

**THE MALAYSIAN JOURNAL OF
Medical Sciences**

Volume 17, No. 2, 2010
ISSN 13-94-195X | e-ISSN 2180-4303



Penerbit Universiti Sains Malaysia

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11800 USM, Pulau Pinang

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Brain in Business: The Economics of Neuroscience

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As a business educator, I am enthralled with the recent advancements by scientists who integrated neuroscience (the study of the anatomy and physiology of the brain) and psychology (the study of the human mind and human behaviour). Such convergence has given birth to a plethora of new interdisciplinary business fields with neuro-prefix such as neuroeconomics, neuromarketing, neuroaccounting, neurogovernance, neuroethics, and neuroleadership. Such an exotic union of science and the arts may provide better understanding of human nature and behaviour change. Imaging technologies such as functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) reveal unseen neural connections in the living human brain along with brain wave analysis technologies such as quantitative electroencephalography (QEEG). We can even theoretically link the brain (the physical organ) with the mind (the human consciousness that thinks, feels, acts, and perceives) through an advanced computer to analyse these connections. As economists and business people always strive for better, faster, cheaper means of production, and demand higher productivity from their employees through effective leadership and supervision, neuroscience is relied upon to provide answers to questions like:

- How can we leverage our brain in business?
- Capitalise/invest on the brain?
- Make the best decision?
- Find the productivity “hot buttons” in the brain?
- Encourage creative and ethical brain?

Such questions give rise to exciting symbiotic developments of business and neuroscience.

Neuroeconomics as an emerging discipline combines neuroscience, economics, and psychology; and uses research methods from cognitive neuroscience and experimental economics. It is “the application of neuroscientific methods to analyse and understand economically relevant behaviour” (1). such as evaluating

decisions, categorising risks and rewards, and interactions among economic agents. Neuroeconomics research draws on the convergence of three major trends. First, using fMRI we can measure brain activity associated with discrete cognitive events and study higher cognitive processes like decision making and reward evaluation. Second, by incorporating economic variables into electrophysiological experiments, we can encode motivationally relevant information through novel recognition of neurons at multiple levels of processing pathways. Third, neuroeconomics draws on behavioural economics to consider psychological variables into economic and decision-making models.

Neuroaccounting is a new way to scientifically view accounting and the brain’s central role in building economic institutions. The measure of brain activity during economic decision-making using neuroscientific methods can prove useful for evaluating the desirability of implementing new policies that run contrary to long-established accounting principles (2). Dickhaut et al. (3) reviewed neuroscientific evidence that suggest the emergence of modern accounting principles based on the mapping of brain function to the principles of modern accounting.

Neuromarketing is the application of neuroscientific methods to analyse and understand human behaviour in relation to markets and marketing exchanges. Applying neuroscience to marketing may form a basis for understanding how human beings create, store, recall, and relate to information such as brands in everyday life. Neuromarketers now use cognitive neuroscience in marketing research that bears implications for

understanding organisational behaviour in a social context (4), for example whether certain aspects of advertisements and marketing activities trigger negative effects such as overconsumption. Going beyond focus groups in traditional advertising methods, we can now use EEG to detect putative “branding moments” within TV commercials and apply brain imaging to discover the “buy button” (5). In notable research emerging from Stanford University, Carnegie Mellon University and the Massachusetts Institute of Technology, scientists are using fMRI to identify parts of the brain that influence buying decisions.

Neuroethics is the investigation of altruism in neuroeconomic research, which suggests that cooperation is linked to activation of reward areas (5). Investigations into such problems could in fact be among the most compelling within neuromarketing. As a new field, it has triggered heated debate and questioned the ethics behind neuromarketing in a 2004 editorial of *Nature Neuroscience*. Now that we have identified certain key regions of the brain that would be implicated in consumer preferences, it may be possible for marketers to “manipulate” their advertisements and target the brain areas that mediate reward processing. One example is the perennial war of the colas (Coca-Cola vs. Pepsi-Cola) whereby studies indicate that Coca-Cola had a more efficient advertising campaign (6). Similar studies were done on the attractiveness of cars or human faces, and how they trigger or activate these “pleasure centres” in the brain that drive social behaviour. As for the marketers themselves, the neuroethical question that arises is whether there is any difference between the brain activity of highly ethical and less ethical salespeople?

Neuroscience has the potential to influence corporate governance; the study of this phenomenon is **neurogovernance**. Neurogovernance is a growing field. In Germany, we now have the Institute for Corporate Governance (ICG Germany) (<http://web.dmz.uni-wh.de/icg/Forschung.html>). Further, since 2001, the Malaysian Code on Corporate Governance has been published by the Malaysian Institute of Corporate Governance (7). Neurogovernance seeks to explain behaviours of directors, auditors, or even those who breach corporate governance. The same explanations can be applied to managers, leaders, and other business people or other professions. For example at Emory, researchers asked 16 executives to respond to PowerPoint slides concerning moral quandaries, such as acting on privileged information, while inside an MRI machine. They found that managers

weighing ethical dilemmas use the part of their brain associated with early memories, which could mean moral thinking is formed early in life. (8).

Stepping away from economics and business sub-disciplines like marketing and accounting, a more recent development is **neuroleadership**, a term coined in 2006 by David Rock, a leadership consultant. Neuroleadership is the study of leadership through the lens of neuroscience and explores central elements of leadership, including: (a) self-awareness (b) awareness of others, (c) insight, (d) decision making, and (e) influencing (9). As a new field of study, neuroleadership brings neuroscientific knowledge into the area of leadership development, management training, education, consulting and coaching. Rock and his collaborator Jeffrey M. Schwartz, a research psychiatrist at the University of California at Los Angeles, apply broader themes from neuroscience to leadership that suggest mindful, focused attention on new management practices, rather than on old habits, can rewire the brain. Another way of applying neuroscience is mapping the individual managers’ brains. In “The Leadership Neuroscience Project”, Pierre A. Balthazard and David A. Waldman from the Arizona State University School of Global Management & Leadership work with neuroscientists to monitor the brains of 44 business leaders while they discussed scenarios such as layoffs. Balthazard seeks to identify brain patterns, and then train managers to replicate the patterns within their own brains (10).

At Universiti Sains Malaysia, we are interested in the study neuroleadership from the perspectives of transformational neuroleadership based on Bass (11) and Burns (12). Unlike transactional leadership, which focuses on exchange that motivates followers by providing rewards and benefits for productivity, transformational leaders make decision based on cognitive rewards, provide a climate of trust, and draw out followers’ higher order needs to perform beyond expectations. Transformational leaders inspire their followers to make decision that transcend self-interests. Can neuroimaging show how transformational versus transactional managers make decision (13)?

The symbiotic development of neuroscience in business is not without challenges. Of primary concern for business researchers in developing countries is the access to EEG and fMRI since these types of equipment are usually in the domain of neuroscientists from the medical faculty. One strategy to overcome this dilemma is

to use interdisciplinary research teams. Another challenge is that the design of experiments required by these projects, which may not agree well with the scientific methods in business—especially in the interpretation of data of the neuroimages for which business researchers have no expertise. Whereas business research and scientific research uphold high ethical standards, the use of neuroscientific methods involving human subjects raises strict ethical issues to which business researchers are unaccustomed. As an academic exercise, after conducting research, interdisciplinary issues arise about where to publish and who to supervise pseudo-science or pseudo-arts candidates.

In conclusion, I am moved by the simple argument by Renvoise and Morin (13) about brain and marketing that captured the essence of brain in business:

The new brain thinks. It processes rational data.

The middle brain feels. It processes emotions and gut feelings.

The old brain decides. It takes into account the input from the other two brains, but the old brain is the actual trigger of decision.

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Observation of Ureteric Diameter in Negative Intravenous Urogram in Hospital Universiti Kebangsaan Malaysia

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Submitted: 18 Aug 2009

Accepted: 19 Sep 2009

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Abstract

Background: This study observed the widest ureteric diameter in negative intravenous urogram (IVU) examinations using low osmolar contrast media.

Methods: We reviewed a total of one hundred and eighty four ureters from 92 negative IVUs.

Results: The results show a mean diameter for the abdominal ureter of 4.19 mm with an SD of 1.27 mm and a mean pelvic ureteric diameter of 4.45 mm with an SD of 1.37 mm. The upper limits for abdominal ureter and pelvic ureter based on a confidence interval of 95% were 4.37 mm and 4.64 mm, respectively.

Conclusions: There was no significant difference between the right and left ureteric diameter in both female and male subjects. There was no significant correlation between ureteric diameters and the age of subjects, from the second to the eighth decades.

Keywords: low osmolar contrast media, negative intravenous urogram, ureteric diameter, medical sciences

Introduction

Assessment of ureteric diameter is important in the diagnosis of urinary diseases. Intravenous urogram (IVU) remains as one of the few modalities that can reliably study the entire course of the ureters. Ureteric dilatation is an important secondary sign that can identify a diagnosis of stone disease even when a stone has recently passed. Chronic vesicoureteric reflux and congenital anomalies of the urinary tract (e.g., posterior urethral valves, megaureter, and prune-belly syndrome) may also result in dilatation of the ureter. Similarly, infectious processes (e.g., *Escherichia coli*, *Pseudomonas* and *Citrobacter*) can impair ureteric peristalsis, causing ureteric dilatation (1). Inflammatory processes adjacent to the ureter may also impair ureteric peristalsis and result in ureteric dilatation (2). Compression of the ureter by a pelvic or an abdominal mass can cause unilateral or bilateral dilatation of the ureter.

Current information about ureteral diameter adopted by most radiological textbooks is mostly from papers published in the 1970's and has

quoted a maximal ureteric diameter of 7 mm, solely based on research in non-pregnant female populations (3,4). A recent review of literature on the techniques and interpretation of IVU also briefly mention that a diameter of less than 8mm is generally considered to be normal (5). But the reference from which this observation is made is also from a study performed more than 30 years ago in which low osmolar contrast media (LOCM) were not commonly used due to the high cost (even in the 1990s, there was only approximately a 50% of penetrance of LOCM into the market) (6). In view of current IVUs which are all carried out using LOCM, a refined observation of ureteric diameter is deemed appropriate as in theory, non-ionic LOCM exerts only a third of osmotic pressure of conventional ionic contrast media. The result therefore should be that of reduced distension of the ureters, compared to high osmolar contrast media. A study of ureteric diameter in infants and young children (up to 16 years of age) has identified linear relationships between advancing age, the height of the lumbar vertebra and ureteric diameter (8). Reviews of literature showed that there has not been a study that looks into the

relationship between ureteric diameter and age in an adult population.

It is a commonly recognized fact that pregnancy is associated with upper urinary tract dilatation due to both physiologic processes and compression of the urinary system by the gravid uterus. The right collecting system was larger in 86% of the affected subjects while the left side was affected in 10% of the subjects (7). It usually occurs during midterm of pregnancy, which is thought to be due to the dextrorotation of the uterus (urologic process during pregnancy). Some authors also assume that such dilatation is not transient but persists long after the post-partum period (3,7).

This study is therefore aimed at providing information about the mean ureteric diameter in negative IVUs to determine if there is a correlation between age and ureteric diameter in an adult population and to ascertain if there is significant difference between the right and left ureteric diameters in male and non-pregnant female patients.

Material and Methods

This study was conducted in the Department of Radiology, Hospital Universiti Kebangsaan Malaysia (HUKM). All patients had undergone intravenous urograms in the radiology department for routine and urgent clinical indications from period of 1 January, 2004 until 31 September, 2006 and fulfilled the inclusion criteria were included in this study. A negative study was defined as an examination that failed to yield positive findings suggesting primary or secondary diseases involving the ureter, such as: obvious dilatation and/or tortuosity of the ureter; asymmetry of right and left ureter; an increasing, dense nephrogram; kidney enlargement; delay calyceal opacification; pelvicaliectasis; a standing column of contrast; a filling defect within the ureter or pelvicalyceal system; and spontaneous pyelosinus extravasation. All negative IVUs included in this study were verified by two independent, qualified radiologists.

Patients with the following exclusion criteria were excluded: history of pregnancy within three months, diagnosed with bladder calculus disease, renal failure, diagnosis of urinary tumour of any type, stenosing ureteric disease, inadequate visualization of the entire ureter on the IVU, and poor opacification of the urinary collecting system. Non-Malaysian foreigners were also excluded.

Equipment

The X-ray apparatus used in this study was a Siemens overhead couch units model (8375040 G2107). IVU was performed with no fluid restriction but with standard oral preparation with diet modification and a prescription of laxatives (bicasodil) two days prior to the examination. Control films were taken in all patients before injection with contrast material (Omnipaque, Iohexol 300) at dose of 1–2mL/kg body weight. All films were taken at a standard of 100 cm FFD, with the centering ray at the iliac crests for full-length films. Full-length films were taken five minutes post-injection. Abdominal compression was then applied and a 10-minute renal area radiograph was obtained. A 15-min full-length film was taken after the release of compression; any subsequent films were taken at the discretion of the supervising radiologist/attending medical officer.

The mean abdominal ureteric diameter was defined as the largest transverse dimension within 6 cm from the pelviureteric junction (PUJ), measured on either on 5-minute film or compressed film, whichever measurement was larger, in accordance with the method adopted by Bradley et al. (4,8). The PUJ is defined as the transition between the renal pelvis and upper ureter. Mean pelvic ureteric diameter was defined as largest the transverse dimension from the level of sacrum to its insertion point in the urinary bladder, measured either in 5-minute or released film, whichever measurement was larger. All measurements were made with aid of a 5x magnifying glass and a standard transparent ruler.

Results

A total of 92 patients were included in this study. The mean age of the study population was 40.6 ± 14 years (range 14–70 years). There were 53 males (57.6%) and 39 females (42.4%). The racial distribution in this study mirrored the racial distribution typically found in this community, 77.2% were Malays; 16.3% were Chinese; and 6.5% were Indians.

Correlation between ureteric diameter and age

Data on abdominal and pelvic ureteric diameter was plotted against subject age in a scatter plot. Pearson's correlation test indicated poor correlation between age and ureteric diameter, as summarized in Table 1.

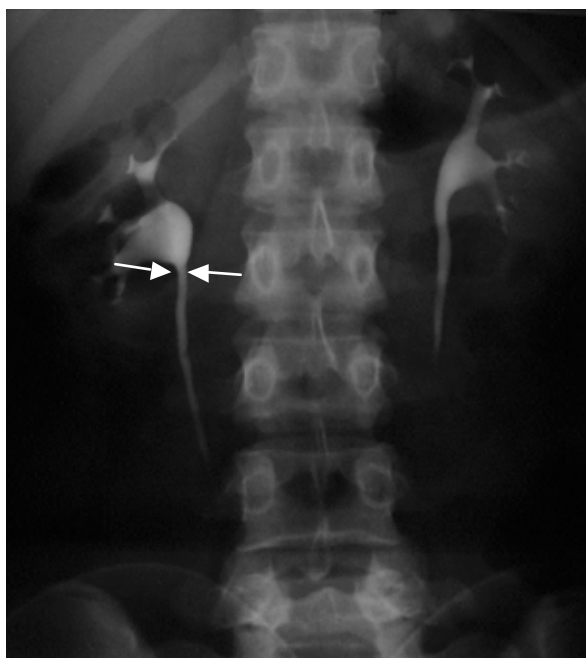


Figure 1: Right abdominal ureter measurement (arrows)

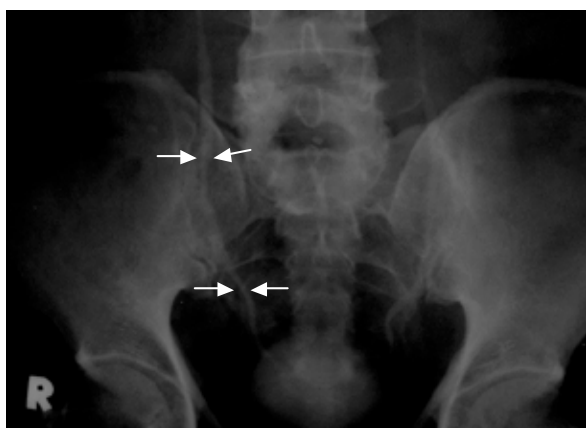


Figure 2: Right pelvic ureter measurement (arrows)

Table 1: Correlation analysis between age and ureteric diameters

	Pearson's correlation coefficient
Age and right abdominal ureter	0.129
Age and left abdominal ureter	0.073
Age and right pelvic ureter	0.025
Age and left pelvic ureter	0.102

Mean ureteric diameter

The measurement of the abdominal and pelvic ureter divided into the right and left side ranges from 1 to 9 mm, as summarized in Table 2.

Measurement according to gender

There were 53 males and 39 females in this study. The mean right and left ureteric diameters of male and female were analysed with independent T-tests to ascertain any significant differences between them.

Female

The mean of the right abdominal ureteric diameter was 4.05 mm and the left was 3.90 mm. The mean of the pelvic ureteric diameter was 4.21 mm on the right and 4.18 mm on the left (Table 3). Although both the right abdominal and pelvic ureters appeared to be larger than the left, the difference is not statistically significant, with a P-value of 0.438 for the abdominal ureter and 0.891 for the pelvic ureter.

Male

The mean of the right abdominal ureteric diameter was 4.30 mm and the left was 4.75 mm. The mean of the pelvic ureteric diameter was 4.38 mm on the right and 4.51 mm on the left (Table 4). Although the left abdominal ureter appeared larger than the right, and the right pelvic ureter appeared larger than the left, the difference was not statistically significant, with a P-value of 0.699 for the abdominal ureter and 0.229 for the pelvic ureter.

Female/Male Differences

The means of measured ureteric diameters appeared to be larger in male subjects for both the right and left abdominal and pelvic ureters, compared to their female counterpart (Table 5). Comparing the means of right abdominal ureter, left abdominal ureter, right pelvic ureter and left pelvic ureter between female and male subjects using independent T-test, there is no significant difference between right and left abdominal as well as pelvic ureter for both the sexes.

Discussions

In the genitourinary system, it is known that the kidney size continues to grow until the seventh decade of life, when it starts to shrink (9). As for the ureter, previous research has documented that the ureteric diameter increases with age until 16 years of age (8). However,

Table 2: Ureteric diameter measurement, according to sidedness and region

Ureter	Minimum (mm)	Maximum (mm)	Mean (mm)	Std. Deviation (mm)	95% confidence interval for mean	
					Lower limit	Upper limit
Right abdominal	2	8	4.2	1.37	3.9	4.5
Left abdominal	2	9	4.17	1.17	3.9	4.4
Right pelvic	2	9	4.5	1.36	4.2	4.8
Left pelvic	1	8	4.37	1.37	4.1	4.7

Table 3: Mean ureteric diameter (mm) in females

Ureter	Right side (mm)	Left side (mm)	P-value
Abdominal	4.05	3.90	0.438
Pelvic	4.21	4.18	0.891

Table 4: Mean ureteric diameter (mm) in males

Ureter	Right side (mm)	Left side (mm)	P-value
Abdominal	4.30	4.75	0.699
Pelvic	4.38	4.51	0.229

Table 5: Mean ureteric diameter (mm) in females and males

Ureter	Female	Male	P-value
Right abdomen	4.05	4.30	0.548
Left abdomen	4.21	4.75	0.235
Right pelvic	3.90	4.38	0.296
Left pelvic	4.18	4.51	0.756

no previous study has examined if there is a significant change in ureteric diameter with age. It has been assumed that the ureteric diameter could be wider in the elderly due to laxity of the smooth muscles, similar to those of the common biliary duct. However, the findings in this study demonstrated that in an adult population, there is no progressive increment in ureteric diameter up to the seventh decade. This is an important finding, as the ureter is a structure for which measurement of its diameter reveals information regarding its condition. Combining data from this study with those of previous similar studies, it can therefore be concluded that the ureter reaches its maximum diameter at the end of growth spurt in the teenage years.

Other intravenous urogram studies have cited different numbers. These figures range from as small as 2mm to as large as 8mm (3,4,5). Some

of these figures are derived from a study of a specific sample population e.g., from post-partum females (3,4,5).

Anecdotal observation of the ureteric diameter in IVUs suggests that the actual number is less than that described in previous reports citing 7 or 8 mm (3,5). In light of current IVU studies using LOCM—versus 1970s studies using HOCM (3,5)—a new study is deemed necessary, as LOCM should, in theory, produces less distension of the ureters, in comparison to HOCM (5).

Findings from the data collected in this study suggest that mean of the abdominal ureteric diameter is 4.19 mm, with an SD of 1.27 mm, and the mean for pelvic ureter is 4.45 mm, with an SD of 1.37 mm. The upper limits of the abdominal and pelvic ureters are 4.37 mm and 4.64 mm respectively, calculated to be within the

95% confidence interval for the given means. A maximal diameter of 7 and 8 mm (suggested in previous papers as being normal) may no longer be acceptable (3,5). These study findings are also supported by the work of Zelenko and colleagues, who observed a mean diameter of 1.8 mm with standard deviation of 0.9 mm, after having examined 212 patients who had undergone CT examinations (10). Even with radiographic magnification using the conventional radiographic technique, the distension caused by the osmotic and diuretic effect of excreted contrast media is unlikely to reach a maximal diameter of 8 mm, which is almost 300% more than the CT measurement.

