Case Report

Breast Carcinoma Occurring from Chronic Granulomatous Mastitis

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Abstract

Chronic granulomatous mastitis is known as a benign and relatively rare disorder that is often difficult to differentiate from breast carcinoma. We highlight the case of a 34-year-old woman who had recurrent episodes of right breast swelling and abscess for 8 years. These were proven to be chronic granulomatous mastitis by tissue biopsies on 3 different occasions. Her condition improved on similar courses of antibiotics and high-dose prednisolone. However, she subsequently developed progressive loss of vision due to an orbital tumour. She then underwent a craniotomy and left orbital decompression with excision of the tumour, which proved to be a metastatic carcinoma. A trucut biopsy of the right breast was then done and showed features consistent with an infiltrating ductal carcinoma. This case illustrates the possibility that chronic granulomatous mastitis could be a precursor for malignancy and the difficulty in differentiating one from the other. The possible mechanisms of development and the implications for future management are also discussed.

Keywords: *breast, carcinoma, disease progression, granulomatous mastitis, surgery*

Introduction

Chronic granulomatous mastitis (CGM) is a relatively rare and benign chronic condition of unknown aetiology, with several cases reported in the literature. It occurs in women of child bearing age and is not associated with the classical risk factors of malignancy such as smoking, hormonal therapy, or family history. Clinically, the condition can present as an abscess or can mimic breast cancer and therefore is often difficult to differentiate from breast carcinoma. The diagnosis is by exclusion and is best made by tissue histology. Radiological modalities commonly used to diagnose other pathologies of the breasts, such as ultrasonography and mammography, have not been successful in diagnosing CGM (1). The management of the disease consists of high-dose, short-term steroid treatment, either with or without surgery. However, recurrence rates are as high as 50% (2). This is a report of a case in which recurrent chronic granulomatous mastitis subsequently presented with an infiltrating breast carcinoma. This complex progression illustrates the difficulty in diagnosing and managing the disease.

Case Report

A 34-year-old pre-menopausal woman presented 8 years previously with a right breast abscess that was treated with an incisional drainage and a course of antibiotics. The first biopsy done had shown fragments of breast tissue heavily infiltrated by chronic and acute inflammatory cells with several collections of epithelioid cells indicative of CGM. The patient was subsequently treated with a 3-week tapering course of high-dose prednisolone and recovered well. However, she developed another 3 recurrences over the next 8 years, which were also treated with incision and drainage along with similar courses of antibiotics and prednisolone. Two repeat biopsies taken during these recurrences were similar to the initial results of CGM (Figure 1). The patient did not report any history of fungal infections or tuberculosis exposure and had no previous history of breast disease or any other medical illnesses. She also has no history of breast cancer in her family, is a non-smoker, and was never on any hormonal contraception.

In between these recurrences of CGM, she was regularly followed up in our clinics

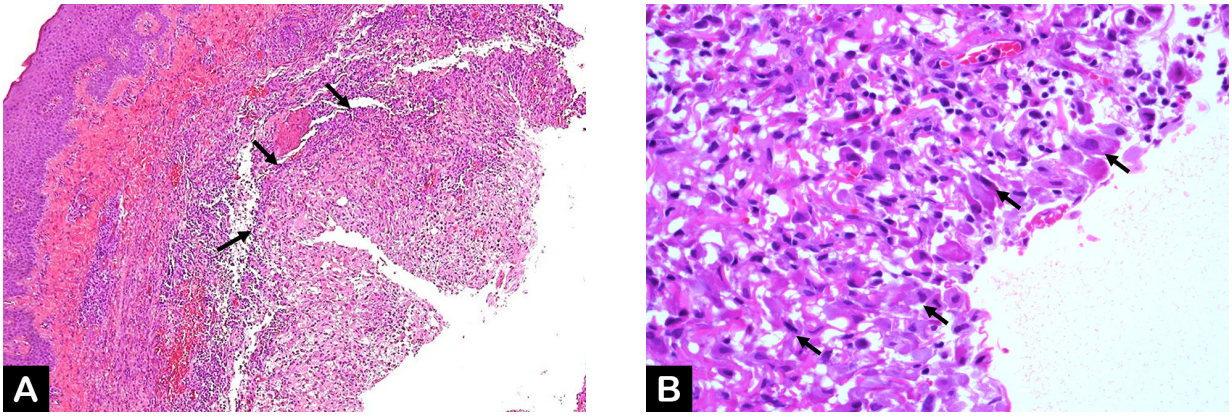

Figure 1: Breast tissue showing chronic granulomatous mastitis. (A) Vague granuloma formation (arrow) composed of epithelioid cells at the centre and lymphocytes at the periphery. No central necrosis or multinucleated giant cell is apparent (haematoxylin and eosin staining, 40× magnification). (B) The epithelioid cells (arrow) have abundant eosinophilic cytoplasm (haematoxylin and eosin staining, 400× magnification).

with routine physical and ultrasonographic examinations. These were unremarkable except for the presence of extensive fibrous scarring due to the repeated surgeries and inflammation. She was last seen and examined 2 months prior to her latest presentation. At the time, she was on another tapering course of prednisolone and was clinically asymptomatic.

