Case Report

Mesenchymal Chondrosarcoma: A Case Report

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Abstract

Mesenchymal chondrosarcoma is a rare disease with poor prognosis. Treatment including wide or radical excision is very important. Radiotherapy and chemotherapy are additional treatment options, but no conclusive results for their efficacy have been shown until date. Imaging modalities can give important clues for diagnosis and management planning. Angioembolization before surgery could be useful as prophylaxis to control intraoperative bleeding, increasing the likelihood of complete resection.

Keywords: *mesenchymal chondrosarcoma, extraskeletal, therapeutic embolization*

Introduction

Mesenchymal chondrosarcoma (MC) was first described as an occurrence in the bone by Lichtenstein and Bernstein in 1954. It is a subtype of chondrosarcoma and is assumed to arise from remnants of the embryonic cartilage or metaplasia of meningeal fibroblasts (1). MC mostly affects children and young adults between the ages of 15 and 35 years and accounts for less than 1% of all sarcomas (2). One-third of the cases occur outside the bone and are seen more in young patients (23 years). Occurrence is mostly seen in the central nervous system, meninges, maxillary sinuses, eyelid, eye socket, and thyroid (3). We present a case of anterior skull base MC with intracranial involvement.

Case report

A 30-year-old male first presented with right proptosis five years ago at another hospital. He was diagnosed as having a right anterior skull base tumour, and subsequently, underwent craniotomy and tumour excision followed by 25 cycles of radiotherapy after histopathology examination (HPE) indicating MC. He presented five years later at the University Kebangsaan Malaysia Medical Centre (UKMMC) on 28 July, 2008 with right proptosis, loss of vision, third and seventh cranial nerve palsy, and hearing impairment.

Contrast-enhanced CT (Figure 1a and 1b) showed a lobulated heterogeneously enhancing mass at the right anterior cranial fossa with foci of calcification. The mass extended to the right infratemporal fossa inferiorly, right maxillary sinus anteriorly, and right ethmoid sinus medially. There was associated bone destruction, including the greater wing of the right sphenoid, right ethmoid, maxillary, frontal, and right temporal bones. Superiorly, the mass extended to the brain parenchyma of the right frontal and temporal lobes with no fat plane between them. T1-weighted (T1W) images of magnetic resonance imaging (MRI) showed a hypointense mass that was isointense to hyperintense with dark areas of calcification on T2W images (Figure 1c and 1d). After administration of gadolinium (Figure 1e), the mass showed intense enhancement. The right lateral rectus muscle was compressed anteromedially, indicating that the tumour originated from the extraconal space (Figure 1d). Since the epicentre of this mass was at the right spheno-orbital region, it was assumed to originate from the right sphenoid or lateral orbital wall of the right orbit. Anteromedially, the tumour extended into the right orbital cavity and compressed the right orbital contents, causing proptosis of the right globe. There was no clear fat plane between the mass with the right lateral and superior rectus muscles. Part of the mass encased the proximal part of the right optical nerve. Medially, the adjacent meninges were enhancing and had no clear plane with the mass, however, this part of the meninges was not significantly thickened, suggesting the tumour infiltrating into rather than originating from the meninges. Parts of the adjacent brain also showed no clear plane with the tumour (Figure 1d).

The patient was diagnosed as having recurrent MC and underwent right fronto-orbito-

zygomatic craniotomy for tumour debulking and right eye enucleation on 26 September, 2008. During surgery, the tumour was incised. The right orbital roof and right temporomandibular joint were removed. The estimated blood loss was approximately 5 L. CT after surgery (Figure 1f and 1g) showed a residual tumour and minimal subdural haemorrhage over the surgery site. The patient remained stable with full Glasgow coma scale (GCS) and was discharged on 30 September, 2008. HPE result (Figure 1h and 1i) showed a bimorphic histological pattern of well-differentiated cartilage and an abrupt boundary from undifferentiated stroma comprising small primitive round/oval cells with occasional spindle cells. The primitive cells had scant cytoplasm and mildly pleomorphic nuclei that exhibited irregular chromatin clumping and small nucleoli. Few mitotic figures were seen. The malignant cells were surrounded by fibrous cartilaginous tissues. Immunohistochemical staining with Ki-67 showed a high proliferative index (60%). These findings were consistent with MC.