The likely explanation for the finding of reduced maximal ureteric diameter in this study is that current IVUs are performed with non-ionic contrast media, which in theory exert less of an osmotic effect onto the urinary collecting system, thus producing less diuresis and distension of the ureters, in comparison with high osmolar contrast media used in studies in the 1970s.

It is a well-recognized fact that pregnancy is associated with upper urinary tract dilatation due to both physiologic processes and compression of the urinary system by the gravid uterus (2,3,7). The right-side urinary tract is involved in 86% of cases, with the left side affected in 10% of cases (7).

Some authors also observed that such dilatation is transient while others argue that dilatation persists long after the post-partum period, analogous to the physiological changes that occur in the breast and the uterus (7). If this proves to be true, it may pose diagnostic difficulties – for example, such ureteric dilatation in post-partum females during IVU studies may mimic obstructive and other non-obstructive causes of ureteric dilatation.

The mean of the right abdominal ureteric diameter was 4.05 mm, and the left was 3.90 mm. The mean of the pelvic ureteric diameter was 4.21 mm on the right and 4.18 mm on the left. Although right abdominal and pelvic ureters appeared to be larger than the left, the difference was not statistically significant. We therefore conclude that the data from female subjects in this study showed no significant differences between the right and left ureters. In other words, dilatation of the urinary collecting system during pregnancy is transient and does not persist beyond the post-partum period. In future IVU studies in post-partum women, such findings for ureteric dilatation must be viewed with a consideration for the obstructive and non-obstructive causes of abnormal dilatation.

We further tested to see if there was a significant difference between the mean ureteric diameters of male and female subjects to validate the fact that each ureter unit could be individually sampled for calculation of an overall mean and SD for the abdominal and pelvic ureteric diameters.

The additional clinical implication of the above findings is that the fact that there is no significant difference between the right and left ureteric diameters in both male and female subjects, emphasizes the fact that symmetry in the ureteric diameter of both adult males and females is an expected normal finding in IVU research, and deviation from such findings should be considered abnormal.

Limitations of study

This study had certain limitations. It is a retrospective study of already-taken record images. Additional information could not be retrieved from the subjects, such as the weight and height of each patient.

The sample was a group of patients who underwent IVU for routine indications at HUKM. Many of these subjects were referral cases from the satellite clinics around HUKM for which, in some of them, the IVU film was not returned to HUKM for record purposes. Many subjects also had incomplete sets of IVU films, with one or more films missing from their record. In those with complete sets, there are some with inadequate visualization of the entire ureter or poor quality of the opacification of ureter. Due to these limitations, and compounded by our strict exclusion criteria, many potential candidates were excluded, thus reducing the sample size.

Within the limits of this clinical study, the IVUs of the examined subjects were reported to be normal. This study examined ureters in which there were no secondary signs of obstructive or non-obstructive dilatation of any part of the urinary collecting system, including the ureters. However, it must be remembered that all the patients were investigated for possible illness in their urinary collecting systems.

All IVU examinations were done without fluid restriction. However, the actual fluid intake may vary amongst patients. Ureteric distension may thus vary depending on the hydrational statuses of patients. This is a limitation in IVU examinations in all previous studies, as fluid intake is difficult to quantify given the diversity of body mass/types of different patients.

As different patients have different adipose tissue thicknesses, the magnification factor may vary between patients—a fact which was not

corrected in this study. However this limitation is not of significant concern, as the aim of this study is not to examine the anatomical diameter of the ureter, as can be achieved by ultrasound or computed tomography examination, but rather to observe the range of projected diameters on radiographs in the sample population.

Conclusion

In conclusion, the mean abdominal ureter diameter was 4.19 mm with an SD of 1.27 mm, and the mean pelvic ureteric diameter was 4.45 mm, with an SD of 1.37 mm. Upper limits for the abdominal and pelvic ureteric diameters (based on confidence interval of 95%) are 4.37mm and 4.64mm, respectively. This study also finds no correlation between age and ureteric diameter. There is no statistically significant difference between the right and left ureters, particularly in females. Therefore, in a normal, non-pregnant female and in male subjects, symmetry of ureter is expected.

Acknowledgements

I wish to thank the following for their help in the preparation of this project report:

Dr. Hamzaini Abdul Hamid, senior radiologist and lecturer, Radiology Department, HUKM for his invaluable guidance and supervision in the course of this project. Prof. Dr. Zulfiqar Mohd Anuar for generously giving her input and corrections and sharing her knowledge and opinions. Prof. Madya Zahiah Mohammad, Head of Radiology Department, HUKM for her consent to allow this study. Dr. Loi Hoi Yin, fellow radiologist and lecturer, radiology department, HUKM for his support and invaluable advice. Prof. Dr. Syed Zulkifli Syed Zakaria Al-Juffry, senior consultant and research fellow, UKM Medical Molecular Biology Institute, HUKM for his expert opinion on data interpretation and statistical analysis.

I would also like to convey my heartfelt gratitude to the lecturers, colleagues, and staff of the radiology department, who have contributed in one way or another, to the completion of this project.

Authors' contributions

Conception and design, provision of study materials or patients, data collection, analysis,

and interpretation, statistical expertise, drafting of the article, final approval of article: WSL.

Administrative, technical or logistic support; critical revision of the article: HAH

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Preventing HIV Transmission in Nigeria: Role of the Dentists

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Submitted: 13 May 2009
Accepted: 1 Feb 2010

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Abstract

Background: As healthcare providers, dentists are in a unique position to foster behavioural changes that are needed to stem the spread of HIV infection. This study was conducted to assess the role of dentists in the prevention of HIV transmission in Nigeria.

Methods: This descriptive cross-sectional survey was conducted from June 2006 to January 2007. A multi-stage sampling technique was used to select 300 practising dentists from all parts of Nigeria. Data were collected through a self-administered questionnaire that focused on dentist demographic details, attitudes towards treating HIV-infected persons, involvement in public or clinic-based patient education on HIV and infection control.

Results: Two hundred and fifty-seven questionnaires were returned completed, constituting an 86% response rate. The majority of respondents (77.8%) had their dental practice in the southern part of Nigeria, and 89% were in the age bracket of 21–40 years. HIV education by dentists was ranked as poor, as less than a quarter of respondents routinely educated patients on HIV in the clinic. Only a few dentists (33.3%) were involved in public enlightenment programme on HIV in the previous 12 months. Most of the respondents (93%) reported a willingness to treat HIV-infected patients while observing universal precautions. Good infection barrier practices were adopted by 89.9% of dentists, and disposable cartridges for local anaesthetic agents and dental needles were not reused by 93.4% of the respondents. Autoclaving was the most widely used sterilization method (73.2%), but less than half of the respondents knew how to ascertain whether sterilization was effective.

Conclusion: This study revealed that efforts by Nigerian dentists to prevent HIV transmission are presently less than optimal. Therefore, there is a need for sensitisation and motivation through seminars, workshops and lectures.

Keywords: HIV, infection transmission, Nigeria, dentists practice patterns, prevention and control, dental sciences

Introduction

HIV/AIDS is the leading infectious cause of adult mortality in Africa (1). Africa is the most affected continent, accounting for 70% of the global HIV/AIDS pandemic (2). The magnitude of HIV/AIDS infection in Nigeria presents an alarming trend. Nigeria has the third highest number of people living with HIV/AIDS in the world after South Africa and India (3). Public perception of the HIV epidemic has culminated in heightened and persistent public anxiety. This anxiety is attributed to the high mortality rate of AIDS and the fact that there is, to date, no proven vaccine or cure. If the epidemic continues at its current rate or worsens, its effects could spread across

the whole continent. Prevention is therefore a critical issue in Nigeria. HIV prevention must be a multidisciplinary approach involving physicians, dentists, pharmacists, nurses, health educators, therapists and other health care providers.

National data on the utilisation of oral health services per annum in Nigeria were not available, but more than half of the population in America visit dentists yearly (4). A great percentage of HIV-infected patients and those at risk are in the age range between 15 to 49 years. The majority of patients visiting dental clinics are in a similar age range (5). Approximately 18–20% of young men and women in Nigeria between the ages of 15 and 24 correctly identified ways to prevent HIV transmission (6). Those infected with HIV

may relapse to risky behaviour when preventive counselling is less than optimal. Provider-delivered risk reduction counselling has been shown to reduce risky behaviour by people living with HIV/AIDS in other settings. Dental health workers are well placed to provide information about HIV. The public is willing to discuss AIDS with dentists and is favourably disposed to the information dentists' supply. Patients see dental practices as a place where they can discuss and receive valuable and trusted information about HIV. Studies consistently demonstrate that patients view their dentist as a trusted and authoritative source of health information (7). Studies in other disease prevention areas have shown that brief intervention delivered by dentists can translate into behavioural change (8). Dental patients are particularly receptive to health messages at their periodic check-up (9). For these reasons, dental clinics provide an excellent venue for HIV prevention and intervention services.

There is a high possibility that dentists treat HIV-infected patients unknowingly because most patients are probably unaware of their HIV status. The undiagnosed, untreated patient may unknowingly be a hazard to dentists, dental staff and other patients, especially because everyday dental practices involve invasive procedures and instrument reuse. There is documented evidence of HIV transmission in dental operations (10). Only effective infection control measures in a clinical setting can prevent the spread of HIV and other highly infectious diseases. Failure to adequately clean, disinfect and/or sterilize dental instruments contaminated with HIV from previous patients will endanger subsequent patients. If adequate precaution is not taken to prevent blood and body fluid contamination, the risk of HIV transmission increases tremendously. Studies have documented that 70–90% of HIV-positive individuals display oral manifestations of HIV, (11) but Nigerian-based studies reported a 48.8–53% prevalence of oral lesions in HIV-infected adults (12,13). Many different oral lesions may occur at different stages of the infection.

Poor oral health could complicate the management of the medical conditions of HIV-infected patients and may create or exacerbate nutritional problems. Oral prophylaxis improves the oral health and quality of life of individuals with HIV/AIDS infection. There is therefore a need for HIV-infected patients to receive dental care at different times during the course of the disease. The AIDS INSTITUTE stated that the treatment of oral manifestations of HIV infection could improve a patient's attitude, quality of

life and general well being (14). Dentists have an ethical, moral and professional obligation to protect themselves, co-workers, patients and society at large from any avoidable harm, including exposure to HIV infection. Dental services may therefore have a role in the primary prevention of HIV by providing information about HIV and promoting health through early diagnosis and treatment of oral manifestations of HIV/AIDS.

Several researchers have documented the multiple roles of dentists in the HIV/AIDS pandemic (15–19), which include the following: the provision of routine dental care to HIV-infected patients; preventing the spread of HIV through proper infection-control practices; providing education to the community and clinic; oral lesion screening, diagnosis, treatment and recognition of its significance; educating other health care workers; acting as a resource to HIV-infected health care workers; collaborating with other health care workers and social support systems in delivering psychological counselling and drug rehabilitation; conducting research concerning HIV/AIDS; and finally, screening for HIV infection using a rapid oral fluid HIV antibody test.

Oral health priority areas of the World Health Organisation (WHO) focus on the dissemination of information on HIV/AIDS and its prevention through every possible means of communication. The WHO advises the involvement of oral health personnel in the documentation of HIV/AIDS to ensure appropriate medical evaluations in prevention and treatment (20). The WHO established a task force to focus on key regions including the African Union and Southeast Asia. Nigeria is Africa's most populous nation and ranks tenth in the world with a population of 140 million (21).

The objective of the survey was to assess the role of dentists in the prevention of HIV transmission in Nigeria.

Materials and Methods

This study was designed as a cross-sectional descriptive survey. The survey population was 300 dentists practicing in private and government-owned dental centres in Nigeria. The sample population was divided into north and south groups. A multi-stage proportionate sampling technique was used because there are more dentists practicing in the southern part of the country. Data were collected using a pre-tested, self-administered questionnaire that contained

open and closed-ended questions. The questions focused on dentist demographic data, dentist-to-patient education on HIV issues, participation in public enlightenment campaigns on HIV, attitudes to treating HIV-infected patients, infection barrier practices and sterilization. Questionnaires were hand-delivered by the authors to dentists at their dental centres, while some were delivered by mail. Informed consent was obtained from the participants. There was an introductory note in the survey that explained that the co-operation of respondents would be highly appreciated, and their responses would be treated with strict and the utmost confidentiality. The survey was anonymous. The duration of the study was seven months from June 2006 to January 2007. Data were analysed with SPSS version 13.0, and graphs were plotted with Microsoft Excel.

Results

Out of 300 questionnaires, 257 were returned completed, resulting in a response rate of 86%.

Demographic characteristics

Table 1 shows the demographic characteristics of respondents.

HIV education

Less than a quarter of respondents (21.8%) routinely educate patients on HIV in the clinic, and only one third of dentists (33.1%) were engaged in any HIV public enlightenment in the last 12 months (Figure 1). They were mostly males (24.7%) and younger dentists with 1–5 years experience (30.0%). HIV public enlightenment was organised by non-governmental organisations in almost 70% of cases (Figure 2).

Willingness to treat HIV-infected patients

The majority (93%) of respondents reported a willingness to treat HIV-infected patients observing universal precautions (Figure 1).

Infection barrier usage

Good infection barrier practice was adopted by 89.9% of the respondents (Figure 1). However, the most commonly used gloves during patient examination were non-sterile latex gloves (58.4%), while the least commonly used were sterile latex gloves (22.5%). Disposable cartridges for local anaesthetic agents were not reused by 93.4% of the dentists, and 95.7% of dentists did not reuse disposable dental needles.

Sterilization

Appropriate sterilization techniques were used by 86.4% of respondents (Figure 1). Dry heat accounted for 13.2%, and autoclaving was the most popular method (73.2%). Inappropriate methods were reported and included boiling water (5.1%), cleaning with bleach alone (3.1%) and cleaning with soap and water alone (0.4%). Those respondents that were unaware of the sterilization method used in their dental centre made up 1.6% of the total respondents, and only 2.7% gave no response. Less than half (33%) knew how to ascertain whether sterilization was effective, while 43.6% reported no knowledge. The efficacy of sterilization was monitored with the use of colour-coded autoclaving packs (16.7%), thermometers (14.0%) and pressure gauges (2.3%) (Figure 3).

Discussion

The role of dentists in the prevention of HIV transmission is largely ignored in the literature. To our knowledge, this report is the first comprehensive survey on the preventive roles of dentist in the HIV/AIDS pandemic.

The response rate in this study was higher than other dentist-based studies reported in Nigeria (22) and other African countries (23). The high response is consistent with the impact that HIV has had on dental practices in Nigeria. The non-response rate in some questions was similar to that documented in a questionnaire-based survey of American dentists (24). The distribution of dentists in Nigeria may be a result of the location of dental schools. Only 12.4% of the dentists in this study had additional qualifications other than the basic dental degree. This result may be attributed to limited vacancies and the unattractive nature of dental postgraduate training prior to the new millennium.

There are a limited number of counsellors and health educators in Nigeria. Nigerian dentists' involvement in public education is very low (33.1%), and only 21.8% routinely educate patients on HIV in their clinics, as shown in this study. This level of involvement is inadequate, especially because it has been documented that this type of information giving can be effective (25), and dentists have a great deal of contact with potentially high-risk patients (26).

The findings from this study are surprising because dental students have agreed to the adoption of public education as a preventive measure for HIV transmission (27). The currently low participation of dentists in public education

Table 1: Demographic characteristics of respondents

Characteristics	Frequency	Percentage
Age group (years)		
<31	85	33.1
31-40	135	52.5
41-50	32	12.5
>50	5	1.9
Gender		
Male	174	67.7
Female	83	32.3
Marital Status		
Single	110	42.5
Married	146	56.8
Separated	1	0.4
Education		
Bachelor Degree	225	87.5
Masters Degree	7	2.7
Fellowship	25	9.7
Position		
House Officer (Intern)	63	24.5
General Practitioner	102	39.5
Junior Registrar	41	16.0
Senior Registrar	25	9.7
Consultant	26	10.1
Practice		
Private Clinic	32	12.5
FMC/Teaching Hospital	148	57.6
General Hospital	69	26.8
School of Dental Technology	1	0.4
Military Hospital	7	2.7
Location		
Southern Nigeria	200	77.8
Northern Nigeria	57	22.2
Years of Practice		
<6	129	50.2
6-10	73	28.4
11-15	25	9.7
>15	30	11.7
Total	257	100

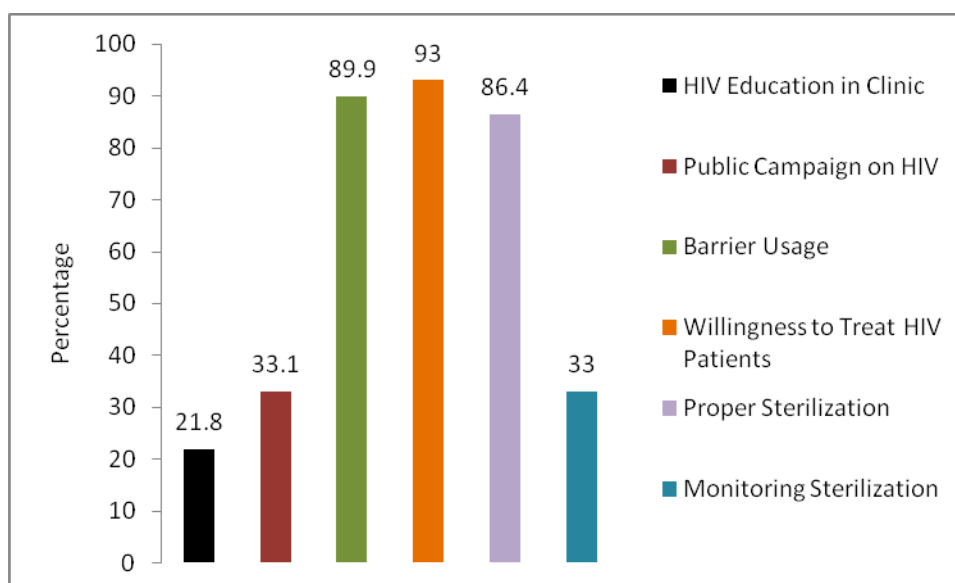


Figure 1: Assessment of the roles of dentists in HIV prevention

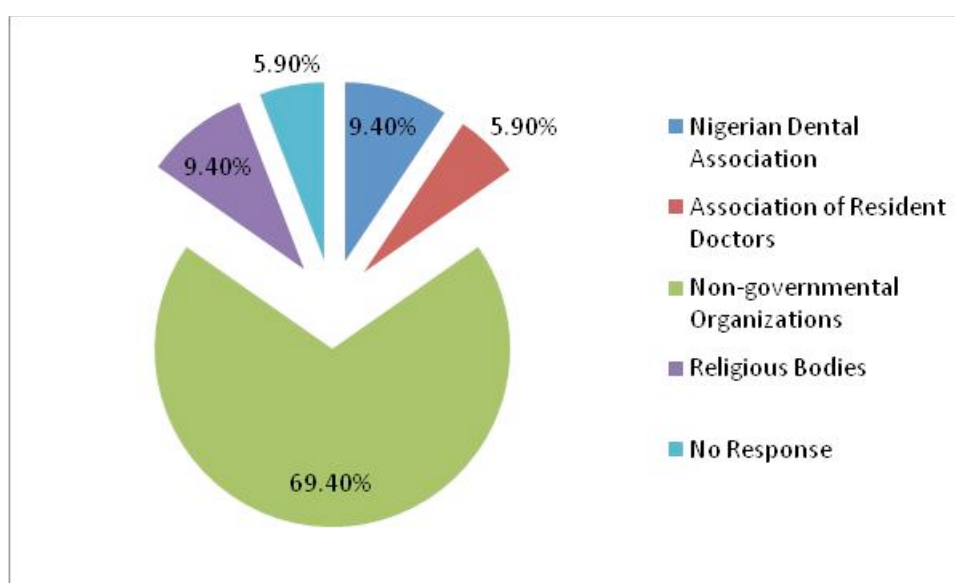


Figure 2: Organizers of HIV public enlightenment campaigns

may be a result of the poor coordination by their professional associations and governmental agencies. Most dentists who were involved in public education did so under the auspices of non-governmental organisations (65.9%).

A positive attitude towards HIV patients and preparedness to advise these patients are essential elements for dentists to play a successful role in the management of HIV/AIDS. Providers' attitudes about HIV/AIDS are an important factor in the delivery of quality care to people with HIV/AIDS. The willingness to treat patients while observing universal precautions was quite high

(93%). This willingness is about 30% higher than reported by Uti et al. (28) and also higher than reported in a South African study (29), in which only 42% of dentists were willing to treat HIV-infected patients. In contrast, a Kenyan study (23) reported that 87% were willing to treat this group.