Subsequently, the patient presented with a progressive loss of vision of the left eye. This was associated with intermittent headaches, anorexia, and a significant loss of weight. Magnetic resonance imaging (MRI) showed the presence of a left orbital apex tumour compressing the optic nerve (Figure 2). The patient then underwent a craniotomy and left orbital decompression with excision of the tumour. Biopsy results revealed metastatic carcinoma. In the search for a primary tumour, an MRI of the breasts showed extensive scarring of the right breast that looked suspicious of malignancy. A trucut biopsy of the right breast was then performed and revealed infiltration of malignant cells arranged in a vague tubular pattern and cords displaying large hyperchromatic nuclei with prominent nucleoli. These were indicative of the presence of an infiltrative ductal carcinoma of the right breast (Figure 3). The tumour was estrogen and progesterone receptor positive and c-erb negative (++). Staging radiological investigations then showed multiple bony metastases to the vertebrae with no evidence of hepatic or pulmonary spread.

The patient was then referred for palliative chemotherapy, but she declined treatment or any follow up and subsequently expired after 6 months.

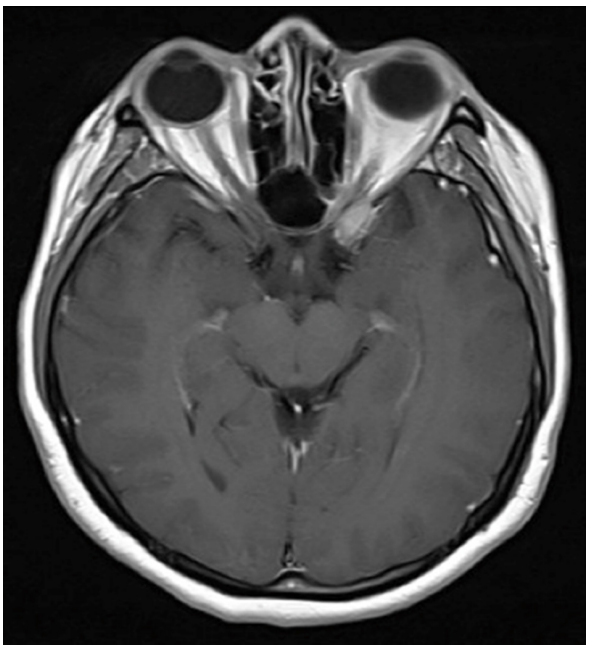

Figure 2: Gadolinium-enhanced T2-weighted magnetic resonance image showing a soft tissue lesion at the left orbital apex involving the intracallicular portion of the left optic nerve.

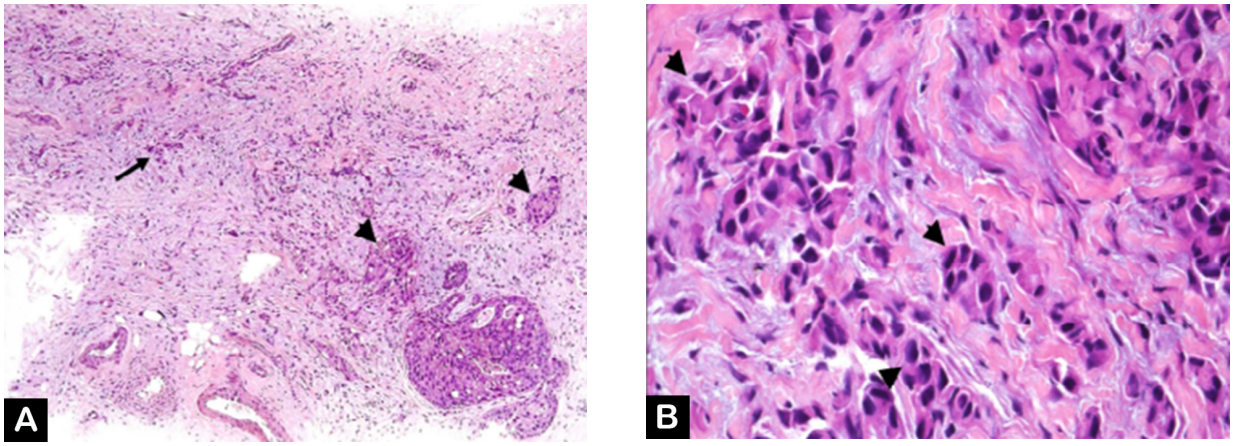

Figure 3: Infiltrating ductal carcinoma in breast biopsies. (A) Infiltration of malignant cells arranged in cords (arrow) and groups (arrow head) (haematoxylin and eosin staining, 40× magnification). (B) The groups of malignant cells (arrow head) display hyperchromatic nuclei with moderate amount of cytoplasm (haematoxylin and eosin staining, 400× magnification).