On 10 February, 2009, the patient returned

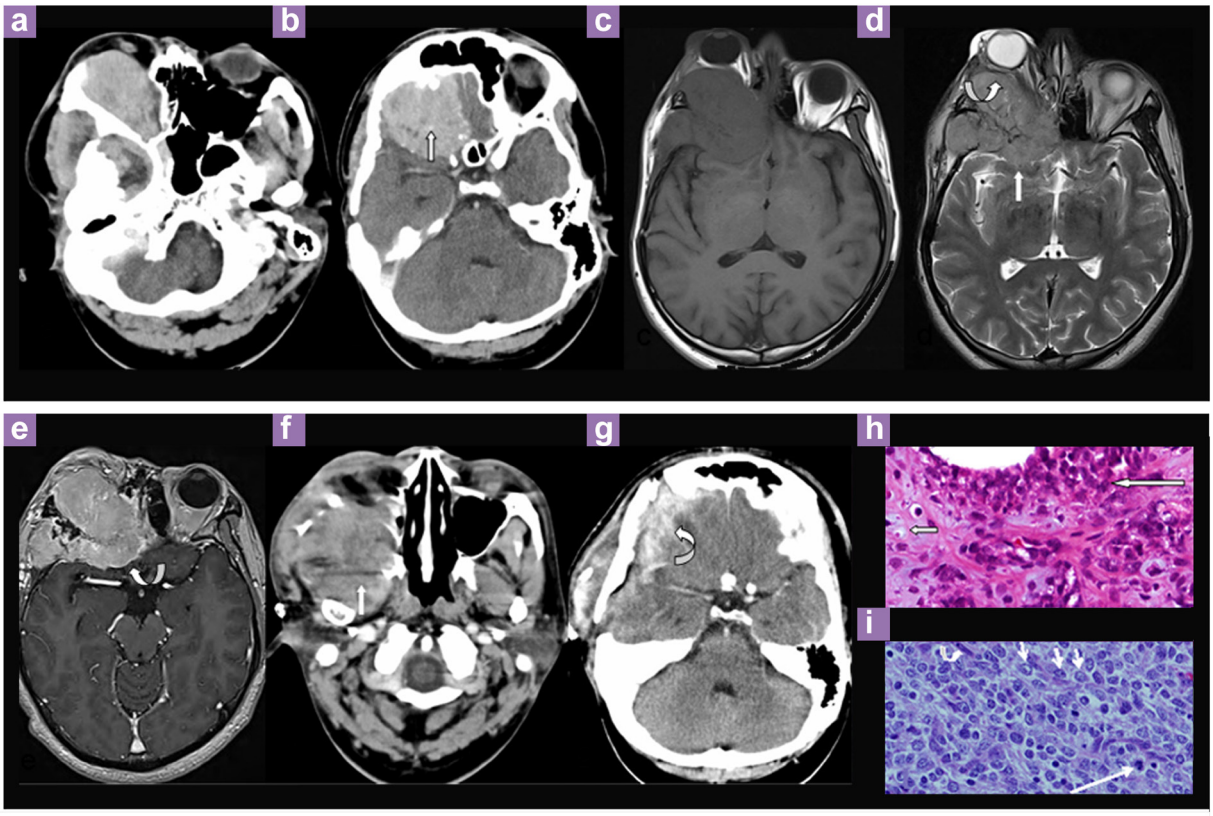

Figure 1: First admission contrast-enhanced CT: A heterogeneously enhanced mass at the anterior cranial fossa. The mass extended to the right infratemporal fossa, right orbit (1a) and right frontal lobe with foci of calcification (1b-arrow). MRI: A soft tissue mass that is hypo to isointense on T1W imaging (1c), iso to hyperintense on T2W imaging (1d) and intensely enhancing after administration of gadolinium (1e). The right lateral rectus muscle was compressed anteromedially (1d-curve arrow). Part of the tumour had no clear plane with the brain parenchyma. (1d-arrow). The adjacent meninges were enhanced with no clear plane with the tumour (1e-curve arrow). Contrast-enhanced CT after surgery: A residual tumour at the right infratemporal fossa (1f-arrow). Post-operative changes with subdural haematoma (1g-curve arrow) at the right frontotemporal region. HPE result: a bimorphic histological appearance of well-differentiated cartilage with chondrocytes (1h-short arrow) and undifferentiated stroma (1h-long arrow). The undifferentiated stroma comprised of small primitive-appearing oval/round cells (1i-short arrows) and spindle mesenchymal cells (1i-curve arrow). These primitive-appearing mesenchymal cells had scant cytoplasms and mildly pleomorphic nuclei that exhibited irregular chromatin clumping and small nucleoli (1i-short arrows). Few mitotic figures were seen (1i-long arrow).