Improved knowledge of HIV/AIDS in dental health workers over the last few decades may be the reason for the increased willingness to provide care and the more positive attitude towards HIV-infected individuals. Interestingly, 100% of the respondents that refuse to treat HIV-infected patients were female dentists. This finding is

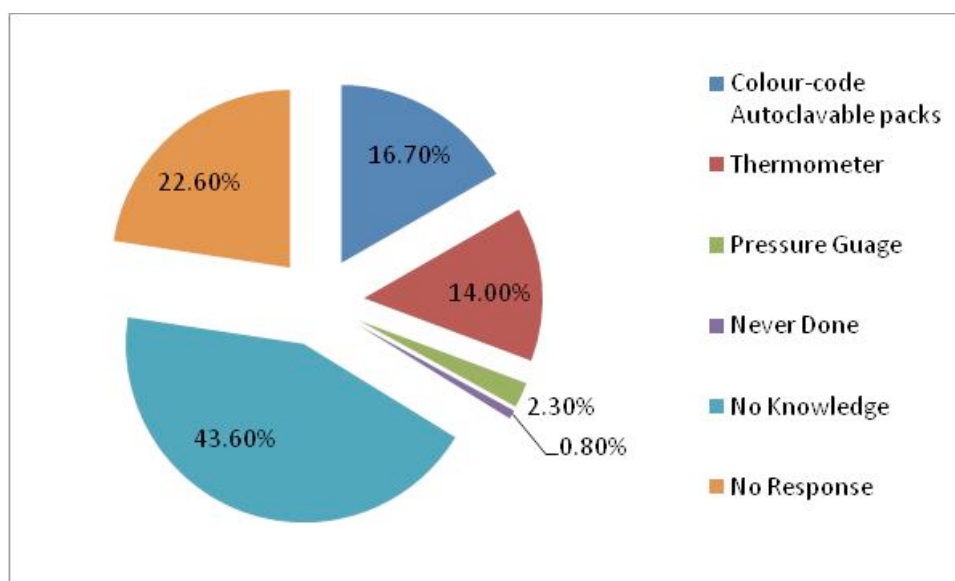


Figure 3: Methods used for monitoring sterilization efficacy

consistent with previously documented gender differences in caring for infected individuals (30). Interestingly, 100% of the respondents that will treat patients without observing universal precautions are male dentists. This finding may be because males are more likely to take risks in general than females.

The proper use of infection barriers, like hand gloves (89.9%), reported by respondents in this study was higher than reported in 2003 among public hospital dentists in Lagos, Nigeria (70.6%) (22). The accepted universal practice is to use a fresh cartridge containing the local anaesthetic agent and a new disposable needle for each patient. Most dentists in this survey do not reuse needle and cartridges, but a significant few (16.7%) still reuse needles (chi-square test, $P=0.002$). Approximately 6% of private dental practitioners reuse anaesthetic cartridges, and 1.5% reused needles (31). Sterilization is the destruction of all forms of micro-organisms (vegetative and spores) for a given object, and it is the best method to prevent cross infection from patient to patient in oral health care. All critical and semi-critical dental operative instruments that are heat stable should be cleaned, debrided and then sterilized in a steam autoclave or dry-heat hot air oven at a specified temperature and duration. Autoclaving is the most popular sterilization method among respondents (73.2%), which is consistent with previously reported findings (22,23,29). Boiling water is presently seen as an inappropriate method of sterilization in dentistry because it kills vegetative bacteria within 2 or 3 minutes, but bacteria spores and

viruses may take many hours. Despite the fact that the use of boiling water is being discouraged, 5.1% of the respondents reported boiling water as their mode of sterilization.

Ideally, tests should be conducted routinely to check that sterilization is adequate. These tests may be performed with chemical indicators such as Browne's autoclave tape, a standard test pack containing a thermocouple or by using standardised spore papers. Only about a third of dentists (33%) who use appropriate sterilization methods can ascertain whether their sterilization is optimal. Poor monitoring of sterilization was also reported in a study on university dental clinics in Nigeria (32), where it was discovered that sterilization ovens did not have thermometers and biological monitoring (spore testing) was not conducted.

Conclusion

Educating patients in Nigeria on HIV prevention by dentists both inside and outside clinics is at a very low level, while infection control based on barrier usage, appropriate sterilization methods and the willingness to treat HIV patients are relatively high. Inadequate monitoring of sterilization was evident, and a few dentists still use poor practices that may put themselves and their patients at risk. The overall assessment revealed that efforts by Nigerian dentists are still less than optimal.

Recommendations

The role of dentists in preventing HIV should be adopted as a topic in continuing education courses. Sensitisation and motivation of Nigerian dentists through seminars, workshops and lectures is advocated. The National Dental Association should actively disseminate information to educate members on their roles in the prevention of HIV and other blood-borne infections. The few practitioners that constitute the greatest risk should be targeted, and legislation should be enacted to prevent bad practice. Additionally, existing laws should be properly enforced.

Acknowledgements

The authors wish to thank Prof. M.A Ojo, Head of the Department of Oral Medicine and Pathology, Dr. N.O. Obuekwe, Acting Dean of the School of Dentistry and Dr. V. A. Omuemu, Public Health Physician in the Department of Preventive Medicine, University of Benin, Benin City, Nigeria, for reviewing this manuscript before it was presented at the 4th International AIDS Society Conference on Pathogenesis, Treatment and Prevention in Sydney, Australia.

Authors' contributions

All authors contributed equally to the conception and design of the study, data collection, analysis and interpretation, as well as drafting and critical revision of the article.

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The Prevalence of Urinary Incontinence among the Elderly in a Rural Community in Selangor

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Submitted: 7 Sep 2009
Accepted: 1 Apr 2010

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Abstract

Background: Urinary incontinence is a common but poorly understood problem in the elderly population. The aim of this study was to determine the prevalence of urinary incontinence and its associated factors among the elderly in a community setting.

Methods: A cross-sectional study design was used. Stratified cluster sampling was used in this study. All elderly residents aged 60 years old and above who fulfilled the selection criteria were included as respondents. The translated Malay version of the Barthel's Index (BI) was used to identify the presence of urinary incontinence.

Results: The prevalence of urinary incontinence was 9.9% among the elderly respondents. Urinary incontinence among the elderly was significantly associated with age, gender, depression, functional dependence, and diabetes mellitus ($P < 0.05$).

Keywords: associated-factors, community, elderly, prevalence, urinary-incontinence, medical sciences

Introduction

Urinary incontinence is a common problem among the elderly (1). Many studies have recorded the prevalence of urinary incontinence in old people living in the community as well as those living in institutions. The prevalence rate in the community has ranged from 7% to 42%, (2–8) and the rate has typically been higher in institutions (9). The prevalence of incontinence may be significantly underestimated. The elderly may assume that urinary incontinence is a normal consequence of aging. Some elderly may be embarrassed by their incontinence or fear invasive testing, and thus, avoid evaluation. In primary health care clinics and hospitals, medical and health personnel rarely ask patients about urinary incontinence. Furthermore, patients seldom initiate discussions about incontinence (10).

Urinary incontinence commonly results in medical, social, and economic consequences. Incontinence is a common reason for the institutionalisation of the elderly. The care of incontinent nursing home residents is significantly more expensive than continent residents, and requires more nursing time. Urinary incontinence can result in skin irritation and contribute to skin breakdown or pressure sores. The social consequences include guilt and isolation, with some elderly afraid to leave their homes (10).

Though the younger age group comprises a large part of the population, the proportion of the older age group is substantially increasing (11). The health problems associated with the elderly in this country are a major cause of concern for health care providers. Urinary incontinence is a health condition that affects the elderly. We hypothesise that the prevalence of urinary incontinence among the elderly is not uncommon. The aim of this study was to determine the prevalence of urinary incontinence among the elderly in a rural community in Selangor. In addition, factors related to urinary incontinence were also studied.

Materials and Methods

A cross-sectional study was conducted in Sepang District, Selangor between 17th June and 20th August 2002. Stratified cluster sampling was used in this study; living areas in Mukim Sepang were stratified into traditional villages, small towns and one "Orang Asli" village. Three out of 6 traditional villages, 1 out of 2 small towns and 1 "Orang Asli" village were randomly selected. The study population consisted of elderly residents aged 60 years old and above who were Malaysian citizens. Exclusion criteria included elderly who were not Malaysians and those with significant communication problems such as deafness and stroke.

The respondents who fulfilled the selection criteria were personally interviewed using a structured questionnaire. The questionnaire consisted of three parts. Part 1 consisted of questions on age, gender, ethnicity, marital status, living arrangement, educational level, occupation, family income and history of chronic illness. Part 2 consisted of the Malay version of the Barthel's Index (BI). Part 3 consisted of the Malay version of the Geriatric Depression Scale. Data were collected via face-to-face interview by trained personnel. Interviews were approximately 20 to 30 minutes in length.

The translated Malay version of the BI was used to identify the presence of urinary incontinence. This questionnaire was modified after the original BI (12) and was pre-tested in a locality not included in the study area. The internal reliability of the translated version was assessed using Cronbach's alpha coefficient and was found to be satisfactory (coefficient alpha of 0.71). The questionnaire consists of 10 questions measuring basic Activities of Daily Living (ADL), including urinary incontinence. Functional dependence in basic ADL implied that the respondent required assistance in one or more of these tasks (8). Based on the BI, the presence of urinary incontinence was determined by asking the respondents whether they had problems with their bladder control. Answers of "yes" or "occasional" were grouped as having urinary incontinence.

The translated Malay version of the Geriatric Depression Scale (GDS), which consists of 30 questions, was used to screen for depression. The total scores range from 0 to 30. Based on the GDS guidelines, a cut-off score of more than 10 was used to identify depression (13). The internal reliability of this translated version was also found to be satisfactory (coefficient alpha of 0.69).

Written consent was obtained from each respondent. Ethics approval was obtained from the Faculty of Medicine and Health Sciences Ethics Committee of University Putra Malaysia. Data was analysed using SPSS version 10.0. The statistical significance was set at $P < 0.05$. Chi-square test with a confidence interval of 95% and odds ratio (OR) were used to determine the association between urinary incontinence and age, gender, ethnicity, marital status, living arrangement, occupation, family income, functional dependence, depression, presence of chronic illness and types of chronic illness.

Results

Of the 263 elderly residents, 223 agreed to participate, resulting in a response rate of 84.8%.

Socio-demographic profile

The age of the respondents ranged from 60–99 years, with a mean of 69.7 ± 6.8 years and a median of 68 years. The majority of the respondents were females (55.2%), Malays (53.8%), married (60.1%), living with family (91.5%), had formal education (55.2%), were not working (83.4%), and had a monthly family income of more than RM 300 or USD 91.70 (62.3%) (Table 1).

Barthel's Index

The most common type of functional dependence was urinary incontinence ($n=22$ or 9.9%) (Table 2). This was followed by problems with steps ($n=20$), poor mobility ($n=17$), problems with transferring (from bed to chair or chair to chair/commode) ($n=12$), using the toilet ($n=12$), bowel incontinence ($n=8$), and bathing ($n=1$). None of the respondents were dependent in feeding, dressing or grooming ($n=0$).

Urinary incontinence

Urinary incontinence was found to be significantly associated with age, gender, functional dependence, depression and diabetes mellitus ($P < 0.05$) (Table 3).

Discussion

The prevalence of urinary incontinence among the elderly in this study was 9.9%. This is comparable to the studies conducted by Poi, which found the prevalence in Malaysia to be 9.1%, and by Chia at 9.0% (10,14). However, among the elderly in Singapore, Chan et al. found that the prevalence of urinary incontinence was 14.5% (15). Mayo estimated that at least 15% of community-dwelling elderly individuals and 50% of institutionalised elderly persons have significant urinary incontinence (16). All of the Malaysian studies reported a lower prevalence of urinary incontinence compared to other countries. This may be an underestimate of the actual situation as elderly in this country may not be as forthcoming in revealing their health problem (13,15).

Age was found to be associated with urinary incontinence. The odds of the elderly aged 80 years and above having urinary incontinence compared to those aged 60 to 79 years were 4:1.

Table 1: Socio-demographic profile of the respondents (N=223)

Socio-demographic profile	Number	Percentage (%)
Age		
60-69 years	122	54.7
70-79 years	69	30.9
80 years and above	32	14.4
Gender		
Females	123	55.2
Males	100	44.8
Ethnicity		
Malays	120	53.8
Chinese	52	23.3
Indians	45	20.2
Orang Asli	6	2.7
Marital Status		
Married	134	60.1
Single /Widowed/Divorced	89	39.9
Living Arrangement		
Living alone	19	8.5
Living with family	204	91.5
Occupation		
Not working	186	83.4
Working	37	16.6
Family Income		
Less than RM 500	152	68.2
RM 500 and above	71	31.8
Level of education		
No education	100	44.8
Primary education	110	49.3
Secondary education	13	5.9

Table 2: Prevalence of functional dependency among the elderly respondents (N=223)

Activities of Daily Living	Prevalence of functional dependence (%)
Feeding: unable or needs help	0.0
Dressing: unable or needs help	0.0
Grooming: unable or needs help	0.0
Bathing: unable or needs help	0.4
Bladder control: incontinence or occasional incontinence	9.9
Bowel control: incontinence or occasional incontinence	3.6
Transfer to bed: unable or needs help	5.4
Using the Toilet: unable or needs help	5.4
Mobility on level surfaces: immobile, or using wheelchair, or needs help	7.6
Climbing Stairs: unable or needs help	9.0

In this study, urinary incontinence may be related with difficulty in mobility and transferring. Many studies have shown very high prevalence rates of urinary incontinence in those aged 85 and older (2,4,5,7,17). Normal aging causes changes in urinary anatomy and patho-physiology, which allows incontinence to occur more easily. Aging results in the reduced size of the urinary bladder, producing a decreased bladder volume and a need for more frequent bladder emptying (urinary frequency). Many elderly individuals experience early detrusor contractions, even at low bladder volumes. This results in a sense of urgency to empty the bladder. Elderly individuals are, in general, less able to suppress early detrusor contractions (15).

This study found that males had a higher risk of urinary incontinence compared to females (OR 5.5:1). This contrasted with other studies that found that urinary incontinence was more common among females as compared to males (1,2,4,5,7).

Urinary incontinence was also found to be significantly associated with functional dependence. Nearly two-thirds of the elderly with functional dependence had urinary incontinence. Among the respondents without functional dependence, none complained of urinary incontinence. Studies have documented that as the degree of functional dependence increases, the prevalence of incontinence increases as well (15).

Depression was also found to be associated with increased risk of urinary incontinence (OR=2.7). Research has shown that urinary incontinence can adversely affect quality of life,

leading to depression, negative affect, low life satisfaction, and restriction of activities (1). The elderly tend to be embarrassed of their problem and may even experience a sense of guilt. They are reluctant to go out and socialise because of their problem. This eventually leads to self-imposed social isolation (15).

There was no association between chronic diseases and urinary incontinence. However, diabetes was found to be associated with a higher risk of urinary incontinence ($P<0.05$). Studies have shown that in addition to changes of normal aging, diseases such as dementia and cognitive impairment, which are commonly experienced by the elderly, may contribute to the problem of urinary incontinence. Urinary tract infections, diabetes mellitus, benign prostatic hyperplasia, and immobility are also typical examples of conditions that may impact urinary incontinence (10,15).

Conclusion

The prevalence of urinary incontinence in this study is most likely underestimated due to the study's limitation in determining the presence of urinary incontinence by a self-report method based on the BI. It is possible that mobility problems contributed to the presence of urinary incontinence among the respondents in this study. Another problem in the elderly age group is cognitive impairment, which also contributes to urinary incontinence. However, this risk factor was not examined in this study.

Despite the limitations of this study, we acknowledge the fact that urinary incontinence is

Table 3: Factors associated with urinary incontinence among the respondents (N=223)

Socio-demographic Factors	Urinary incontinence (n = 22)	No urinary incontinence (n = 201)	Prevalence (%)	95% Confidence Interval	Odds Ratio
Age					
60-79 years old	13	178	6.8	1.93, 8.85	4.1
80 years and above	9	23	*28.1		
Gender					
Male	18	82	*18.0	1.94, 15.83	5.5
Female	4	119	3.3		
Race/Ethnicity					
Malays	17	103	14.2		
Chinese	4	48	7.7		
Indians	1	44	2.2		
Orang Asli	0	6	0.0		
Marital Status					
Married	15	119	11.2	0.58, 3.78	1.4
Single/Divorced/Widowed	7	82	7.9		
Living Arrangement					
Living alone	3	16	15.8	0.55, 5.21	1.7
Living with family	19	185	9.3		
Education Level					
Education	14	109	11.4	0.31, 1.61	1.4
No education	8	92	8.0		
Occupation					
Retired	19	167	10.2	0.36, 4.60	1.3
Working	3	34	8.1		
Family Income					
RM300 and above	14	125	11.4	0.38, 2.35	1.1
Less than RM300	8	76	8.0		
Chronicle Illness					
Present	17	117	12.7	0.86, 5.90	2.3
Absent	5	84	5.6		
Depression					
Yes	4	13	*23.5	1.03, 7.04	2.7
No	18	188	8.7		
Functional Dependence					
Yes	22	13	*62.9	1.75, 4.14	2.7
No	0	188	0.0		

* significant (P<0.05)

a common and poorly understood problem in our community. Based on the self-reported evidence in this study, urinary incontinence occurred in approximately 1 in 10 elderly respondents. A larger and more in-depth study might reveal a much higher prevalence. Detection of this problem is essential for preventing complications and improving the quality of life of the elderly.

Acknowledgement

We would like to express our gratitude to the Dean of the Faculty of Medicine and Health Sciences, Universiti Putra Malaysia for his support and permission to publish.

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Effect on Antioxidant Levels in Patients of Breast Carcinoma during Neoadjuvant Chemotherapy and Mastectomy

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Submitted: 17 Sep 2008

Accepted: 4 Apr 2010

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Abstract

Background: Breast cancer is the most common cancer in Indian women. The aim of this study was to assess the levels of red blood cell (RBC) superoxide dismutase (r-SOD), RBC catalase (r-CAT), RBC glutathione peroxidase (r-GPx) and the ferric reducing ability of plasma (FRAP) in advanced breast cancer patients post mastectomy before and after chemotherapy.

Methods: Female breast cancer patients between 27 and 65 years of age who were admitted to the Department of Surgery of the All India Institute of Medical Sciences in New Delhi were enrolled in the study. This study included two arms: a control group of healthy age-matched females ($n=20$) and patients undergoing treatment with a combination of the anticancer drugs cyclophosphamide, doxorubicin, and 5-fluorouracil (CAF) ($n=55$). No treatment was given to the control group. The CAF group received CAF treatment at weeks 0, 3, and 6, then surgery at week 9 followed by CAF treatment at weeks 12, 15, and 18. A three-week drug-free interval was included between each cycle of drug treatment. Blood samples were collected from control subjects and from patients in the CAF group before administration of drugs at week zero to establish a baseline, again weeks 12 and 18, and once more at the end of the 26-week treatment. Blood samples collected from the control subjects and CAF patients were analysed to determine levels of the endogenous antioxidants, r-SOD, r-CAT, r-GPx, and FRAP.

Results: Levels of r-SOD, r-CAT, r-GPx, and FRAP in CAF-treated patients at 12, 18, and 26 weeks were significantly decreased ($P<0.001$) in comparison to the baseline levels observed at week zero.

Conclusion: The results from the present study show that a change in the enzyme antioxidant systems in patients after chemotherapy and mastectomy causes an overall decrease in antioxidant levels. Chemotherapeutic agents induce oxidative stress that damages many cellular targets.

Keywords: antineoplastic combined chemotherapy protocols, antioxidants, breast neoplasms, medical sciences

Introduction

Breast cancer is reported to be the most commonly occurring cancer, with an annual age-adjusted incidence of 22–28 in 100 000 women per year in Indian urban areas, and 6 in 100 000 women per year in rural areas. More than 75 000 new cases of breast cancer are reported in India each year, and the majority of breast cancers in India (50–70%) present with locally advanced disease (1). Free radical-induced oxidative stress in cancer patients has attracted a great deal of scientific attention in the last two decades. Free radicals are chemical species possessing an unpaired electron and are generally very

reactive. They are produced continuously in cells either as by-products of metabolism, or during phagocytosis in the extra-nuclear compartment by the mitochondrial respiratory chain and the mixed function oxidase system. Free radicals can be detected by electron spin resonance spectroscopy, however this is not possible in vivo. Detection of free radical activities in vivo can be determined using antioxidants as markers. All aerobic organisms have mechanisms by which they can minimise free radical toxicity, for example reaction of superoxide radical with the enzyme superoxide dismutase (SOD), breakdown of hydrogen peroxide (H_2O_2) to water and oxygen (O_2) by catalase; and glutathione-mediated

detoxification. Thus the markers for antioxidant defence system include r-SOD, r-CAT, and r-GPx.

Neoadjuvant chemotherapy is currently a common approach for treatment of cancer patients. Despite the fact that the vast majority of patients show a clinical response to chemotherapy, its benefit is only realised in a small number of patients who achieve optimal tumour burden reduction. At our institute, every breast cancer patient presenting with a locally advanced tumour undergoes mastectomy after three cycles of chemotherapy. Following mastectomy, these patients received three further cycles of chemotherapy. Most patients with breast cancer are treated with a combination of the anticancer chemotherapy drugs cyclophosphamide, doxorubicin, and 5-fluorouracil (CAF) (2–3). These antineoplastic agents cause a reduction in antioxidant levels because their toxicity increases the peroxidation of the unsaturated fatty acids of membrane phospholipids (3). The aim of the present study was comparison of antioxidant enzymes levels in breast cancer patients at different intervals of treatment with normal subjects.