Discussion

CGM was first described by Kessler and Wolloch in 1972 (2) as a benign and rare disorder. To date, less than 150 cases have been reported. A significant number of these reports have addressed the issue of the diagnostic difficulties faced in confirming CGM. Researchers have suggested that the diagnosis of CGM is a diagnosis of exclusion and that CGM can mimic breast carcinoma (3,4). With the exception of a case by Handley in 1938 (5), no reported cases have suggested the possibility of an association between CGM and malignancy.

It is well accepted that the risk factors of developing breast cancer can be broadly divided into hormonal and non-hormonal factors. The former involve estrogen, and the latter include radiation exposure as well as the inheritance of the germline mutations BRCA-1 and BRCA-2. A literature search of infections associated with breast cancer has revealed only cross-species infection by the mouse mammary tumour virus initiating pathogenesis of breast cancer, although research establishing this connection remains preliminary (6). As mentioned earlier, chronic granulomatous inflammation by any cause has not been shown to lead to malignancy of the breast.

The theory that chronic inflammation leads to cancer is well documented (7). It is postulated that in response to infection from an offending microorganism, the host's defence mechanisms produce free radicals, which lead to DNA damage through oxidative processes and nitration of DNA bases. This could eventually lead to cell dysplasia and, subsequently, the development of cancer. It has been reported that nearly 15% of worldwide cancer is associated with microbial infection (8); however, breast cancer is not associated with such infections.

There are several indications that our patient initially had CGM, and this could have led to breast carcinoma rather than a missed diagnosis. First, 2 different histopathology biopsies taken approximately 3 years apart after the initial histopathological diagnosis of CGM indicated the presence of foamy macrophages and multinucleated giant cells forming granulomas and microabscesses, confirming the initial diagnosis. Second, the patient responded to steroid therapy after every recurrence and had periods in which she was completely asymptomatic. Finally, the long nature of the disease beginning from the first presentation to the diagnosis of malignancy, a total of 8 years, makes it unlikely she had breast cancer from the beginning.

The difficulty in differentiating breast carcinoma and CGM as well as the possibility that CGM could have led to cancer in our patient prompts us to raise the question of whether current management with regard to monitoring and surgical therapy is adequate and appropriate. Current practice indicates that following careful confirmation of the diagnosis of CGM, the initial treatment should be non-operative and that in patients with more severe symptoms, a course of prednisolone may be started. In more persistent cases, either further immunosuppressive therapies like methotrexate or azathioprine may be used or the patient may be offered surgical management,

such as a wide surgical excision or a mastectomy. In a previous report (9), only 3 recurrences were noted in 18 cases diagnosed with CGM, suggesting that surgical excision has a higher success rate. Whether a more radical surgery is needed will remain a matter of debate, unless it can be proven that CGM can lead to cancer.

The patient in this case was regularly followed up in 4 to 6 month intervals by ultrasound and clinical examination, as is standard for a patient in her mid-30s. The affected breast was extensively scarred, rendering clinical examination and ultrasound findings less sensitive. In retrospect, annually imaging the patient with MRI would have helped in identifying malignancy at an earlier stage because extensive fibrous scarring would reduce the sensitivity of a mammogram. In such circumstances, MRI may be useful; although studies have shown mixed results. Kocaoglu et al. (10) showed that MRI produced varied appearances in patients diagnosed with CGM and thus might limit its utility as a diagnostic tool. However, in general, MRI is known to be more sensitive than mammograms in detecting lesions in fatty and dense breasts.

In summary, 3 different scenarios are possible in our patient. First, the patient had breast carcinoma throughout the years that was misdiagnosed as CGM. However, this is highly unlikely for the reasons mentioned earlier. Second, she was unfortunate enough to have developed breast carcinoma as a second, separate pathology in the same breast. Third, she developed breast carcinoma as a result of chronic inflammation leading to dysplasia and subsequent malignant change.

This case illustrates the difficulty in identifying and diagnosing breast cancer in a patient with a background history of CGM. Whether the patient could have developed cancer from CGM will be a matter of debate unless more cases are encountered and subsequent research can link breast cancer and CGM. The results of future research could affect the diagnosis and treatment of CGM and would certainly alter the course of its management.

Authors' Contributions

Conception and design, critical revision of the article: LM, SNAS, SJJ, NHML, SA, RM
Drafting of the article: LM
Final approval of the article: SNAS, NHML, SJ, RM

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