to UKMMC complaining of epistaxis, headache, and lethargy. He was found to have right seventh cranial nerve palsy and decreased hearing. MRI (Figure 2a, 2b, and 2c) showed tumour recurrence with further extension into the right frontal, bilateral ethmoid, bilateral sphenoid sinuses, right cavernous sinus, and part of the clivus. Part of the mass was seen extending into the brain parenchyma of the right frontal lobe with no clear plane in between (Figure 2c). He was diagnosed as having a new recurrence and underwent debulking surgery again on 17 February, 2009 by the Neurosurgery and Ear-Nose-Throat (ENT) team (Figure 2d and 2e). The estimated blood loss this time was approximately 3 L. He developed cerebrospinal fluid rhinorrhoea seven days after surgery. A lumbar drain was inserted and removed on 5 March, 2009 after the rhinorrhoea resolved. He had normal vital signs, full GCS and was discharged on 10 March, 2009.

On 17 July, 2009, he returned to UKMMC for the third time, with pus and blood discharge at the pre-auricular punctum, blocked right nostril, and swelling of the right periorbital region. This time, MRI showed artifacts because of previous surgical clips. CT (Figure 3a and 3b) showed markedly larger tumour recurrence at the previous tumoral site. The tumour crossed the midline and involved the bilateral frontal, ethmoid, and sphenoid sinuses. It extended posteriorly involving the entire clivus and bilateral cavernous sinuses. It also extended into the bifrontal and right temporal lobes with no clear fat plane with the brain parenchyma (Figure 3b).