Materials and Methods

Female breast cancer patients who were admitted to the Department of Surgery of the All India Institute of Medical Sciences in New Delhi were enrolled in this study. The study included two arms: a control group consisting of healthy age-matched females ($n=20$), and patients undergoing treatment with CAF: cyclophosphamide 500 mg/m² + doxorubicin 50 mg/m² + 5-fluorouracil 500 mg/m² treatment + mastectomy ($n=55$). No treatment was given to the control group. The patient group received CAF treatment at weeks 0, 3, and 6 and underwent surgery on week 9 followed by CAF treatment on weeks 12, 15, and 18. As per protocol, a drug free interval of three weeks was given between two chemotherapy cycle treatments.

Patients were between 27 and 65 years of age (mean age 42.8 ± 10.4 years). Of the enrolled patients, eleven were pre-menopausal and 14 were post-menopausal. Patients with associated illness that are known to alter free radical levels in cancer patients such as diabetes, hypertension, myocardial ischemia, myocardial infarction, renal disorders, pancreatic disorders, pulmonary disease, and pregnancy; and patients with fibroadenomas or with any previous treatment were excluded from this study. The criteria for inclusion in this study was presentation of a

palpable mass in the breast that was observed with mammography and further confirmed by fine needle aspiration cytology (FNAC) at our institute. The study was conducted after obtaining the appropriate clearance from our institutional ethical committee.

Blood samples taken from 20 healthy females ranging from 26 and 60 years old (mean age 42.8 ± 9.8 years) were used for control measurements. Blood samples were collected in heparinised vials and centrifuged at 5000 rpm in order to separate erythrocytes from plasma. Plasma was stored at -80°C , and the erythrocytes were washed three times with normal saline and used for estimation of the endogenous antioxidants r-SOD (4), r-CAT (5), and r-GPx (6). Plasma was used for estimation of the FRAP as per the procedure laid by Benzie and Strain (7).

Chemicals

All chemicals used were of analytical grade and were obtained from Sigma Chemicals (St. Louis, USA). Double distilled water was used for all biochemical assays.

Statistical Analyses

Data are expressed as Mean $\pm$ SD. One-way analysis of variance (ANOVA) followed by a post-hoc test was used for comparison of experimental values. Values of $P < 0.001$ was considered statistically significant.

Results

The present study was conducted to investigate the effect of mastectomy and chemotherapy regimen on antioxidant status in red blood cells in breast cancer patients. The antioxidant status was determined using r-SOD, r-CAT, r-GPx, and FRAP as markers of antioxidant activity.

Erythrocyte r-SOD levels

At week zero, there was significantly higher r-SOD activity in breast cancer patients (323.54 ± 43.34 U/g Hb) in comparison with the control group (297.67 ± 38.29 U/g Hb). After 12 weeks of treatment the r-SOD level in patients undergoing CAF treatment was observed to decrease to 249.08 ± 54.31 U/g Hb, which is lower than the r-SOD activity observed in healthy controls. In CAF-treated patients, r-SOD activity was lower than in controls at 18 weeks (Table 1). After completion of CAF treatment and mastectomy, r-SOD activity was decreased to 240.06 ± 49.69 U/g Hb. All patients showed a statistically significant ($P < 0.01$)

Table 1: Time-dependent effect of CAF chemotherapy on markers of antioxidant activity in breast cancer patients. Values are expressed as Mean $\pm$ SD.

	n	r-SOD (U/g Hb)	r-CAT (U/g Hb)	r-GPx (U/g Hb)	FRAP (mEq)
I Control	20	297.67 $\pm$ 39.29	3010.90 $\pm$ 746.52	7.84 $\pm$ 1.04	782.60 $\pm$ 112.08
II Day 0 (Baseline)	55	323.54 $\pm$ 43.34	4287.65 $\pm$ 737.49 ^a	7.78 $\pm$ 1.01	819.98 $\pm$ 110.75
III 12 weeks from baseline	55	249.08 $\pm$ 54.31 ^{a,b}	3348.04 $\pm$ 842.79 ^c	6.49 $\pm$ 1.18 ^{d,e}	657.30 $\pm$ 100.68 ^{b,f}
IV 18 weeks from baseline	35	252.72 $\pm$ 49.83 ^{b,f}	3360.85 $\pm$ 835.54 ^c	6.41 $\pm$ 1.22 ^{d,e}	641.37 $\pm$ 95.99 ^{b,e}
V 26 weeks from baseline	35	240.06 $\pm$ 49.69 ^{b,e}	3350.36 $\pm$ 835.87 ^c	6.26 $\pm$ 1.21 ^{b,e}	630.75 $\pm$ 95.99 ^{b,e}

^a P < 0.05 vs. control^b P < 0.001 vs. baseline^c P < 0.001 vs. baseline^d P < 0.001 vs. baseline^e P < 0.001 vs. control^f P < 0.01 vs. control

decrease in r-SOD activity in comparison to the control group.

Erythrocyte r-CAT levels

At week zero, a statistically significant difference was found in r-CAT levels in CAF-treated patients (4287.65 $\pm$ 737.49 U/g Hb) in comparison to the control group (3010.90 $\pm$ 746.52 U/g Hb) as shown in Table 1 ($P < 0.05$). As treatment continued, r-CAT levels remained decreased in CAF-treated patients in comparison to control subjects; r-CAT activity levels were measured at 12 weeks (3348.04 $\pm$ 842.79 U/g Hb), 18 weeks (3360.85 $\pm$ 835.54 U/g Hb) and at 26 weeks (3350.36 $\pm$ 835.87 U/g Hb).

Erythrocyte (r-GPx) levels

At week zero, no statistically significant difference was found in r-GPx levels in CAF-treated patients (7.78 $\pm$ 1.01 U/g Hb) in comparison to the control group (7.84 $\pm$ 1.04 U/g Hb). After beginning CAF treatment, r-GPx levels were observed to decrease; activity levels were measured at 12 weeks (6.49 $\pm$ 1.18 U/g Hb), 18 weeks (6.41 $\pm$ 1.22 U/g Hb), and at 26 weeks (6.26 $\pm$ 1.21 U/g Hb). These activity levels are significantly decreased ($P < 0.001$) in comparison to baseline levels measured at week zero as shown in Table 1. r-GPx activity levels show a statistically significant difference in comparison to the control group at 12 weeks, 18 weeks, and at 26 weeks ($P < 0.001$).

Plasma FRAP levels

No statistically significant difference was found for FRAP levels CAF-treated patients at week zero in comparison to the control group (819.98 $\pm$ 110.75 mEq vs. 782.60 $\pm$ 112.08 mEq) as shown in Table 1. Here "mEq" stands for milliequivalents of Fe²⁺. After beginning CAF treatment, FRAP levels began to decrease in the plasma of breast cancer patients in comparison to week zero levels; FRAP levels were measured at 12 weeks (657.30 $\pm$ 100.68 mEq, $P < 0.001$), 18 weeks (641.37 $\pm$ 95.99 mEq, $P < 0.001$) and at 26 weeks (630.75 $\pm$ 95.99 mEq, $P < 0.001$). FRAP levels were significantly lower in CAF-treated patients in comparison to the control group at 12 weeks ($P < 0.01$), 18 weeks ($P < 0.001$) and at 26 weeks ($P < 0.001$).

Discussion

In the present study, we have investigated levels of various enzymes with antioxidant activities at different intervals—after 12 weeks of chemotherapy (after three cycles of chemotherapy and mastectomy), after 18 weeks of chemotherapy (after five cycles of chemotherapy were given), and after 26 weeks from the beginning of chemotherapy (i.e., two months after mastectomy and completion of the chemotherapy regimen). Baseline measurements (week zero) of antioxidant activities were also obtained before beginning chemotherapy. Changes in the activity levels of r-SOD, r-CAT, r-GPx, and FRAP were observed during chemotherapy treatment and mastectomy in comparison to baseline values measured before treatment.

Under conditions of oxidative stress, an increased concentration of reactive oxygen species may cause damage to many biomolecules including antioxidant enzymes (8). It is believed that increased H_2O_2 production in breast cancer patients may be due to an increase in production of superoxide anion ($O_2^{\cdot-}$) and elevated SOD activity. This increased H_2O_2 production may lead to accumulation of damage through formation of $OH^{\cdot}$ and other highly toxic reactive oxygen species which may form from metabolism of H_2O_2 . H_2O_2 may be detoxified by transformation into water by the catalytic activity of r-GPx and r-CAT. r-GPx is a selenium-dependent enzyme that catalyses the reaction of glutathione and H_2O_2 . A study has reported enhancement of lipid peroxidation and antioxidant status along with significant elevation in both enzymatic and non-enzymatic antioxidants in breast cancer tissues from patients with breast tissue adenocarcinoma in comparison to adjacent uninvolved tissues (9). The authors of this study suggest that upregulation of antioxidant activities induced by oxidative stress confers a selective growth advantage to tumour cells over adjacent normal counterparts.

In our study, r-SOD, r-CAT, and r-GPx activities and FRAP levels were observed to decrease after CAF treatment. These chemotherapeutic drugs are hydrophilic and cannot penetrate into the inner membrane of cells where they would be reduced by NADH located on the inner membrane surface (10–11). Chemotherapeutic drugs, particularly doxorubicin used in CAF treatment are able to enter the outer mitochondrial membrane and enter the cytosol. Intramolecular rearrangements result in formation of a lipophilic deoxyglycone that can penetrate the inner membrane of the mitochondria. There doxorubicin competes with coenzyme Q_{10} as an electron acceptor and diverts electrons to molecular oxygen resulting in formation of superoxide radicals (11). Doxorubicin intercalates DNA coils and interferes with normal cellular metabolism through a diverse set of biochemical mechanisms that may explain its toxicity. It causes an increase in peroxidation of unsaturated fatty acids of membrane phospholipids which leads to a decrease in the level of antioxidants and generates a high level of oxidative stress. In addition, doxorubicin is able to divert electrons from the mitochondrial electron transport system in addition to generating reactive oxygen species (ROS) at the cellular sites.

Studies have shown that chemotherapy causes thiobarbituric acid reactants to increase significantly, and that retinol and alpha-tocopherol

levels are lower at the end of chemotherapy (12). Another study found that the concentration of blood glutathione, plasma glutathione peroxidase activity, and plasma zinc and selenium levels were decreased in patients with cancer but were not further modified by chemotherapy (13). Antioxidant levels are significantly decreased in chemotherapy-treated breast cancer patients compared with control groups (14–15). Another study found that r-CAT activity was significantly decreased after chemotherapy along with higher oxygen free radical production (16). Following chemotherapy, both stimulated and unstimulated human polymorphonuclear leukocytes were observed to generate increased amounts of superoxide anion and hydrogen peroxide, accompanied by increased formation of lipid peroxidation products measured by thiobarbituric acid assay. Results from this study confirm that many anti-cancer drugs augment free radical generation and lipid peroxidation in vivo where the erythrocytes are under continuous oxidative stress (17).

FRAP levels in our patients are lower after chemotherapy and mastectomy in comparison with pre-chemotherapy baseline levels, indicating that chemotherapy induces lowering of plasma antioxidant levels that may be due to the failure of antioxidant defence mechanisms to respond to the oxidative damage induced by commonly used anticancer drugs. This failure probably results from both the consumption of antioxidants caused by chemotherapy induced-oxidative stress as well as renal loss of low molecular weight, water-soluble antioxidants such as uric acid (18).

The results from the present study show that a change in the enzyme antioxidant systems in patients after chemotherapy and mastectomy causes an overall decrease in antioxidant levels. Chemotherapeutic agents induce oxidative stress that damages many cellular targets. This major side effect of chemotherapeutic agents may be due to generation of superoxide and hydroxyl radicals during treatment. Oxygen free radicals, particularly $OH^{\cdot}$, are thought to be produced from genomic material and attack it directly. It will be very useful to study the effect of antioxidant supplementation to alleviate the depletion of antioxidant enzyme levels in CAF-treated patients.

Acknowledgements

We are thankful for financial support from Indian Council of Medical Research (ICMR), India (Project No. 3/2/2/98/NCD-III/2006).

Authors' contributions

Conception and design, obtaining of funding: SKM, PK

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Computed Tomography (CT) Imaging of Injuries from Blunt Abdominal Trauma: A Pictorial Essay

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Submitted: 27 Aug 2009
Accepted: 6 Jan 2010

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Abstract

Blunt abdominal trauma can cause multiple internal injuries. However, these injuries are often difficult to accurately evaluate, particularly in the presence of more obvious external injuries. Computed tomography (CT) imaging is currently used to assess clinically stable patients with blunt abdominal trauma. CT can provide a rapid and accurate appraisal of the abdominal viscera, retroperitoneum and abdominal wall, as well as a limited assessment of the lower thoracic region and bony pelvis. This paper presents examples of various injuries in trauma patients depicted in abdominal CT images. We hope these images provide a resource for radiologists, surgeons and medical officers, as well as a learning tool for medical students.

Keywords: blunt abdominal trauma, computed tomography, injuries, medical sciences

Introduction

The rapid identification of life-threatening injuries and prompt initiation of appropriate care may increase the chance of survival for patients with trauma. However, it is often difficult to accurately clinically evaluate blunt abdominal injuries, which may be masked by other more obvious external injuries. CT imaging is the diagnostic tool of choice for the evaluation of abdominal injury due to blunt trauma in haemodynamically-stable patients (1). CT scans can provide a rapid and accurate appraisal of the abdominal viscera, retroperitoneum and abdominal wall (2). In addition, an abdominal CT scan can assist in the evaluation of coexisting abdominal injuries such as thoracic injuries (3) and unsuspected pelvic and spinal fractures. The ability of CT to perform and produce fast-processing images, such as multiplanar reconstruction (MPR), is important for the accurate interpretation of abnormalities.

A variety of comments, reports and studies on the accuracy and efficacy of CT in the evaluation of blunt abdominal trauma are available in the medical literature; this topic is highly debated and has generated much discussion (4–11). CT has been reported to be valuable for the diagnosis of solid organ injuries and for the detection of active bleeding. The accurate detection of bowel and mesenteric injuries has also improved with

the development of thin-section multidetector CT (MDCT) (7). The use of CT to evaluate blunt trauma has influenced current trends in the management of solid organ injuries, prompting a greater focus on non-surgical management (12). Although the decision to surgically intervene is usually based on clinical criteria rather than findings from images (13), CT information often increases diagnostic confidence and decreases rates of unnecessary exploratory laparotomy (14).

In 2008, 92 abdominal CT scans were performed to assess blunt abdominal trauma in a tertiary referral centre (Hospital Tengku Ampuan Afzan (HTAA) in Kuantan, Pahang). In all of these cases, CT scans were performed based on the clinical suspicion of intra-abdominal injury. CT films and each patient's case notes were followed and retrospectively reviewed. Of these 92 scans, CT images showed injuries involving various organs in 72% of cases; the remaining images did not show any injuries.

All of the scans were performed using a four-row multislice CT scanner (Somatom Siemens Volume Zoom, Siemens Medical Systems, Erlangen, Germany) with a slice width of 10 mm, a 2.5 mm collimation, a 0.75 s rotation time, a table feed of 15 mm and a 3 mm reconstruction interval. Pre- and post-contrast scans were routinely performed and patients received 2 mL/kg of intravenous contrast medium (Iohexol,

300 mg/mL). Oral contrast was not routinely given. The CT scans were acquired during the portal venous phase approximately 80 seconds after the contrast injection. When necessary, sagittal and coronal images were acquired using the maximum intensity projection (MIP) and MPR techniques. Full thoracic CT scans were not routinely performed when lower thoracic injuries were observed on the abdominal CT.

The various injuries seen on the CT images were grouped and examined based on the injury site and the organs involved.

Haemoperitoneum and the detection of active haemorrhage

CT has high sensitivity and specificity for the detection of blood in the peritoneal cavity (15). Haemoperitoneum starts near the site of injury and spreads along the expected anatomic pathways (16). When the patient is in a supine position, blood from the liver collects in Morison's pouch and passes down the right paracolic gutter to the pelvis. From the spleen, blood passes via the phrenocolic ligament to the left paracolic gutter and the pelvis (Figure 1a). Blood from a splenic injury also goes to the right upper quadrant (16). Although peritoneal lavage is a sensitive indicator of intraperitoneal haemorrhage, it is unable to detect the source or origin of the bleeding (17). The 'sentinel clot' sign indicates adjacent, focal higher attenuation clotted blood as a marker for the organ that is the cause of haemorrhage (16) (Figure 1b). A large amount of blood may collect in the pelvis without much haemoperitoneum seen in the upper abdomen.

Active haemorrhage can appear as a region of extravasated contrast material and is indicated on a CT scan by an area of high attenuation, with values ranging from 85 to 350 Hounsfield units (HU) (Figure 1c) (18). The site of contrast extravasations noted on CT scans corresponds to the site of bleeding seen on angiography (19).

Splenic injury

The spleen is the most frequently injured abdominal organ during blunt abdominal trauma and accounts for up to 45% of all visceral injuries (20). A CT scan following the power injection of intravenous contrast is highly accurate (98%) in diagnosing acute splenic injuries (21). CT scans can detect a variety of splenic injuries, including laceration, a non-perfused region, intra-parenchymal haematoma and subcapsular

haematoma (22) (Figures 2a, 2b and 2c). Several CT grading scales for splenic injury are available, but these grading scales have become less clinically important with the increasing popularity of non-surgical management of splenic injury (23–24). These scales are now most important for research and database use.

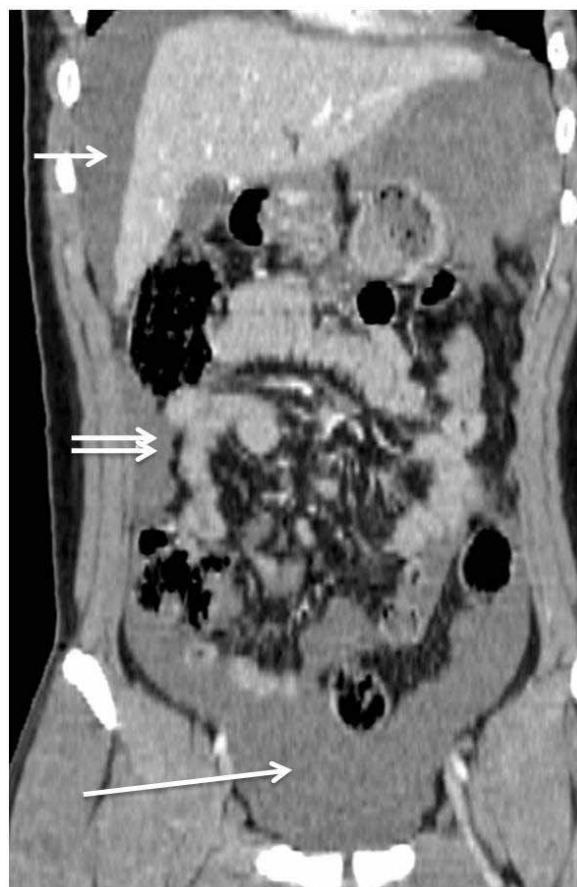


Figure 1a: CT coronal MPR in 18-year-old boy whose motorbike skidded. He had a Grade V splenic injury (images not shown). Splenectomy was performed and about 2 liters of haemoperitoneum was noted intraoperatively. This image demonstrate the possible pathway of blood flow, from the splenic injury to perihepatic (single arrow) regions and passes down the right paracolic gutter (double arrows) to the pelvic cavity (long arrow).



Figure 1b: CT scan showing haemoperitoneum from liver injury in a 23-year old man who was involved in a motor vehicle accident (MVA). The 'sentinel clot' sign is seen as a high-attenuation collection adjacent to the liver surface (arrow). Liver injury was confirmed surgically with estimated blood loss of 3 litres.



Figure 2a: CT scan of a 32-year-old man following MVA showing splenic injury. Subcapsular hematoma (θ) appears as a region of low attenuation that compresses the normal splenic parenchyma. Note also multiple lacerations of the spleen. Splenectomy was performed in this patient.



Figure 1c: CT scan demonstrating active haemorrhage in a 20-year -old man following MVA. CT shows contrast extravasation (long arrows) and pooling of the extravasated contrast in the dependant area (short arrows). This patient died 2 days after surgery from excessive blood loss.

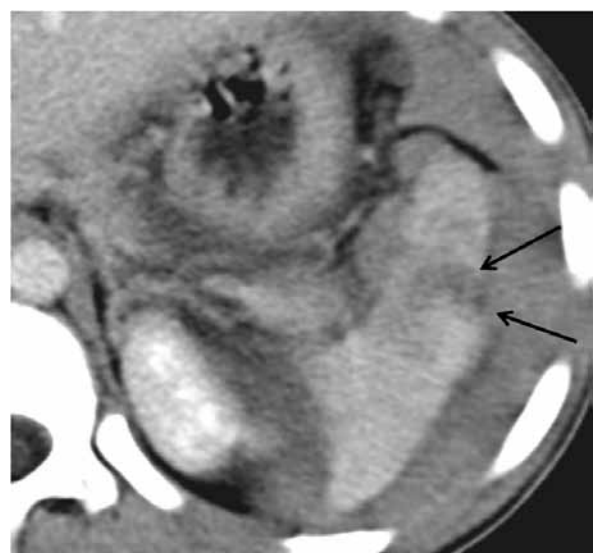


Figure 2b: CT scan showing splenic laceration in a 13-year-old boy, a pillion rider of a skidded motorbike. Splenic laceration is seen as irregular, linear region of low attenuation (arrows). A 4 cm laceration was identified at the tip of the spleen during surgery and splenectomy was performed.