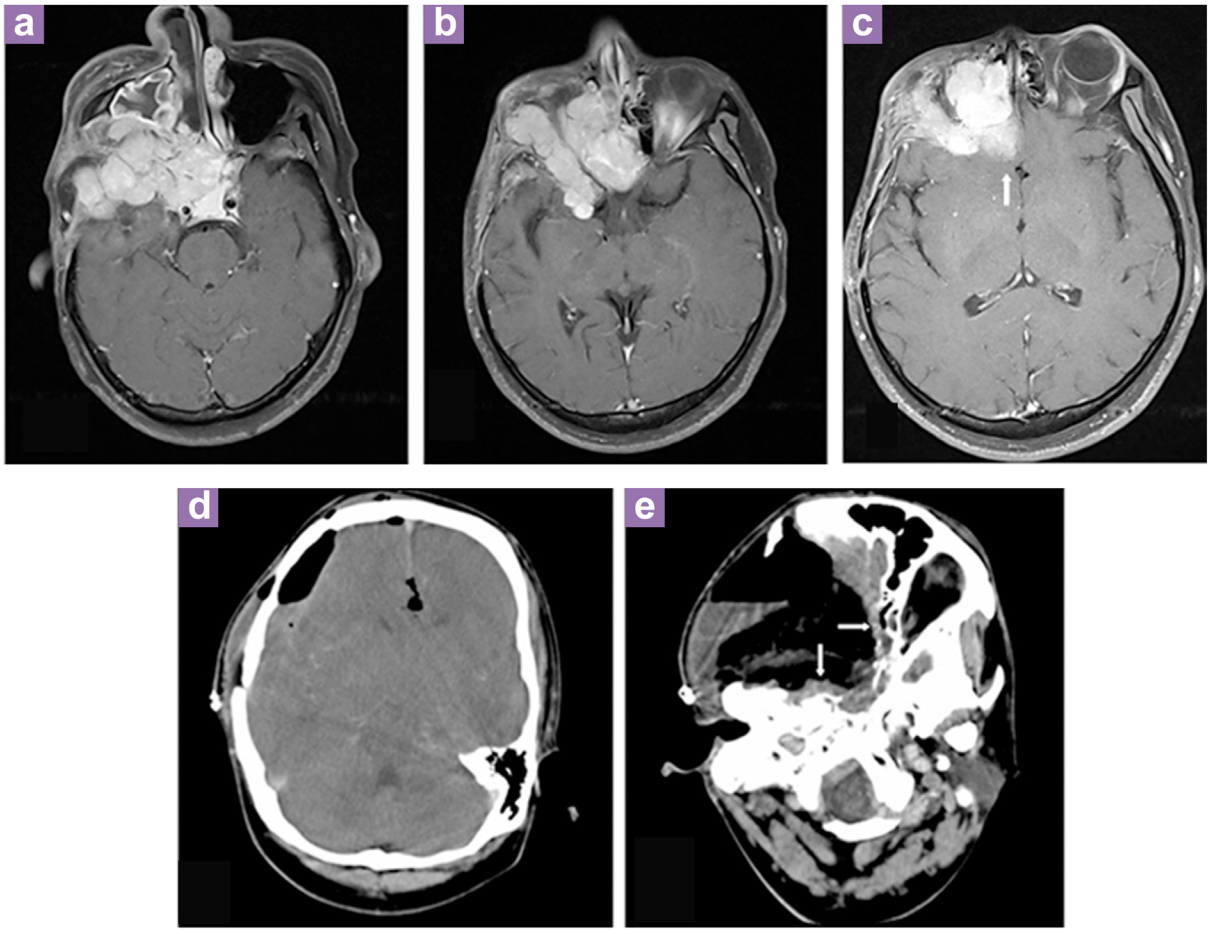

Figure 2: Contrast-enhanced MRI at second admission: A tumour recurrence with extension into the right cavernous sinus, part of the clivus, ethmoid and sphenoid sinuses (2a, 2b). Part of the mass is seen extending into the brain parenchyma with no clear plane in between (2c-arrow). Contrast-enhanced CT after second surgery: Post-operative changes with minimal subdural bleed, fluid collection and cerebral oedema (2d). Fluid is also seen at the right frontal scalp (2d), extending to the right infratemporal fossa (2e). Soft tissue density along the ethmoid sinus and right temporal fossa could represent residual tumour (2e-arrows).

The patient underwent debulking surgery for the third time on 7 August, 2009. During surgery, he experienced massive blood loss that was estimated to be at least 15 L. This resulted in cardiac arrest with one episode of CPR in five minutes. The mass was partially resected and then closed with packing for haemostasis. His blood pressure (BP) was increased with the assistance of inotrope and blood transfusion. The pack was removed five days later. Subsequently, he experienced wound infection with *Pseudomonas* that resolved after two weeks of antibiotics (Figure 3d). He achieved normal vital signs and full GCS three weeks after surgery. He was discharged on 28 August, 2009 uneventfully. CT after surgery showed a residual tumour (Figure 3e).

Discussion

Four types of chondrosarcoma have been cited in the literature: grade I, grade II, mesenchymal, and myxoid. The mesenchymal type is the most malignant because of its tendency for intradural and cerebral growth (4). The extraskeletal locations of MC vary in different studies, but the orbital MC remains an extremely rare entity (5), and shows no sex dominance (6).

The clinical presentation of MC depends on the location and size of the tumour. In this study, the patient presented with right proptosis because of the mass effect on the right orbit. He also had loss of vision of the right eye, and right third and seventh nerve palsy probably because of the mass effect and/or tumour involvement.