Figure 2c: CT scan demonstrating a shattered spleen in a 21-year-old male motorcyclist following MVA. Multiple hypodense areas that connect to the visceral surfaces are shown. This patient had failed conservative treatment and splenectomy was performed two days following the trauma which confirmed the CT findings of shattered spleen.

Liver injury

The liver is the second most frequently injured intra-abdominal viscus (2). The worldwide incidence of liver injuries is not known (9), although penetrating injuries (gunshots and stab wounds) account for the majority of liver injuries in North America and South Africa while blunt injuries cause the majority of liver injuries in Europe and Australasia (8).

Although elevated transaminase levels are 100% sensitive and 92.3% specific in predicting hepatic injuries (25), CT is currently the diagnostic modality of choice. CT scans can be used to accurately diagnose parenchymal injuries and exclude surgical lesions such as bowel or pancreatic injuries (26) (Figures 3a and 3b). CT grading criteria have been proposed for liver injuries, but, as with splenic injury, these criteria do not correlate well with the need for surgical intervention or risk of subsequent complications. Surgical analyses have shown that up to 80% of liver injuries in adults and up to 97% of liver injuries in children can be treated without surgery (27).



Figure 3a: CT scan of liver injury in a 48-year-old man with MVA. CT demonstrates a subcapsular hematoma that appears as a hypodense collection, compressing on the underlying liver parenchyma (arrows).



Figure 3b: CT scan of liver injury in a 23-year-old man with MVA. Liver laceration is shown on CT as a non-enhancing irregular linear low attenuation area (arrow) with associated intraparenchymal hematoma (θ), which appears as a region of decrease attenuation compared to the rest of the enhanced liver parenchyma. He was managed surgically.

Urinary tract injury

Renal injury occurs in about 10% of cases of abdominal injury and the majority of renal injuries (80% to 90%) result from blunt trauma (28). CT can provide a precise delineation of renal laceration, haematoma and perinephric collection (29); in addition, CT scans can be used to differentiate trivial injuries from those requiring intervention (28) (Figures 4a, 4b and 4c).

To evaluate bladder injuries, CT cystography with retrograde bladder filling can be added to the routine CT abdominal examination (30). Bladder injuries have characteristic CT cystographic features that can be used to accurately classify injuries and plan treatment (Figures 5a, 5b and 5c). CT differentiates between extraperitoneal and intraperitoneal bladder ruptures and helps determine the management of these injuries.



Figure 4b: CT of renal laceration in a 32-year-old man with MVA. The right renal lacerations are shown as irregular, linear low attenuation areas within the parenchyma (arrow), which does not involve the collecting systems. He was managed conservatively with an unevenful recovery.



Figure 4a: CT scan of renal injury in a 20-year-old man with MVA. A right contusion which appears as a focal patchy area of decreased enhancement (arrows) was observed on CT. A liver laceration is present adjacent to the kidney. He was managed conservatively with an uneventful recovery.



Figure 4c: CT scan of renal injury in a 17-year-old girl with MVA. Subcapsular hematoma of the right kidney (arrows) appears on CT as a superficial, crescentic, low attenuation area that compresses the adjacent renal parenchyma. She was managed conservatively with uneventful recovery.

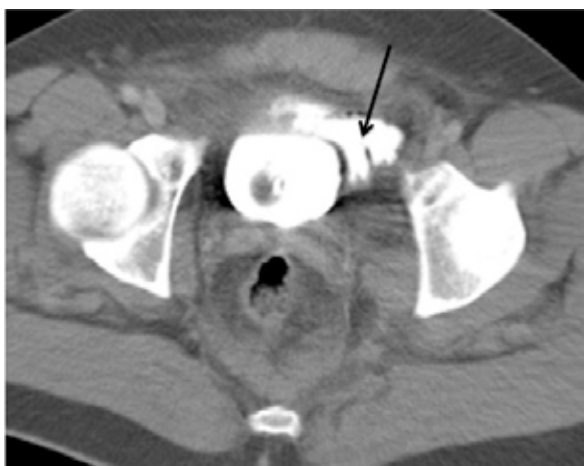


Figure 5a: CT cystogram of urinary bladder truma in a 28-year-old man following MVA. There is extravasation of contrast (arrow) in the perivesical fat indicating an extra peritoneal bladder rupture.



Figure 5b: CT scan showing fracture of the pelvic bone. A lower scan of the same patient in Figure 5a shows the pelvic fracture (arrow). He was managed conservatively with unevenful recovery.



Figure 5c: CT scan of urinary bladder injury in a 26-year-old man with industrial accident. He fell and was run over by a tractor. This image shows extravasation of contrast from a urinary bladder injury, which outline the bowel loops (arrows). This indicates an intraperitoneal bladder rupture. Note fracture on the right side of the sacrum and diasthesis of left sacroiliac joint. Urinary bladder perforation at two sites with about 1 litre of haemoperitoneum was confirmed at surgery.

Pancreatic injury

Pancreatic injury is encountered in only 3% to 12% of all abdominal injuries (31). Pancreatic injury is more common in children and young adults, possibly because these individuals have less retroperitoneal fat to act as a protective buffer (2). The identification of blunt pancreatic injury may be difficult because image findings are often subtle (32). Initial CT findings may be normal, even with pancreatic transaction, because the elastic pancreatic parenchyma resumes its normal contour (33). A repeated CT abdominal scan at 24 to 48 hours can help reveal evolving injuries (2). A delay in diagnosis can often result in recurrent pancreatitis, pseudocyst, fistula or abscess formation (27)(Figure 6).



Figure 6: CT scan of pancreatic transection in a 9-year-old girl with 'bicycle-handle' injury. Diagnosis was delayed and CT scan performed 2 days after the incident showed a total transection of the body of pancreas (arrow). This was later complicated by a pseudocyst formation that required a percutaneous drainage.



Figure 7a: CT scan of perforated bowel in a 26-year-old man with MVA. Note subtle extraluminal air (single white arrows) with focal bowel wall thickening (double white arrows) at the rectosigmoid region that was missed on initial review of the CT images. Also note air pockets in the urinary bladder (black arrows). Urinary bladder perforation and transection at the rectosigmoid junction were detected intra operatively.

Bowel and mesenteric injury

The sensitivity of CT to traumatic bowel injury varies from 69% to 92% and CT is 94%–100% specific for the diagnosis of bowel and mesenteric injuries (10, 34–35). CT findings can include focal bowel wall thickening, mesenteric infiltration, free air, the presence of intraperitoneal fluid without solid organ injuries and extravasated contrast material (10–11,34,36) (Figures 7a and 7b). CT images must be carefully examined to detect injuries and close attention should be paid to scanning techniques and optimal bowel contrast (37).

Injury to the retroperitoneum, spine, abdominal wall and lower chest

Before the use of CT, haemorrhage into the retroperitoneal space was difficult to diagnose (1). CT is valuable in the detection of retroperitoneal and abdominal wall injuries (38) (Figures 8a and 8b). In addition, CT scans can reveal various fractures involving the pelvis (Figures 9a and 9b) and spine (Figure 10) and can offer information about significant unsuspected or underestimated thoracic injuries (Figures 11a and 11b) that are common in patients with blunt abdominal trauma (3,39).



Figure 7b: CT scan of bowel injury in a 23-year-old lorry driver with MVA. CT scan showed focal small bowel thickening (arrows) but no free air was identified. Small bowel perforation was found intra operatively.



Figure 8a: CT scan of retroperitoneal injury in a 23-year old man with MVA. CT shows an anterior displacement of the right kidney by a retroperitoneal haemorrhage. Both kidneys are otherwise intact. He was managed conservatively with uneventful recovery.

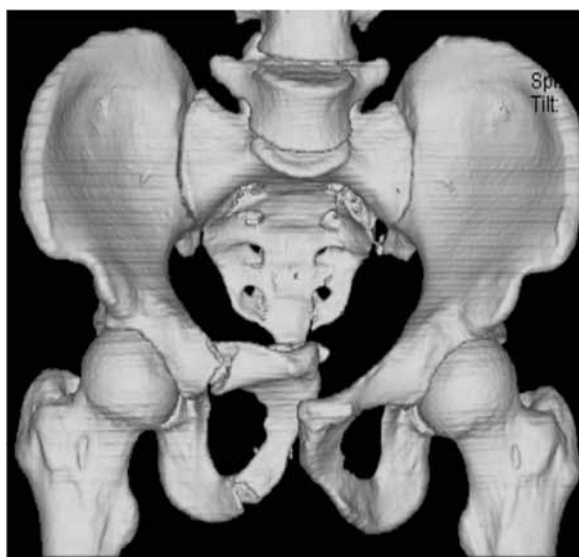


Figure 9a: CT scan showing fracture of the pelvic bone in a 29-year-old lorry driver following MVA. This volume-rendered CT coronal MPR image clearly depicts fracture of the right pubic rami with displacement of the fractured fragments.



Figure 8b: CT scan of the same patient in Figure 8a showing the soft tissue injury. There is haematoma and thickening of the abdominal wall (short arrows). The soft tissue injury is extensive involving the right iliopsoas muscle (long arrows) and extends inferiorly to the high region, which compresses the right femoral artery and vein (images are not shown). Note also comminuted fractures of the right iliac bone.



Figure 9b: CT demonstrating soft tissue injury associated with pelvic fracture. A coronal MPR CT image in soft tissue window of the same patient in Figure 9a showed the fractured fragment (short arrow) compressing at the base of the urinary bladder. Note the mal-positioned Foley's catheter balloon within the urethra (long arrow). Urethrogram demonstrated a membranous urethral injury.

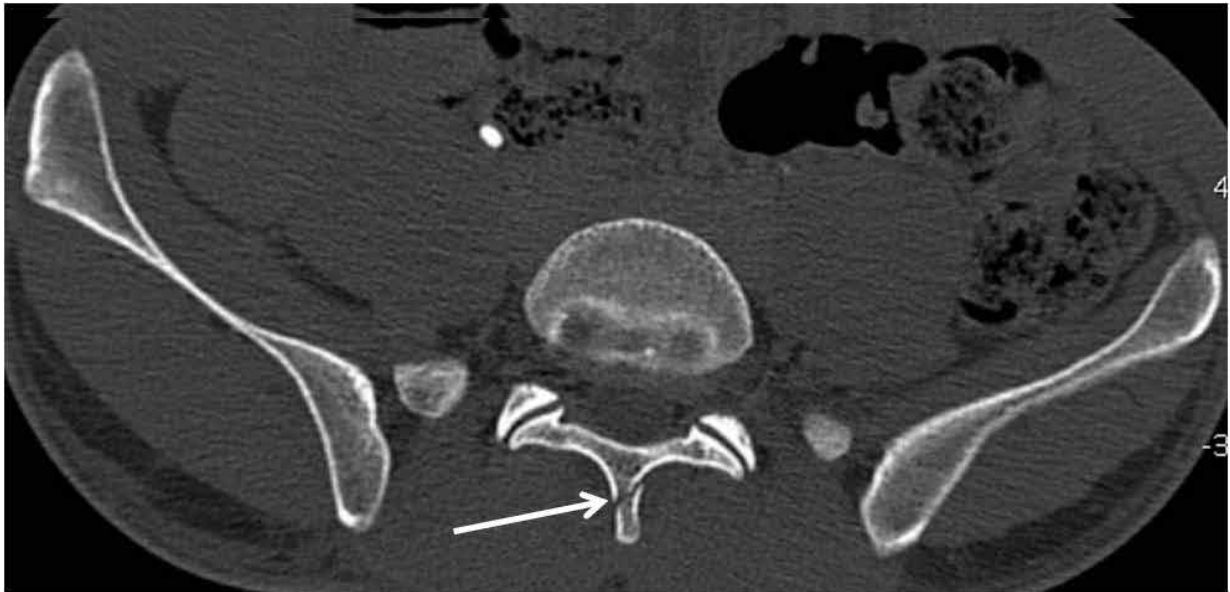


Figure 10: CT scan of spine fracture in a 29-year-old man who fell from height at the workplace. He complained of pain at the lumbar region. CT scan shows no intra abdominal injury but demonstrated a subtle of L5 spinous process (arrow), which was missed on the plain radiograph. He was managed conservatively with unevenful recovery.



Figure 11a: CT of a 15-year-old boy with MVA. The limited evaluation of the lung bases reveals bilateral lung contusions with a left lung laceration (arrow). He sustained a Grade 1 liver injury (not shown) and was managed conservatively.

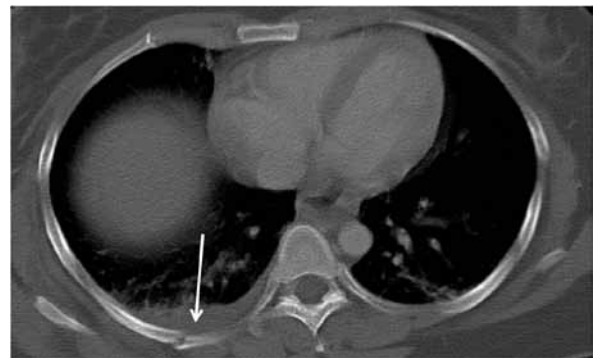


Figure 11b: CT evaluation of the lower thoracic region in a 25-year-old man with MVA revealed fracture of right posterior rib (arrow) with associated pleural effusion, possibly a haemothorax.

Conclusion

The examination of CT scans is extremely useful for the evaluation of blunt abdominal injuries in haemodynamically-stable patients. CT scans can reveal a wide variety of injuries. In addition, CT examination is fast and widely available. With appropriate scanning protocol, CT can provide good resolution images with MPR.

Acknowledgements

We would like to thank the surgical and radiological staff of HTAA and Kulliyyah of Medicine, IIUM for their continuous effort and assistance in the care and treatment of patients. The data obtained in this pictorial essay is part of a project funded by the IIUM Research Endowment Fund (Type A).

Authors' contributions

RH and AAA had contributed equally towards drafting and revising the manuscript.

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Submitted: 29 Jun 2009

Accepted: 25 Dec 2009

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Abstract

Background: Kernicterus occurs in infants around the world. This study examined the outcomes of various treatments for neonatal hyperbilirubinemia (NH) used in the Khulna Medical College Hospital in Bangladesh.

Methods: All of the jaundiced newborns in the neonatal ward between 2005 and 2008 were included in the study. Total serum bilirubin and fractional levels were measured in all cases, regardless of the degree of jaundice. NH was classified as mild, moderate or severe depending on the bilirubin level; mild NH was treated with a sunbath, moderate NH was treated with phototherapy, and severe NH was treated with exchange transfusion.

Results: Of 1981 neonates, 426 (22%) were diagnosed with NH. Physiological jaundice (26.7%) was most common, followed by the jaundice of prematurity (20.9%). Haemolytic jaundice was primarily caused by ABO incompatibility (11.3%) and Rh incompatibility (5.4%). Exchange transfusion (ET) was performed in 22 patients; four (18.2%) died as a result of hazards that could have been avoided with skilled monitoring. Twelve (2.8%) individuals with jaundice died. Kernicterus developed in nine (2.1%) children, four of whom survived with neurological sequelae.

Conclusion: ABO incompatibility is twice as common as Rh incompatibility. The majority of kernicterus patients died in the acute phase.

Keywords: exchange transfusion, kernicterus, neonatal hyperbilirubinemia, medical sciences

Introduction

Neonatal hyperbilirubinemia (NH) is a common problem that occurs in about 60% of newborns during the first week of life (1). Bilirubin is a known antioxidant at low concentrations but a potent neurotoxin at high concentrations (2). The transition from progressive hyperbilirubinemia to acute bilirubin encephalopathy is often rapid and unpredictable because of a very narrow margin of safety. Studies in the early 1990s suggested that kernicterus from NH was rare in developed countries, and researchers argued that too many children were being treated unnecessarily (3,4). After new guidelines that recommended the treatment of NH at higher levels than before were published, the incidence of kernicterus increased in several countries (5,6).

Many changes have occurred in the management of NH. The hour-specific nomogram, introduced by Bhutani et al. and supported by the American Academy of Paediatrics (AAP), was found to be an effective means of predicting NH (7,8). Many studies have questioned the accuracy of visual assessments used in developing countries (9) but non-invasive bilirubin estimation by

transcutaneous bilirubinometry is not available everywhere. At the same time, as the incidence of severe jaundice due to Rh incompatibility has declined, ABO incompatibility has become the most common cause of haemolytic jaundice in newborns (10). These changes in global and national contexts have prompted this work. The objective of this study was to evaluate the effect of different treatment modalities on jaundice outcomes in a tertiary care hospital in Bangladesh.

Material and Methods

This prospective cross-sectional study examined patients admitted to the Khulna Medical College Hospital (KMCH) between July 2005 and June 2008. All of the newborns with visible jaundice in the neonatal ward were included in this study. These neonates were either admitted with jaundice or developed it after they were hospitalised for other reasons. Patients with jaundice who were over the age of two weeks were excluded from the study. A careful general examination was carried out to explore possible aetiologies. All of the patients with clinical jaundice, regardless of the severity,

were assessed for total serum bilirubin as well as for direct and indirect fractions. The serum collected from venous blood samples was tested in an automated analyser with the colorimetric method. Additional tests, including a full blood count, peripheral blood film, blood group, Coombs test, blood culture, serum electrolytes and neuroimaging, were completed in all cases of severe NH; these tests were used to determine the causes or effects of NH. Neuroimaging was used only in survivors with neurological sequelae. Lab tests for G-6-PD, pyruvate kinase and glucuronyl transferase could not be completed because of a lack of facilities. Twenty-four hours after birth, mild NH was defined as a total bilirubin level of up to 10 mg/dL (171 μ mol/L) in preterm infants and up to 12 mg/dL (205 μ mol/L) in full-term infants. Bilirubin levels above 18 mg/dL (308 μ mol/L) in preterm infants and above 20 mg/dL (342 μ mol/L) in full-term infants were used to identify severe hyperbilirubinemia. Bilirubin levels between these values indicated moderate NH (10). Kernicterus was diagnosed in severely jaundiced infants on clinical grounds; poor sucking, stupor and hypotonia were symptoms in the early phase, while hypertonia, retrocollis and opisthotonus were symptoms in the late phase (11).

The Paediatric Association of Bangladesh has advocated for the simplified management of NH outside of neonatal intensive care units (12). This study used the recommended therapies according to total serum bilirubin. Mild NH cases were treated conservatively with breast-feeding and sunbaths. Infants were exposed to the sun for a brief period (1–2 hours) in the early morning and afternoon; a filter of tinted glass was used to avoid the possible hazards of radiation. Infants with moderate NH were treated with phototherapy applied in a standard cycle (45 minutes of therapy and 15 minutes of rest). Exchange Transfusion (ET) and phototherapy were used to treat severe NH. Total serum bilirubin was measured each morning. The risk factors for kernicterus, such as prematurity, birth asphyxia, acidosis, hypothermia and hypoglycemia, were monitored to determine whether the treatment needed to be intensified. The clinical course and treatment outcome were noted twice daily. The data at the end of study were analyzed with SPSS-11.5 (SPSS Inc., Chicago). Ethical approval was obtained from the Ethical Review Committee of the KMCH.

Results

During the three-year study period, 1981 patients were admitted to the neonatal ward; 426 (22%) of these infants had jaundice. Of these jaundiced infants, 179 (42%) had a low birth weight (<2.5 kg) and 158 (37%) were preterm (<37 weeks). The male-to-female ratio was 1.3:1. The mean age at the appearance of jaundice was 4.5 ± 2.3 days. Physiological jaundice was most common and was diagnosed in 114 (26.7%) cases. These individuals had mild jaundice persisting from days three to seven after birth. Prematurity (20.9%) and sepsis (17.6%) were also major causes of jaundice. No correlation was found between prematurity and sepsis. Premature infants observed in the study period were between 30 and 36 weeks gestational age. *Escherichia coli* and *Klebsiella* were the most common organisms isolated in cultures from septic infants. ABO incompatibility was responsible for jaundice in 48 cases (11.3%) and Rh incompatibility was responsible for only 23 (5.4%) cases of jaundice.

One hundred and thirty-seven (32.2%) infants were treated conservatively; most (48) of these infants had physiological jaundice (Table 1). Phototherapy was the most common treatment and was used in 267 (62.6%) cases. ET was used in 22 (5.2%) cases; most (68.2%) of these patients suffered from Rh incompatibility. Four hundred and one (94.1%) infants improved satisfactorily, including all those with physiological jaundice and cephalhaematoma. Twelve (2.8%) patients died in the hospital, five of whom developed kernicterus before death (Table 2). Three of the fatal cases were admitted to the hospital in a very late stage with neurological symptoms. ET resulted in the death of four (18.2%) patients: in sepsis (1 case), of ABO incompatibility (1 case) and of Rh incompatibility (2 cases). The rest of the fatalities were attributed to co-morbidities (4) or an unknown cause (1). A shortage of fresh blood and electrolyte imbalance were the principal obstacles and dangers during the ET procedure. Four (0.9%) survivors had neurological sequelae; MRIs of their brains revealed evidence of neuronal atrophy of the basal ganglia, particularly in the globus pallidus and, in two cases, the cerebellum.

Among the 28 infants with severe NH, six did not receive ET due to either their frail state (2) or delayed admission (4). Table 3 compares the characteristics of infants with severe NH who developed kernicterus with those of infants who did not develop kernicterus. Although the proportions of premature infants and those with low birth weight were higher in the group

Table 1: Modalities of treatment for various conditions

Cause	Modalities			Total, (%)
	Sunbath	Phototherapy	Exchange Transfusion + Phototherapy	
Physiological	48	66	0	114 (26.8)
Prematurity	27	62	0	89 (20.9)
Sepsis	24	49	2	75 (17.6)
ABO incompatibility	13	30	5	48 (11.3)
Rh incompatibility	0	8	15	23 (5.4)
Cephalhaematoma	3	7	0	10 (2.3)
Others	22	45	0	67 (15.7)
Total (%)	137 (32.3)	267 (62.6)	22 (5.2)	426 (100)

Table 2: Outcome of neonatal hyperbilirubinemia

Cause	Outcome					Total
	Improved	Expired	Expired with Kernicterus	Kernicterus	Absconded	
Physiological	114	0	0	0	0	114
Prematurity	84	1	1	0	3	89
Sepsis	69	2 ^a	1	1	2	75
ABO incompatibility	46	1 ^a	0	1	0	48
Rh incompatibility	17	2 ^a	2 ^a	2	0	23
Cephalhaematoma	10	0	0	0	0	10
Others	61	1	1	0	4	67
Total (%)	401 (94.1)	7 (1.6)	5 (1.2)	4 (0.9)	9 (2.1)	426 (100)

Total deaths: 12 (2.8%); Total Kernicterus cases: 9 (2.1%)

^aSingle death from Exchange Transfusion; Total deaths from Exchange Transfusion: 4 (18.2%)

developing kernicterus; this difference was not statistically significant. Aetiology, gender and feeding patterns were similar in the two groups.

Discussion

This study found that approximately one in five (22%) infants admitted to the neonatal ward had jaundice. Among these jaundiced infants, 37% were preterm. Khatun et al. reported a similar observation in the neonatal unit of a university hospital, where 35% of newborns had jaundice and 31% of jaundiced infants were preterm (12). ABO incompatibility (11.3%) was more than twice as common as Rh incompatibility (5.4%);

this finding is similar to those reported a study (10). The incidence of Rh isoimmunization has decreased as a result of the introduction of Rh (D) immunoglobulin to Rh-negative mothers. However, Hoque studied haemolytic disease in newborns and found that 39% of cases were the result of ABO incompatibility and 34% cases were the result of Rh incompatibility (13).

One-third (32.2%) of our patients improved with conservative treatment alone. Phototherapy was applied in most (62.6%) cases with good success. A small portion (5.2%) of patients underwent ET. Our findings are consistent with those of other medical centres, where 61% of patients required only phototherapy (12). Fifteen years ago, Rh incompatibility was the

Table 3: Risk factors for kernicterus in severe neonatal hyperbilirubinemia (n=28)

Factors	Kernicterus-9 (% within group)	No kernicterus-19 (% within group)	P-value ^a
Aetiology			
Prematurity	1 (11)	1 (5)	0.426
Sepsis	2 (22)	2 (11)	
ABO incompatibility	1 (11)	5 (26)	
Rh incompatibility	4 (44)	11 (58)	
Unknown	1 (11)	0 (0)	
Gender			
Male	5 (56)	11 (58)	0.907
Female	4 (44)	8 (42)	
Birth weight			
1 - 1.5 kg	2 (22)	2 (11)	0.301
1.5 - <2.5 kg	5 (56)	7 (37)	
≥ 2.5 kg	2 (22)	10 (52)	
Gestational age			
30–32 weeks	2 (22)	1 (5)	0.292
33–<37 weeks	4 (44)	7 (37)	
≥ 37 weeks	3 (33)	11 (58)	
Feeding			
Formula	1 (11)	2 (11)	0.996
Mixed	2 (22)	4 (21)	
Exclusive Breast milk	6 (67)	13 (68)	

^aAssociation between risk factors and kernicterus were calculated using Chi-Square test

most common (40%) cause of ET, followed by ABO incompatibility (35%) (12). Although the incidence of Rh incompatibility has decreased, ET was used most frequently (68%) in cases of Rh incompatibility.

Twelve (2.8%) patients in this study died in the hospital and four (0.9%) neonates were discharged with neurological sequelae. Two studies found that mortality from NH decreased from 36% to 5% over ten years as a result of the wide-spread use of phototherapy, improved ET techniques and increased awareness among health workers of the importance of early management (10,12). ET itself may cause severe complications like acidosis, hypoglycemia, air embolism, arrhythmia and death (14). The mortality from ET in this study (18.2%) is consistent with the ranges (from 8% to 20%) found in other studies (13,15). The clinical features of kernicterus vary, and overt neurological signs have a grave prognosis: 75% of the affected infants die and 80% of survivors bear several neurological complications (14). The

majority (55.6%) of infants developing kernicterus in this study died as well.

It is quite alarming to note that nine patients developed kernicterus and five of them died in the hospital. G-6-PD deficiency is common in Bangladesh and is an important contributor to kernicterus; this deficiency may have been an unmeasured factor that led to the high incidence of severe hyperbilirubinemia and kernicterus. Most of the fatalities resulted from delayed admission. The proportion of infants dying from ET was also high in comparison to those in developed countries (7,14). While sterile procedures and thermal stabilisation were maintained during the procedure, the availability of fresh blood and electrolyte monitoring could not be properly ensured; this may have increased the rate of fatality.

ET is the definitive therapy for the prevention of kernicterus in patients with severe NH. However, 22% of children in this study could not receive ET because of the advanced stage of

the disease. The development of kernicterus may be attributed to several potential risk factors (14,15). In this analysis, no significant association was found with aetiology, gender, birth weight, gestational age, and feeding patterns. While infants with a normal birth weight were the least susceptible to severe NH, premature infants (30–32 weeks gestation) were most vulnerable; this finding highlights the need for early and vigorous intervention in these cases.

The primary limitations of this study include the use of absolute bilirubin values in the grading of jaundice, the lack of extensive investigations to determine the cause of jaundice and the lack of follow-up for kernicterus cases. However, this study shows that NH should be regarded as a potentially dangerous problem. Early and appropriate treatment is essential to prevent disastrous neurological sequelae.

In conclusion, kernicterus due to severe hyperbilirubinemia causes permanent neurological damage. In certain parts of the world, kernicterus is still a major cause of mortality and long-term morbidity.

Authors' contributions

Conception and design; drafting, critical revision and final approval of the article: CHR
Provision of study materials or patients: MAH
Data analysis and interpretation, final
Final approval of the article: CHR, MAH, FY
Data collection and assembly, statistical expertise: FY

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Case Report

Gastric Schwannoma in a Female Patient with Pulmonary Tuberculosis — A Clinicopathological Assessment and Diagnosis

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Submitted: 19 Oct 2009

Accepted: 18 Jan 2010

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Abstract

Schwannomas, or neurinomas, are generally benign, slow-growing, asymptomatic neoplasms originating from the Schwann cells of a nerve sheath. As a part of spindle cell mesenchymal tumours, schwannomas arising from the gastrointestinal tract (GIT) are unusual; however, when they occur, the most common site involved is the stomach, which represents 0.2% of all gastric tumours. We report the case of a 35-year-old female patient with a history of pulmonary tuberculosis presenting with a large palpable abdominal mass reaching up to the peritoneal cavity. The initial clinical impression was a tuberculous abdominal mass, a cyst, or a teratoma. However, intra-operative findings during a subtotal gastrectomy revealed an exophytic gastric serosal mass, which suggested a gastrointestinal stromal tumour (GIST). Post-operative histopathological findings showed a fascicular arrangement of neoplastic spindle cells with palisading nuclei that showed intense positivity for S-100 protein, and were negative for CD117 and desmin in immunohistochemistry studies. These results confirmed the final diagnosis of a gastric schwannoma.

Keywords: gastrointestinal stromal tumours, immunohistochemistry, neurilemmoma, stomach, medical sciences

Introduction

Gastrointestinal mesenchymal tumours are a group of tumours that originate from the mesenchymal stem cells of the gastrointestinal tract (GIT) and consist of gastrointestinal stromal tumours (GIST), leiomyomas or leiomyosarcomas, and submucosal schwannomas (1). Histologically, these tumours form a spindle cellular pattern and were traditionally considered to be of smooth muscle origin; however, the immunohistochemical studies by Sarlomo-Rikala and Christopher showed the differences between these tumours by demonstrating positive desmin and muscle actin immunostaining in leiomyoma or leiomyosarcoma (2,3). No evidence of this positive desmin and muscle actin immunostaining was found in GIST because most of these tumours showed positive staining for CD117 and CD34, whereas S-100 positivity indicated schwannomas (2,3). Diagnosis of primary GIT schwannomas based on the S-100 positivity had been dubious until Daimaru et al. in the year 1992, presented a

series of well-documented cases, in which 24 out of 306 GIT spindle cell tumour cases were found to be schwannomas through immunohistochemistry (IHC). In contrast, only 9 of these cases were diagnosed as schwannomas when stained only with hematoxylin-eosin (H&E) (4). Some of the non-specific histological features supporting schwannomas include the presence of spindle cell tumours lacking epithelioid features and skeinoid fibres that have a peripheral cuff of lymphoid tissue and specific intracellular needle-shaped PAS-positive crystalloids (5,6). This marked difference shown by Daimaru demonstrates the high likelihood for misdiagnosing schwannomas as GISTs when IHC is not used (4). Gastric involvement, though most common among the GIT schwannomas, represents only 0.2% of all gastric tumours and 4% of all benign gastric neoplasms (7). Here, we present the case of a 35-year-old woman with a gastric schwannoma manifesting as a painless palpable mass in the abdomen, which was diagnosed using different immunohistochemical markers.

Case Report

A 35-year-old female with pulmonary tuberculosis presented to the Sharif Medical College Hospital Lahore with a 6-month history of a progressively enlarging but painless abdominal mass. There were no associated symptoms except those related to tuberculosis, including loss of appetite and weight. She had been on anti-tuberculosis therapy for the previous 8.5 months. Her general physical examination was unremarkable, although crepitations and ronchi were heard in the left lung. Upon radiological assessment, both lung fields showed moderate pleural effusion and foci of calcification as a result of pulmonary tuberculosis. The abdominal examination showed a large, freely mobile, firm but smooth-surfaced, non-pulsatile mass that measured 12 x 10 cm and was dull on percussion. Laboratory investigations revealed an erythrocyte sedimentation rate titre three times higher than normal and a haemoglobin level of 8.2 g/dL. Radiographical survey using ultrasound followed by CT scan of the abdomino-pelvic area showed an enlarged, 15 x 13 x 8 cm, well-defined, solid, heterogeneous mass in the abdomen with foci of necrosis and a 15 mm area of dense calcification seen posteriorly. The mass was connected to the stomach but had no link with the bladder or the uterus. The first clinical impression of the surgeon was a disseminated lesion in the abdomen from pulmonary tuberculosis, a mesenteric cyst, or a teratoma. Neurofibromatosis 1 (NF-1) was ruled out by following the criterion suggested by the National Institute of Health (NIH), which specifies the identification of at least two of the seven "Cardinal Clinical Features". These features are as follows: 1) 6 or more café-au-lait macules over 5 mm in largest diameter in pre-pubertal individuals and over 15 mm in largest diameter in post-pubertal individuals, 2) 2 or more neurofibromas of any type, or 1 plexiform neurofibroma, 3) freckling in the axillary or inguinal regions, 4) optic glioma, 5) 2 or more Lisch nodules (iris hamartomas), 6) a distinctive osseous lesion, such as sphenoid dysplasia or thinning of the long bone cortex with or without pseudarthrosis, and 7) a first degree relative (parent, sibling, or offspring) with NF-1 by the above criteria. Initial manifestations most often occur in childhood. Clinical signs may be apparent at birth, however, in some affected individuals, signs may not develop until adulthood. Exploratory laparotomy was planned for the patient, and the pre-operative findings showed a well-circumscribed mass arising from the serosal surface of the distal stomach wall

close to the greater curvature but separated from the liver, pancreas, and major abdominal vessels. The mass was protruding into the peritoneal cavity. A subtotal gastrectomy was carried out to remove the tumour capsule, which was gently and carefully dissected from the fascicles of the nerve. Additionally, adherent omentum and 13 enlarged adjacent draining lymph nodes were resected. Gastro-jejunostomy was performed, and the post-operative course was uneventful. The patient was discharged in stable condition within a week's time. The surgical specimen received by our pathology department was fixed overnight. Gross inspection the next day revealed an exophytic, yellow-tan, bosselated mass measuring 13 x 12 x 7 cm. The cut surface of the specimen was similar to fish flesh with whirling trabeculations (Figure 1). The mucosa overlying the tumour was unremarkable with a tiny, less than 1 cm, focus of ulceration over the tumour area. The tissue sections from the resected tumour specimen were embedded in paraffin blocks. Eleven sections of 4–7µm (five for H&E staining and 2 each for three immunohistochemical markers) were cut from the tumour tissue and collected on poly-L-lysine-coated slides for IHC. Sections from the lymph nodes were subjected to H&E staining only. Histological observations revealed dense lymphocytic infiltration at the periphery of the tumour with predominantly Antoni type A areas. These areas consisted of fascicular arrangements of neoplastic spindle cells bearing palisading nuclei with occasional pleomorphism interspersed within a loose collagenous matrix. Few foci exhibiting Antoni type B changes were also observed. No evidence of necrosis, haemorrhage, cystic degeneration, or any malignant change was seen, along with moderate to severe reactive hyperplasia of all lymph nodes

These findings supported the diagnosis of a GIST or a gastric schwannoma (Figure 2a & 2b). Differential diagnosis was confirmed by applying immunohistochemical markers using the standard 'Avidin Biotin Peroxidase' method. The primary antibodies (AbD Serotec, Germany) employed were purified concentrated mouse monoclonal antibodies to Desmin (HCA071A), CD117 (MCA2598), and the polyclonal antibody to S-100 (AHP385T) protein. The morphologic and immunohistochemical features of the tumour, namely an intense S-100 protein positivity and negativity for desmin and CD117, resemble the diagnostics used in previously reported gastric schwannomas (Figure 3).



Figure 1: Cross-section of the surgical specimen, which shows an enlarged yellow-tan solid mass with whirl like trabeculations originating from the serosal surface of the stomach.

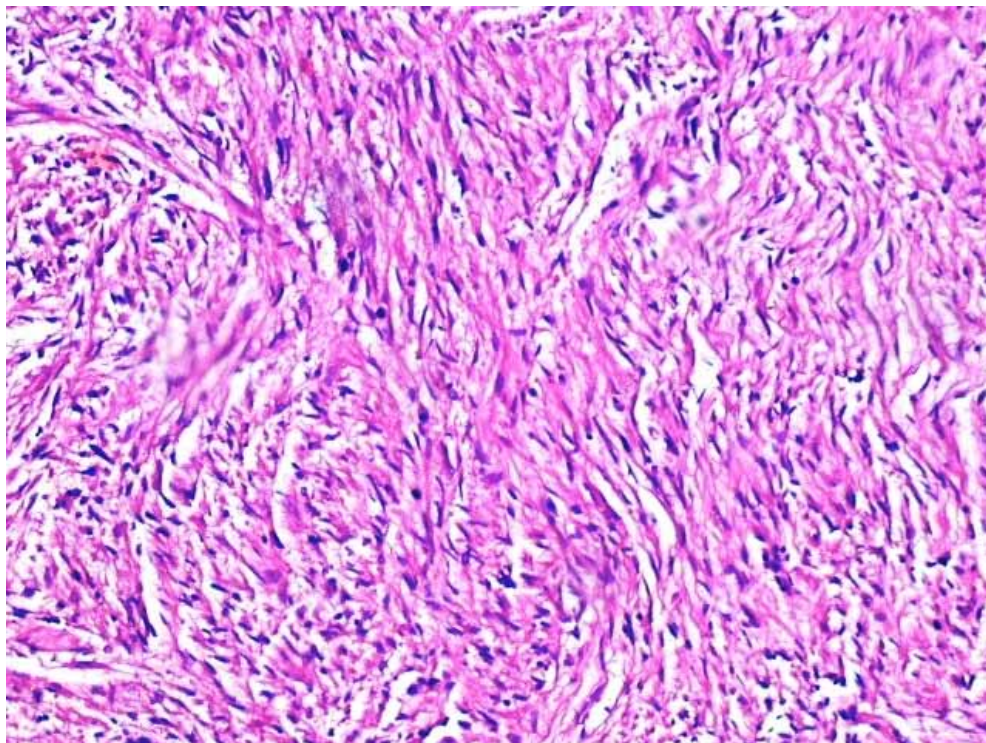


Figure 2a: Photomicrograph of the gastric tumour, which shows interlacing bundles of spindle cells, palisading nuclei with nuclear atypia and no mitosis, interspersed with collagenous strands (H&E, x200).

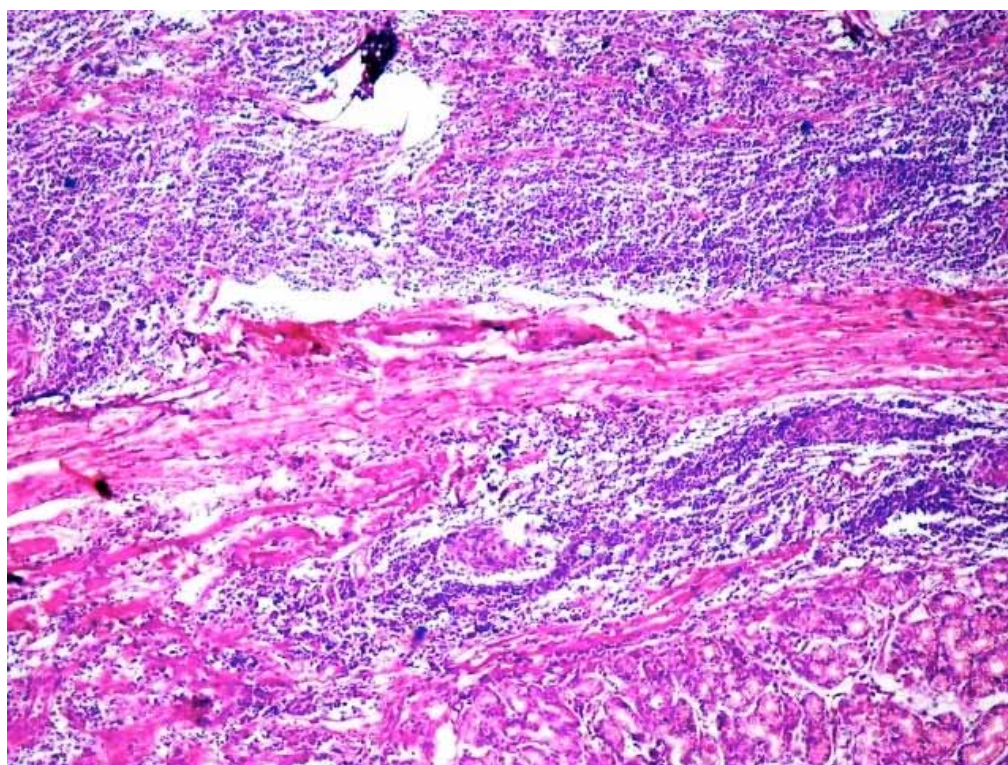


Figure 2b: Dense lymphocytic cuffing at the peripheral part of the tumour, which resembles a tumour of lymphoid origin (H&E, x100).

Discussion

Schwannomas are the most common solitary, encapsulated, and slow-growing peripheral nerve-sheath tumours. Gastric schwannomas originate within the nerve sheath of Auerbach plexus or, less commonly, from Meissner plexus. Histologically, gastric schwannomas are composed of Schwann cells dispersed in a collagenous matrix (7). These tumours arise from the fundus, body, or antrum of the stomach and are commonly intramural, however, they can be extraluminal or endoluminal. Tumours vary from 0.5 cm to 11 cm in diameter and are spherical or ovoid with an occasional multinodular pattern (4,5,8,9). As the tumour enlarges, it displaces the nerve to the periphery of the tumour, preserving neural function. In our case, the tumour was characteristically exophytic, extending from the gastric wall to the abdominal cavity, and the differentiation of the schwannoma from other submucosal tumours was very difficult on pre-operative assessment.

These tumours occur more frequently in females in the fifth to sixth decade of life, although the patient in our study was quite young. These tumours are often asymptomatic and can be discovered incidentally. The most common presenting symptom is an episode of upper GIT bleeding with or without abdominal pain, which

may be secondary to the growing submucosal mass. This mass compromises the blood supply to the gastric mucosa, which then ulcerates secondary to ischemia or a reduced tolerance to the gastric acidity (4,8,9).