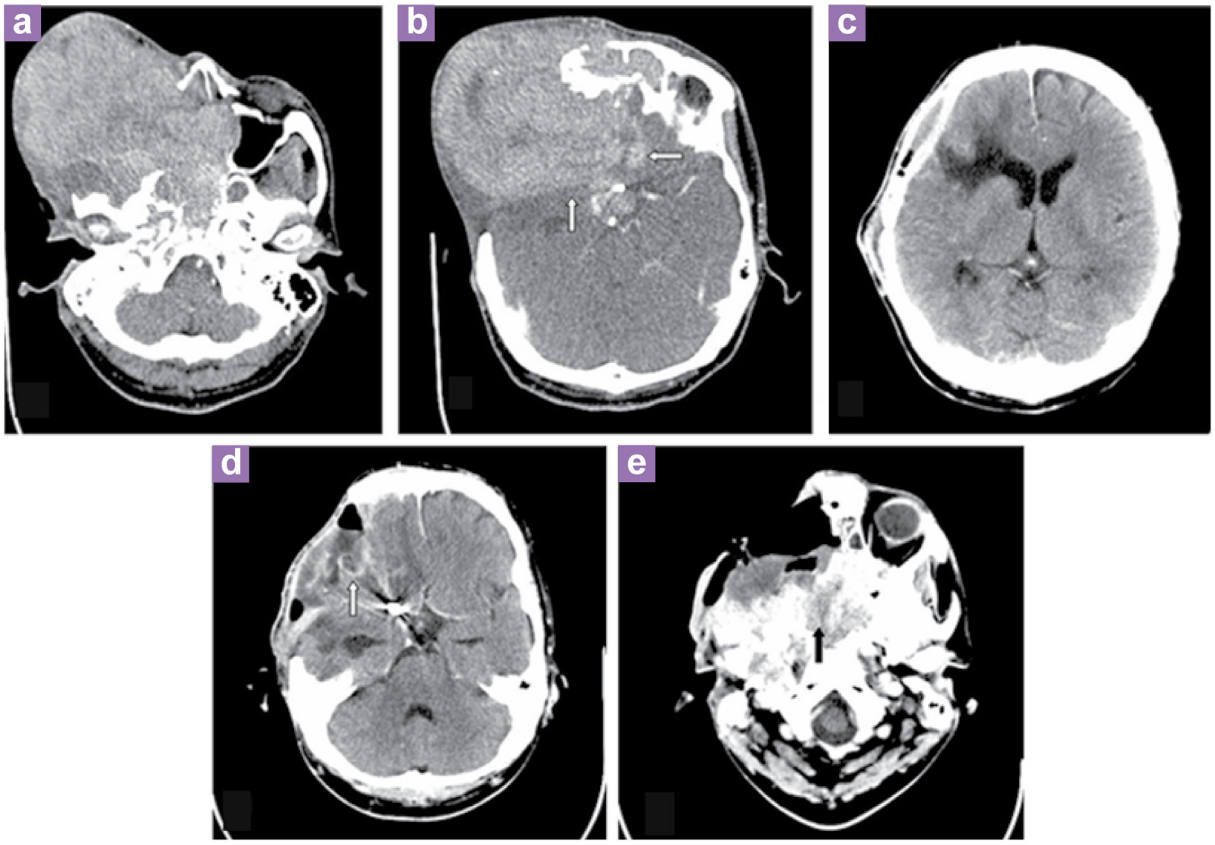

Figure 3: Contrast-enhanced CT at the third admission: The Mass increased in size, crossed the midline and involves the entire frontal, ethmoid and sphenoid sinuses as well as the entire clivus and cavernous sinuses (3a, 3b); it has extended into the bifrontal and right temporal lobes with no clear plane with the brain parenchyma (3b-arrows). Contrast-enhanced CT after third surgery: Hypodensity with fluid density at the right frontal lobe associated with volume loss secondary to tumour removal (3c). Subdural fluid collection at the operative site with peripheral enhancement probably secondary to wound infection (3d-arrow). The soft-tissue lesion is still seen within the remaining ethmoid-sphenoid sinuses, clivus and infratemporal fossa consistent with a residual tumour (3e-black arrow).