Although conventional radiographical procedures can demonstrate the presence or extent of invasion, they cannot provide enough information in the differential diagnosis (10). Similarly, our preliminary clinical impression was different from the actual diagnosis. Surgical resection is the treatment of choice and the prognosis is excellent because malignant transformation is rare (4).

Concordant with our provisional microscopic diagnosis of GIST without employing immunostaining, Fujii reported about 4% gastric schwannomas among 150 GISTs when subjected to IHC (11). Prevot and colleagues also reported three cases (1 male, 2 females; age range of 56–74 years) of gastric schwannomas in which the tumours were well circumscribed but not encapsulated and had sizes ranging from 2 to 11 cm in diameter. A diffuse and intense positivity for vimentin and S-100 protein was detected in all cases along with a variable, sometimes focal positivity for glial fibrillary acidic protein and neuron-specific enolase (4).

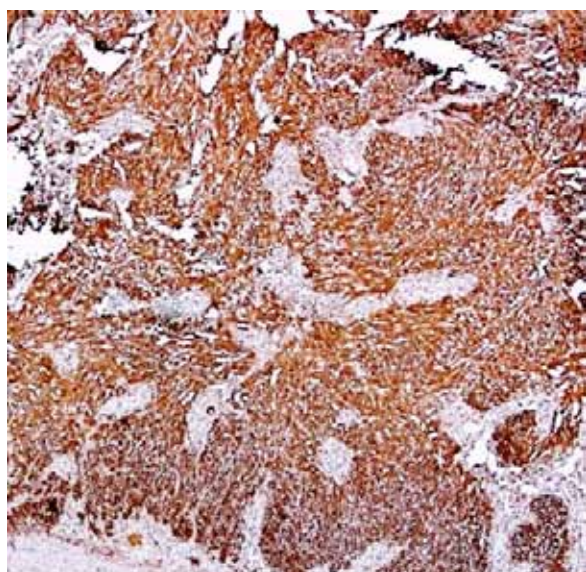


Figure 3: Immunohistochemistry shows the bundles of spindle cells that have a strong positivity for S-100 protein staining (brown colour) (S-100 stain, x200).

Conclusion

Gastric schwannomas, though rare among the spindle cell tumours of GIT, can occur even at a young age and should always be confirmed by IHC, especially to rule out GISTs. A retrospective or a prospective series of GISTs should be analysed using different immunohistochemical markers in our population.

Acknowledgement

The authors are extremely thankful to Professor A.H. Nagi, Head of Pathology Department, University of Health Sciences Lahore, Pakistan for his guidance and co-operation in carrying out the histopathological diagnosis of the case. Authors also acknowledge the support staff of Pathology and Surgery Departments of Sharif Medical and Dental College Lahore, Pakistan, for their assistance in compiling this case report.

Authors' contributions

Conception and design: TMT
Provision of study materials or patients: TMT, SA, HMH
Data collection, administrative, technical, or logistic support: HMH,
Data analysis and interpretation: TMT, SA
Drafting of the article: NN
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Case Report

Necrotizing Fasciitis of the Head and Neck: Surgical Outcomes in Three Cases

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Submitted: 23 Aug 2009
Accepted: 15 Jan 2010

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Abstract

Necrotizing fasciitis of the head and neck is a rare, rapidly progressive infection involving the skin, subcutaneous tissue and fascia. We report three cases of necrotizing fasciitis that differ in their presentation and outcome. The first case involves a patient who presented with progressively enlarging anterior neck swelling that was later complicated by dehydration and reduced consciousness. The second case is a patient with neck swelling and ipsilateral otorrhea. The third case concerns a patient with a buccal ulcer complicated by ipsilateral facial swelling. All of them underwent a fasciotomy with wound debridement with the addition of a cortical mastoidectomy in the second case. Two of these patients recovered well. Unfortunately, the third case succumbed to death due to airway compromise and septicaemia. We advocate the importance of eradicating the source of infection followed by frequent, meticulous wound dressing and strict blood sugar control to obtain better outcomes in managing necrotizing fasciitis of the head and neck. However, involvement of the airway carries a grave prognosis despite aggressive treatment.

Keywords: mastoidectomy, necrotizing fasciitis, otitis media, medical sciences

Introduction

Necrotizing fasciitis is an uncommon, life-threatening, single or polymicrobial infection of the soft tissue characterized by widespread necrosis of the skin, subcutaneous fat and fascia. It typically spares the overlying skin and muscle until late in the disease. It has been recognized for centuries with various names, but the current name 'necrotizing fasciitis' was first used by Wilson in 1952 (1,2). Necrotizing fasciitis commonly affects the abdominal wall, perineum and extremities (2). This disease rarely involves the head and neck region; and if it occurs, it is usually due to the spread of infection from the teeth or pharynx (3). The incidence of necrotizing fasciitis is 0.40 cases per 100,000 people (4). Diabetes mellitus is known to be one of the comorbidities in the progression of the disease. Necrotizing fasciitis of the head and neck has a particularly high mortality rate due to the proximity of many vital anatomical structures. Known complications of cervical necrotizing fasciitis include airway compromise, arterial and venous occlusion and the extension of infection into the mediastinal and pleural spaces (5). Because of its high mortality rate, prompt and aggressive management with immediate surgical

intervention is crucial. Management includes eradication of the source of infection, proper wound dressing, control of blood sugar, and broad spectrum antibiotic coverage. We report three cases of necrotizing fasciitis, which extensively involve the head and neck region with different sources of infection and outcomes.

Case Reports

Case 1

A 65-year-old female presented with a history of progressive neck swelling for one week and dysphagia for 3 days. She also developed recent dysphagia and vomiting. On examination, she was drowsy and dehydrated with poor oral hygiene and no evidence of respiratory compromise. There was necrotic skin on the anterior neck and cellulitis extending to the suprasternal notch. Her blood sugar was high with evidence of metabolic acidosis. She was resuscitated with intravenous fluids and an insulin infusion. Empirical broad spectrum antibiotics (amoxicillin clavulanate, cloxacillin and metronidazole) were started. Computerised tomography scan showed an extensive hypodense collection with air pockets

in the left parapharyngeal space, displacing the midline structures. Wound debridement and drainage were performed after stabilizing her medical condition. A *Klebsiella* species was isolated from the wound. Post-operatively, the wound was cleaned twice daily with hydrogen peroxide and povidone. The wound granulated well after two weeks, and she was discharged home. Subsequently, the wound healed by secondary intention.

Case 2

A 70-year-old Chinese male with underlying diabetes mellitus and hypertension presented with painful progressive left neck swelling for two weeks. The swelling was associated with dysphagia, left otalgia, otorrhea and fever. Clinical examination revealed left neck swelling, extending from the mastoid region (Figure 1). Otoscopy showed features of acute otitis media. His high blood sugar was corrected with insulin infusion. Intravenous ceftriazone and metronidazole were also started. A high resolution computerised tomography scan revealed multiple air pockets within the parotid and submandibular spaces extending medially into the parapharyngeal space and inferiorly along the fascial planes of the posterior triangle. There was also the presence of fluid within the mastoid air cells suggestive of mastoiditis (Figure 2). Cortical mastoidectomy with myringotomy and grommet insertion, including fasciotomy and debridement of the neck, were performed the next day (Figure 3). Intraoperative findings revealed necrotic tissue from the mastoid tip to the supraclavicular region, and the mastoid air cells were filled with granulation tissue. There was no breach of the mastoid cortex. Post-operatively, wound debridement and dressing were performed three times daily with hydrogen peroxide and povidone. *Enterobacter* and *Klebsiella* species were isolated. The wound healed by secondary intention after 10 days.

Case 3

A 70-year-old Chinese female presented with a three-day history of painful left facial and neck swelling associated with odynophagia. She had a recent hospital admission for uncontrolled diabetes mellitus. Examination revealed a dehydrated patient with an inflamed left hemifacial region extending to the submandibular region and crossing the midline. She also had trismus. Intraoral examination revealed a left buccal ulcer and dental carries affecting the left lower canine and premolars. Ultrasonography of the neck showed an ill-defined hypoechoic collection with



Figure 1: Necrotizing fasciitis involving the neck with post-auricular inflammation secondary to acute mastoiditis.



Figure 2: Computerised tomography scan of the temporal bone showing a soft tissue density within the left mastoid air cells suggestive of mastoiditis.

air pockets located at the left submandibular and submental regions. She was started on intravenous amoxicillin clavulanate and metronidazole. Wound debridement and fasciotomy were performed the following day. Extensive necrotic tissue extending to the zygoma, posterior triangle and clavicle was encountered. Swab culture and sensitivity isolated *Klebsiella* and *Candida* species. Post-operatively, she was haemodynamically unstable with signs of septic shock and was ventilated in the Intensive Care Unit. Despite aggressive wound debridement and dressing,



Figure 3: Cortical mastoidectomy performed concomitantly with fasciotomy.

the infection progressed to involve the larynx and mediastinum. Subsequently, she developed septicaemic multi-organ dysfunction. Family members were consulted regarding her poor prognosis, and they requested to bring her home. She then expired at home a few days later.

Discussion

Necrotizing fasciitis of the head and neck region is uncommon (2–3,6). In a large series of 128 cases of necrotizing fasciitis, only five of them involved the head and neck region (1). The severity of necrotizing fasciitis depends on the aetiology, anatomical site, depth of tissue involvement, bacteriology and general condition of the patient. Low immunity plays an important role in determining the initiation, progression and outcome of the disease. Diabetes mellitus is the most common comorbidity in this life-threatening disease. In our series, all patients were elderly and had a history of diabetes mellitus. Another study reported that 58.6% of 75 cases had underlying diabetes mellitus (1). Other risk factors include adrenal insufficiency, liver cirrhosis, cancer, drug abuse, peripheral vascular disease, chronic renal failure, chronic hepatitis and alcoholism (1).

All our patients presented with painful swelling of the head and neck region. Hsiao et al. reported that the most common symptoms were swelling and pain, which occurred in 71.1% and 54.7% of cases, respectively (1). Dysphagia and odynophagia are also common symptoms (6).

The most frequent source of infection for necrotizing fasciitis involving the head and neck region are the teeth or pharynx. Periapical infection of the second or third molar is the

usual culprit for cervicofacial infection. This is because the roots of these molars extend below the insertion of the mylohyoid muscle, which is connected to the submandibular space (7). Other sources include the ear, lymph node, cutaneous infection or extension of infection from adjacent structures.

Once the infection has involved the soft tissues, the spread of the disease subsequently follows the fascial planes. The greatest clinical importance of the cervical fascia is that it divides the neck into potential spaces and involves a number of adjoining areas. Although this infection primarily involves the superficial space, other fascial spaces may be involved depending on the stage of the disease and the portal of entry. The parapharyngeal space communicates with all the major fascial spaces. Thus, it may be involved with infection via direct spread from another space or vice versa. Any delay in the treatment of necrotizing fasciitis of the parapharyngeal spaces will expedite the spread of infection to dangerous spaces and subsequently to the mediastinum inferiorly, causing potentially lethal mediastinitis.

In this series, we postulate that the source of infection for the first and third cases were of dental or oropharynx origin. In the first case, the infection involved the superficial fascial plane and spread into the parapharyngeal space. In the third case, we postulate that the source of infection was the left buccal ulcer and dental carries. Submandibular space infections spread readily beneath the anterior belly of the digastric muscles to involve the adjacent spaces, such as the sublingual, lateral pharyngeal or retropharyngeal space. An infection involving the lateral pharyngeal space may extend into the mediastinum along the carotid sheath or through the risky space. This observation emphasizes the clinical importance of the aggressive nature of the infection in necrotizing fasciitis if it is not treated early.

On the other hand, Chua et al. reported the only other case in the literature of cervical necrotizing fasciitis secondary to a mastoid infection (8). However, in our second case, there was no evidence of a subperiosteal abscess unlike in Chua et al. Therefore, we postulate that necrotizing fasciitis in the neck may be secondary to postauricular lymphadenitis.

Computed tomography is useful in the diagnosis of necrotizing fasciitis. It can detect air pockets, which are difficult to see on plain radiographs, and determine the extent of the infection prior to surgery (7). Although beta haemolytic *Streptococcus* is the most common causative organism, polymicrobial (mixed aerobic

and anaerobic) infections also play an important role in spreading the disease (9). The pathogenesis of the aggressive disease is believed to be due to necrosis and separation of the dermal collagen by mucopeptides, which are present in the bacterial cell wall. There is a synergistic effect between the aerobes and anaerobes in the spread of infection. The aerobes provide a favourable environment for anaerobes through oxygen removal (7). On the other hand, the metabolic substance produced by anaerobes is able to enhance the virulence of the aerobes. However, a single pathogen infection by *Klebsiella* has also been reported (10). Empirical broad spectrum antibiotics should be started without delay while awaiting surgery. This is because most patients require further stabilization before debridement under general anaesthesia.

Early aggressive surgical intervention with eradication of the source of infection is important to achieve good prognosis as demonstrated in our first and second cases. In addition, we also advocate regular and frequent debridement with appropriate wound dressing for better outcomes. Povidone appears to have broad spectrum activity against bacteria and is a common ingredient in topical disinfectants. Hydrogen peroxide is a weak acid with strong oxidizing properties, which can also be used as a disinfectant. We found that this dressing combination allowed adequate wound desloughing in the ward. However, in the third case, this method was unsuccessful because the infection continued to spread to the larynx, leading to mediastinitis, and the patient succumbed to death. Involvement of the larynx and mediastinum carries a higher mortality rate. Those who survive experience prolonged wound healing (6). Death is most often secondary to sepsis, multi-organ failure or respiratory failure (3,6,7).

Hsiao et al. reported five factors that contribute to high mortality, including *Aeromonas* infection, *Vibrio* infection, cancer, hypotension and a white blood count greater than 10% (1). In our case series, we postulate that airway involvement is another predictor of mortality.

Conclusion

Early diagnosis with aggressive surgical intervention, eradication of the source of infection, control of blood sugar, broad spectrum antibiotic coverage and appropriate wound dressing are crucial in achieving a favourable outcome for this fatal disease. Mastoidectomy must be performed concomitantly with fasciotomy if there is evidence of mastoiditis either clinically or radiologically. Involvement of the airway may be associated with poor prognosis.

Authors' contributions

Conception and design: PPSHA
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Case Report

Bilateral Vocal Cord Palsy as the Sole Presentation of Acquired Syphilis

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Abstract

Bilateral vocal cord palsy is almost always caused by neck surgery, particularly surgery of the thyroid. We report a case of bilateral vocal cord palsy requiring emergency surgery to relieve the airway obstruction as the sole presentation of acquired syphilis. As the incidence of syphilis worldwide is rising, this unusual presentation may give clinicians a different perspective on the disease.

Keywords: bilateral vocal cord palsy, syphilis, medical sciences

Introduction

Syphilis is a rare cause of vocal cord palsy. Syphilis manifestation is usually multisystemic, and a sole presentation of syphilis in the larynx is very rare. However, with the growing incidence of syphilis throughout the world, we may be facing more unusual presentations of syphilis. Syphilis is often said to be a great imitator, and Sir William Osler was quoted as saying "He who knows syphilis knows medicine".

Case report

A 45-year-old Malay lady presented with noisy breathing for the past year. The condition was progressively worsening, and at the time of presentation, she had marked stridor that could be heard from the edge of her bed. Her general practitioner had previously diagnosed her with asthma and given her inhalers, but her symptoms did not improve. Over the past month, her voice had become huskier and easily fatigued. She denied any symptoms of aspiration, dysphagia, neck swelling, weight loss, headache or other central neurological symptoms. She did not have any previous neck surgery. Her first husband died ten years ago from pulmonary tuberculosis, and she had since remarried. Her current husband practices polygamy, and she is the second wife of three. They live in a small town bordering Thailand.

She had loud biphasic stridor at rest and was unable to count from one to ten in a single

breath. Her stridor was more marked in the supine position, and she quickly became dyspneic when lying flat. A lung examination revealed no abnormality. Indirect laryngoscopy followed by 70° laryngoscopy showed that both vocal cords were immobilised in a paramedian position, with very little airway patency.

Due to the pending airway obstruction, we proceeded with emergency tracheostomy under local anaesthesia. After securing the airway, we performed a microscopic laryngeal inspection and palpation under general anaesthesia, which revealed bilateral fixed vocal cords in a paramedian position that did not move on palpation. There were areas of granuloma on both sides of posterior vocal cord, more notably on the left side (Figure 1). A biopsy was taken from the vocal cord lesion, and the histology showed the presence of foreign body-type giant cell granulomatous laryngitis (Figure 2). This raised the possibility of several differential diagnoses, with tuberculosis high on the list, given the history of previous contact. However, both Ziehl-Neelsen (ZN) and TB fluorescent stains and the specimen culture were negative. Blood investigations later confirmed the presence of *Treponema pallidum* antibody in the serum and a positive VDRL (Venereal Disease Research Laboratory) test with a titre of 1:128. Other investigations, including sputum for acid fast bacilli (AFB) and rapid HIV ELISA test, were negative. Computerised tomography of the brain to chest revealed no abnormal findings. A cerebrospinal fluid (CSF) analysis for neurosyphilis was not performed, as the patient did not permit it.

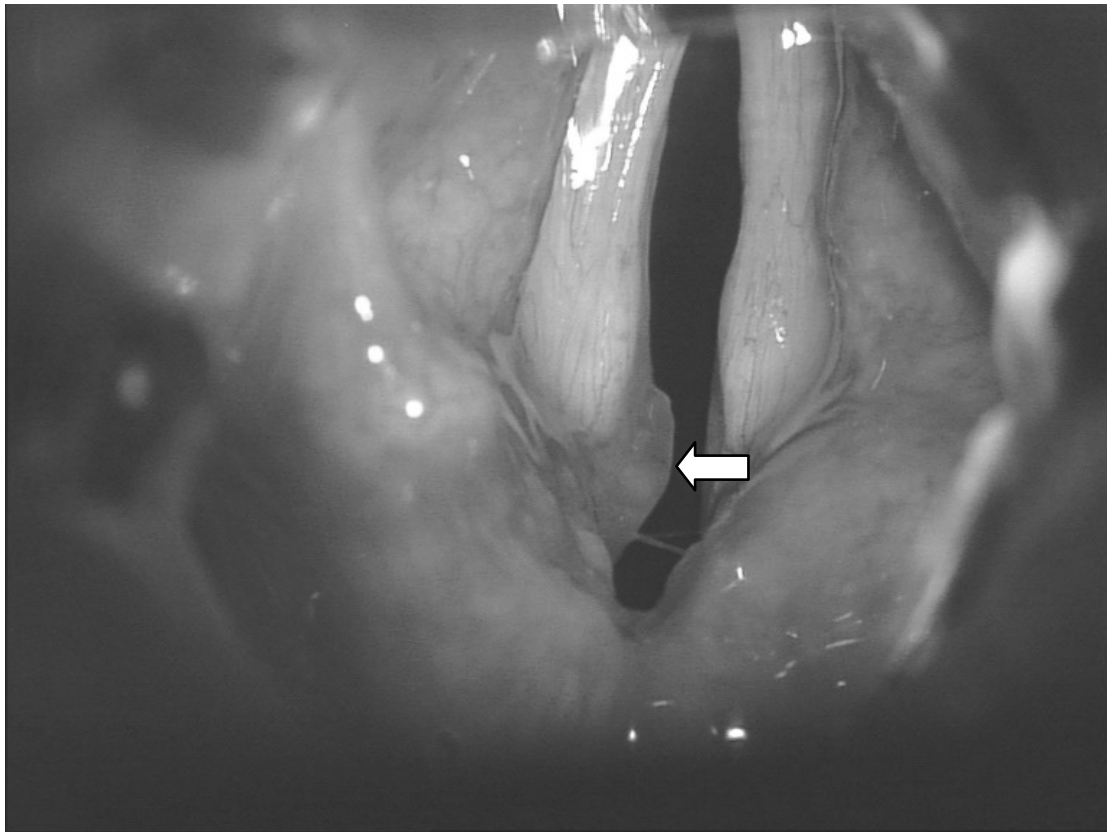


Figure 1: Both vocal cords were in a paramedian position on inspiration and fixed on palpation. There were areas of granuloma on both sides of the posterior vocal cord, more notably on the left side (white arrow).

Laser posterior cordectomy of the left vocal cord was performed after the airway was secured with a tracheostomy. This procedure was performed because the larynx was in a severely fixed position and the patient had earlier expressed the desire to avoid a long-term tracheostomy. The patient was also started on intramuscular procaine penicillin, 2.4 million units daily for 14 days. Following the diagnosis of acquired syphilis, we performed a thorough physical examination to look for other syphilis manifestations; none was found. The patient's husband was screened and also found to be infected with syphilis.

The patient was given a post-operative course of steroids, and tracheostomy decannulation was completed four days post-operation. She was discharged five days post-operatively. Her stridor disappeared after six weeks, although vocal huskiness was still noted. She completed the 14-day course of antibiotics, and a follow-up VDRL test nine months later was seronegative. The final diagnosis was bilateral vocal cord fixation secondary to a tertiary gummatous laryngeal syphilis.

Discussion

Syphilis is a sexually transmitted infection caused by the bacterium *T. pallidum*. In this millennium, the largest numbers of new syphilis infections have occurred in South Asia and Southeast Asia, followed by sub-Saharan Africa, and then Latin America and the Caribbean (1). However, recent data have shown that the incidence of syphilis in the Western world is also on the rise again in this new millennium, after periods of decline in the post-penicillin era of the last millennium (2,3).

Thyroid or parathyroid surgery, which is often performed on both sides of the neck, can injure both recurrent laryngeal nerves and is by far the most common cause of bilateral vocal cord palsy (4). Granulomatous infections, such as tuberculosis and syphilis, can cause unilateral or bilateral palsy, but these account for less than 1% of the total causes (4). A search in PubMed and Scopus for the words "syphilis" and "larynx" yields fewer than 50 publications, and the majority of these were published in the last millennium.

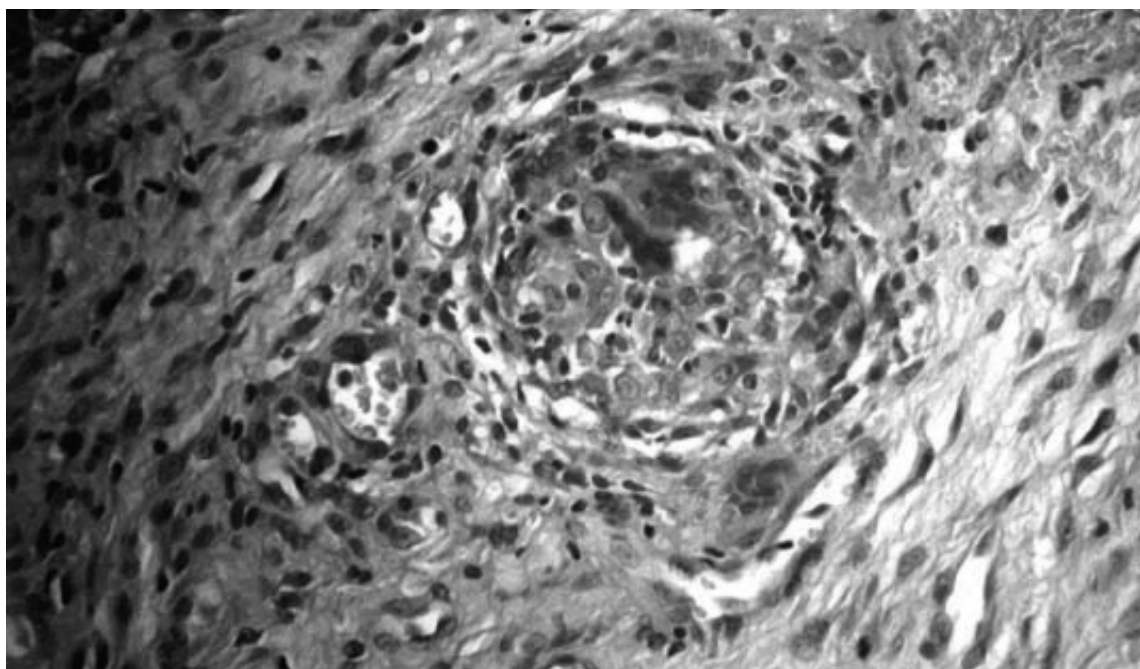


Figure 2: Histology of the laryngeal biopsy (4X magnification)

Syphilis usually has multisystemic manifestations, and it very rarely affects only one system. The interesting feature of this case is that the patient presented with lesions exclusively confined to the larynx. A case of syphilis exclusively presented in the larynx was described in 1917, before the antibiotic era, when the worldwide incidence of syphilis was epidemic (5). Head and neck presentation can be categorised according to the stage of infection. Chancre of the oral and nasal mucosa, nasal septum perforation, and cervical lymphadenopathy are the primary syphilis manifestations (6). Secondary syphilis may also present with mucous lesions and lymphadenopathy and with alopecia, meningitis, headache and ocular lesions (6). Tertiary syphilis can be further divided into cardiovascular syphilis, neurosyphilis and late benign stage (gumma). Neurosyphilis patients may present with headache, vertigo, dementia, delusions, confusions, and cranial nerve palsies (7). Gummatous lesions are monocytic infiltrates with tissue destruction in any organ. In this case, the vocal cord palsy was most likely due to the gummatous lesions on the vocal cords, which fixed both sides in the paramedian plane. However, as we did not do the CSF culture, we could not rule out the concurrent possibility of neurosyphilis causing bilateral recurrent laryngeal nerve paralysis.

Performing routine investigations for granulomatous infections may not be cost-effective in all cases of vocal cord palsy. However, clinicians should remember to do them when the patient's history and clinical examinations indicate their necessity. Medical history interviews should always include questions about contact with people with tuberculosis, syphilis or other granulomatous diseases and include a thorough sexual contact history. Blood examinations for syphilis should be done in all cases without an obvious cause of palsy, in those patients with a history of recent travelling to the endemic countries, in patients with low immunity status, abnormal sexual behaviour or sexual promiscuity and in patients with multiple sexual partners. In our case, we ordered tests to rule out tuberculosis, as it was initially the suspected diagnosis given that the patient's first husband had the disease. These tests included sputum for AFB and ZN and fluorescent stain microscopy on the laryngeal specimens. However, all these tests were negative.

Medical management consisted of a course of penicillin, with the duration of therapy dependent on the severity and stage of the disease. Because neurosyphilis was not ruled out, we followed the Center for Disease Control, USA (CDC) recommendation for neurosyphilis treatment in this patient. Medical management to improve the airway may delay or prevent surgical intervention, and in many centres, a wait-and-see period of six months to a year is usually practiced if the

patient is not in respiratory distress (8). In our case, however, the patient presented with acute airway obstruction, and medical therapy alone could not provide relief. Hence, a tracheostomy was performed to secure the obstructed airway. After we secured the airway with tracheostomy, we needed to choose the best treatment for the underlying cause of the vocal cord palsy. Because the cause in this case was syphilitic infection, the best treatment had to be an antibiotic. A wait-and-see period of three to six months in this kind of case is advocated by many centres to determine how the patient responds to the treatment (8). Surgical repair of the vocal cord can be avoided in most cases if the mechanical obstruction is cleared with antibiotics. In our patient, however, we opted to perform an immediate surgical intervention because the vocal cord damage caused by the disease was so severe that we did not think antibiotics would totally resolve it. More importantly, our patient wished to avoid long-term tracheostomy, so we decided that a cordectomy was the best choice.

Vocal cord surgery options include lateralisation procedures, such as posterior cordectomy, arytenoidectomy or arytenoidopexy. Dennis and Kashima first introduced a posterior partial cordectomy procedure using a carbon dioxide laser (9). This involves excising a C-shaped wedge from the posterior edge of one vocal cord to open up the airway. If this posterior opening is not adequate after six to eight weeks, the procedure can be repeated, or the same procedure can be performed on the other vocal cord. All of their patients achieved a functional airway and preserved voice quality without a tracheostomy, the same outcome that our patient experienced.

Conclusion

Laryngeal involvement is a rare manifestation of syphilis. However, this case shows that acquired syphilis may present solely in the larynx. As the incidence of syphilis worldwide is increasing again in this millennium, clinicians must be aware of uncommon presentations to ensure an accurate diagnosis.

Acknowledgements

We would like to thank the director of Hospital Tengku Ampuan Afzan, Kuantan, Pahang, Malaysia and the director general of health, Ministry of Health Malaysia, for permission to report this case. Written informed consent was obtained from the patient for the publication of this case report and the accompanying images.

Authors' contributions

ZAA was responsible for the overall management of this case and for preparing the manuscript. MSR performed the posterior cordectomy under the supervision of senior surgeon RARLA. All authors contributed to writing this case and have read and approved the final manuscript.

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Case Report

Ketamine-Associated Ulcerative Cystitis: A Case Report and Literature Review

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Submitted: 23 Sep 2009

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Abstract

Ketamine can be abused as a recreational drug, and there has been a recent surge in its usage. The effects of ketamine on the urinary system were unknown until the recent publication of a few case reports. Many doctors are still unaware of this new clinical entity, termed ketamine-associated ulcerative cystitis. We report a case that we encountered and discuss the diagnosis and disease management in addition to a review of the literature.

Keywords: cystitis, hydronephrosis, ketamine, medical sciences

Introduction

Ketamine, an anaesthetic drug, has been abused as a recreational drug since the 1980s. Lately, since 2007, there have been reports of urinary system complications arising from the chronic abuse of ketamine. This new clinical entity, termed ketamine-associated ulcerative cystitis, is characterised by symptoms of lower urinary tract irritation related to ketamine use among young people. It is relatively under-diagnosed because many medical professionals are still unaware of this disease. Here, we report a case of ketamine-associated ulcerative cystitis to highlight the diagnosis, pathology and management of this new clinical entity for clinicians who may increasingly encounter this disease in their practice.

Case report

A 21-year-old man presented with a nine-month history of frequent urination, nocturia and suprapubic pain. There was no history of dysuria or fever. Upon further questioning, he admitted that the onset of his symptoms was approximately concurrent with his beginning to use the recreational drug ketamine. He indicated that the drug was taken in white powder form, snorted about twice a week.

Urine analysis showed microscopic haematuria (10 red blood cells per high powered field). His serum urea level was 3.9 mmol/L, and his creatinine level was 79 µmol/L. The acid fast bacilli (AFB) stain for urine was negative. No *Mycobacterium tuberculosis* was isolated from the urine after 6 weeks of culture. Urine culture also did not grow any other organism.

Initial urinary system ultrasonography showed a small, shrunken right kidney with dilated pelvicalyceal system and distal ureter. This was accompanied by compensatory left kidney hypertrophy and moderate hydronephrosis. The bladder was small in capacity with irregular wall thickening, especially in the right lateral wall. Intravenous pyelography (IVP) showed left hydronephrosis and hydroureter with a non-excreting right kidney (Figure 1a). In the post-voiding pyelogram (Figure 1b), a right vesico-ureteric reflux (VUR) and gross dilation of the right ureter was seen. The left collecting system is still visualised in the post-voiding pyelogram due to vesico-ureteric reflux.

A diethylenetriamine pentaacetate (DTPA) scan showed that the right kidney was non-functioning with severe vesico-ureteric reflux; the left kidney had good function and was not obstructed. The normalised Gate's glomerular filtration rate was 99 mL/min/1.73 m². Although the right kidney was non-functioning, the



Figure 1a: Intravenous pyelogram showing moderate left hydronephrosis and hydroureter with a non-excreting right kidney



Figure 1b: Post-voiding pyelogram showing right vesico-ureteric reflux (VUR) with gross dilatation of right ureter

left kidney was not obstructed despite the hydronephrosis, and the renal function was normal. Therefore, ureteric stenting was not performed.

Cystoscopy showed inflamed bladder mucosa with superficial ulcers. Bladder biopsies (Figure 2) revealed urothelial epithelium with nodular proliferation in the lamina propria. The cells lining the cyst were characteristic of multilayered urothelial epithelium. Dense neutrophil infiltration was seen within the epithelium and lamina propria. Some of the fragments were composed of granulation tissue with eosinophil infiltration (Figure 3). No granuloma, dysplasia or malignancy was seen. On the whole, the biopsies showed changes consistent with severe cystitis with a proliferation of von Brunn's nests.

After cessation of ketamine and a course of antibiotic for a week, the patient noted that his haematuria and lower urinary tract symptoms had resolved. At three months of follow up, he was asymptomatic, and his renal profile remained normal. He declined further imaging of his urinary system.

Discussion

Ketamine is a derivative of phencyclidine and has been used to induce and maintain general anaesthesia for more than 30 years. Unfortunately, since the 1980s, this drug has been abused as a recreational drug in nightclubs. Its popularity has increased tremendously because

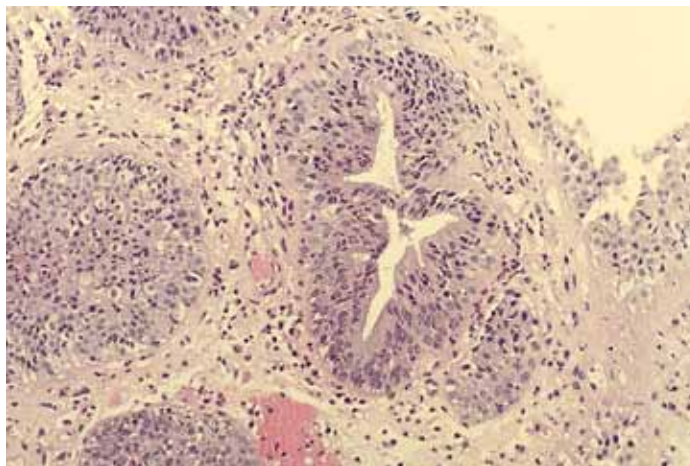


Figure 2: Bladder mucosa biopsy showing tissue lined by urothelial epithelium with nodular proliferation in the lamina propria. Dense neutrophil infiltration also seen. (H&E stain, 100x)

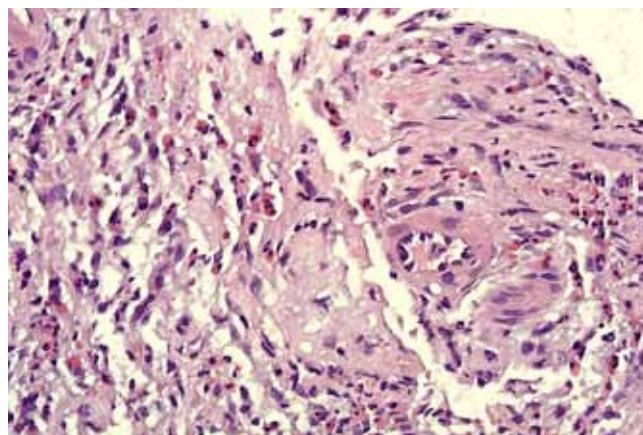


Figure 3: Biopsy of ulcerated bladder mucosa showing eosinophil infiltration. (H&E stain 200x)

it has been erroneously believed to be safer than other recreational drugs. It is available in white powder, tablet or capsule form. When inhaled through the nostril, its effects appear after about ten minutes. When taken orally, its effects appear after about 20 minutes. The psychedelic experience ('trip') includes the sensation of light throughout the body, the sensation of being weightless and floating or hovering, colourful visions and out-of body experiences. The bulk of the 'trip' lasts about an hour and the effects diminish gradually over another hour (1). This is the experience that addicts crave. However, many recreational users are unaware of the detrimental effects of ketamine on the central nervous system, respiratory and cardiovascular systems.

Recently, there have been reports of unwanted effects of ketamine on the genitourinary system. This new clinical entity has been termed ketamine-associated ulcerative cystitis (2). It is characterised by lower urinary tract symptoms related to ketamine use among young adults. It was first identified in 2007; because then, case reports and series have been published from Canada, Belgium, Hong Kong and Taiwan (2–5). Currently, little is known about this disease entity.

The common presentations of lower urinary tract symptoms include dysuria, frequency, urgency, urge incontinence and painful haematuria. Cystoscopic findings include inflammatory changes, neovascularisation, ulceration and small, contracted bladder. Complications include renal impairment with raised serum urea and creatinine levels. Radiological investigations may show unilateral or bilateral hydronephrosis and hydroureter.

The pathophysiology involved in the damage inflicted by ketamine on the urinary system is not well understood, but several possible mechanisms of injury have been proposed. One is the direct toxic effect of ketamine and its metabolites on the interstitial cells of the bladder. Ketamine may also have direct toxic effects on papillary medullary interstitial cells, causing papillary necrosis with interstitial fibrosis and structural damage that will result in renal impairment. The second proposed mechanism involves microvascular changes in the bladder and kidney causing endothelial cell injury of microvessels. This may lead to either compromised intrinsic microcirculation or decreased microvascular density in the subendothelium. The cystoscopic findings of neovascularisation support this hypothesis. Furthermore, the observed suprapubic pain could be attributed to bladder ischemia during bladder filling. The third hypothesis involves an autoimmune reaction of the bladder urothelium

and submucosa triggered by urinary ketamine or ketamine metabolites. This reaction could result in autoimmune-mediated vascular congestion, submucosal oedema and scarring, leading to diminished bladder capacity and poor compliance (6).

The hydronephrosis and hydroureter seen in radiological images could be the result of a long-term decrease in bladder compliance and vesico-ureteric reflux. Moreover, papillary necrosis and the resultant migration of the sloughed papilla into the ureters can cause complete ureteric obstruction. Another proposed mechanism for ureteric obstruction is the immunological mediated fibrosis and stricture of the ureters, which may lead to obstructive uropathy (6). Biopsies are non-specific, showing features of chronic cystitis. Histology reveals infiltrations of granulocytes (mostly eosinophils) and mast cells within the bladder tissue (6).

In our patient, the non-obstructive left hydronephrosis and hydroureter is most likely due to vesico-ureteric reflux as a result of decreased bladder compliance. Severe vesico-ureteric reflux on the right could have damaged the right kidney, causing it to be non-functional. The left collecting system was non-obstructed despite hydronephrosis and hydroureter and was able to compensate for the non-functioning right kidney. Therefore, serum urea and creatinine levels remained normal.

The treatment of ketamine-associated ulcerative cystitis depends on the severity of the disease. In mild cases, cessation of ketamine use is sufficient for the return of normal bladder activity. In patients with obstructive hydronephrosis, early stenting or nephrostomy would be able to preserve renal function before irreversible damage occurs. In patients with markedly diminished bladder capacity due to bladder fibrosis and contracture, an augmentation or substitution cystoplasty may be indicated. Pentosan polysulphate (2) and intravesical instillation of hyaluronan solution (7) has also been shown to significantly reduce irritative voiding symptoms.

In conclusion, ketamine induced ulcerative cystitis is an emerging disease that is threatening to become a major burden on our healthcare system due to the increasing abuse of ketamine as a recreational drug and its therapeutic use in hospice care to palliate complex pain, in addition to its current usage as an anaesthetic drug. Healthcare workers should be alert to this possible diagnosis when seeing young patients with lower urinary tract symptoms in the absence of a urinary tract infection. A thorough history of ketamine use should be obtained. The mainstay of treatment involves cessation of ketamine usage.

Authors' contributions

Conception and design: CCKH
Drafting the article: CCKH, HP
Critical revision of the article, final approval of the article: SP, EHG, BCL, MZZ
Provision of study materials or patients: CCKH, HP

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Antibody mediated immunity — a missed opportunity in the fight against tuberculosis?

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Dear Editor,

Tuberculosis is one of the leading causes of mortality produced by a single infectious agent. Each year 8 million new cases and between 2 to 3 million deaths are reported. One-third of the human population is already infected with *Mycobacterium tuberculosis* — the causative agent of tuberculosis. The disease is increasing at a worrying rate primarily due to the absence of an effective vaccine, the emergence of multi-drug resistant strains, as well as co-infection with HIV; coupled with the low diagnostic and therapeutic coverage in many developing countries.

The role of cell-mediated immunity against mycobacteria, and in particular, *M. tuberculosis* has been fully established. Up to now all the efforts for the development of new or improved vaccines against tuberculosis have been directed toward the induction of an effective cell-mediated immune response. However, the potential role of antibodies for protection against *M. tuberculosis* infection have been underestimated on the assumption that they have limited effect, if any, against intracellular pathogens.

M. tuberculosis gains access to the host through the mucosa of lung alveoli, thus the presence of specific antibodies in mucosal secretions could inhibit bacterial colonization. In fact, our group has demonstrated the protective capacity of secretory IgA monoclonal antibodies directed against *M. tuberculosis* antigens as well as formulations of human gammaglobulins against models of infection with BCG and *M. tuberculosis* in mice (1,2,3). Similar results have been obtained with human secretory IgA in the same animal model (unpublished observations). Using different animal models and antibody formulations, other groups have reported the protective role of antibodies in *M. tuberculosis* infection (4).

Potential mechanisms by which antibodies could modify the outcome of mycobacterial infection could be mediated by interference with adhesion, toxin neutralization, opsonization, activation of complement, increase in cytokine

expression, enhancement of phagosome-lysosome fusion, and enhancement of antigen presentation among others (5).

Future applications of antibody formulations for the control of tuberculosis may include: treatment of patients infected with multidrug resistant strains, combination with the standard treatment in order to achieve shorter therapeutic regimes, and administration to recent contacts of tuberculosis patients and risk groups. Since BCG, the current vaccine against tuberculosis is only protective in the severe forms of the infection in childhood and is not protective against the pulmonary disease in adults — the most common form of the disease. Hence the development of new tuberculosis vaccines is urgently required (6).

The induction of specific antibody responses by vaccination in addition to the stimulation of cell-mediated immunity could be a novel strategy for the development of new generation prophylactic and therapeutic vaccines against tuberculosis. Taking into consideration this possibility, our group has been working on recombinant BCG strains expressing T and B epitopes of *M. tuberculosis*, with some encouraging results with respect to immunogenicity and protection in mice (unpublished results).

Accumulated reports in favour of the protective role of specific antibodies in tuberculosis provide us with potential improvements in prophylactic, therapeutic, and diagnostic methods to enhance future control measures against the disease.

Acknowledgements

Some of the results presented were kindly supported by MOSTI Grant No: 07-01-05-MEB007

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