Diagnostic imaging can give important information for differential diagnosis and management (7). Radiographs may show a soft tissue mass with calcification and possible erosion of adjacent bones. In plain CT, the tumour can be well defined or lobulated, and may be hypo or isodense to muscle because of the mixed composition of tumour cells, well-differentiated cartilage, and highly vascular soft and fibrous tissues. There could be stipple, arc, ring, or coarse dense calcification. MC usually shows heterogeneous and intense enhancement after contrast enhancement (3). MRI shows a soft tissue mass that may be hypo to isointense on T1W imaging, iso or hyperintense in proton density and T2W MRI and intense heterogeneous enhancement after administration of gadolinium. A fat saturation sequence is helpful in analysing and excluding fat containing tumours (i.e. haemangioma). MRI is superior for delineation of lesion demarcation and provides better visualisation of tumour extension, especially when there is neurological involvement (8). Ultrasound can shows a heterogeneous soft tissue mass with calcification.

Angiography often reveals a neovascular pattern, particularly in the periphery, possibly with arteriovenous shunting. Because of its high vascularization, it is often difficult to differentiate this tumour from haemangioma or other hypervascularization. Angioembolization before surgery can be used to delineate feeding and draining vessels. It may also be helpful to provide prophylaxis embolization to reduce blood loss if the patient is planned for surgery. According to some authors, angioembolization before surgery is an effective method to control intraoperative bleeding. It can render the vascularity manageable and make wide tumour excision less formidable (9). This patient unfortunately did not undergo angioembolization before surgery.

There is no specific symptom and radiological findings are similar to tumours with hypervascular characteristics, haemangioma or other sarcoma. Hence, extensive biopsy is helpful for differential diagnosis and to avoid misdiagnosis of this highly recurrent tumour. The pathological classifications of the MC grades I and II are based on differences in characteristics, such as nuclear size, cellularity, mitotic rate, and frequency of lacunae with multiple nuclei. The mesenchymal subtype typically shows the presence of spindle cells. The myxoid type is comprised of a string of round cells in the myxoid matrix (4).

The typical histopathology of MC includes a bimorphic histological appearance, which has both undifferentiated mesenchymal cells and well-differentiated cartilage. The undifferentiated cells include sheets of closely packed small cells with round, oval and short-spindle shapes, scant indistinct cytoplasms and hyperchromatic nuclei. There could be early formation of the cartilage islands at the periphery as a transition between the undifferentiated cells and cartilage. The larger cartilage islands may undergo calcification or ossification (10).

The most important differential diagnosis for a skull-base MC is chordoma (11), which is more aggressive (12) and difficult to differentiate by imaging alone. A chordoma typically contains cohesive nests and cords of large cells with bubbly eosinophilic cytoplasm called physaliphorous cells (11). Chondroid chordoma, a subtype of chordoma, is histologically similar to chondrosarcoma in cartilaginous areas, but it typically contains the cohesive nests and cords of physaliphorous cells. Immunohistologically, chordomas lack vimentin immunoreactivity and chondrosarcoma fails to express cytokeratin, however, S-100 protein expression is present in both (4).

Other small cell tumours should also be differentiated from MC, including haemangiopericytoma and Ewing's sarcoma. Imaging findings of malignant skull base haemangiopericytoma are similar to those for MC with a homo- or heterogeneously enhanced tumour in contrast-enhanced CT with infrequent calcification. MRI shows a tumour with well-circumscribed isointense signal on T1W images, iso to hyperintense signal on T2W images and intense enhancement after administration of gadolinium. Histologically, malignant skull base haemangiopericytoma does not have chondroid components like those of MC and is CD34 positive. Ewing's sarcoma of the skull base is another differential diagnosis of MC, and both have similar radiological findings (13); histologically, Ewing's sarcoma is positive for vimentin and CD99, lacks chondroid areas, and haemangiopericytoma-like pattern. Specifically, it has a tendency to spread to bone (14).

Immunohistochemically, MC is positive for S-100 protein and negative for cytokeratins, which enables differentiation from synovial sarcoma and spindle-cell variants that are usually focally positive for cytokeratins (15).

Treatment of MC includes surgery, adjuvant chemotherapy and radiotherapy. Radiotherapy

helps to improve patient survival when complete resection is impossible (15). Chemotherapy is still under debate. Some studies have concluded that chemotherapy combined with radiotherapy is effective for poorly differentiated MC. Neoadjuvant chemotherapy combined with surgery is effective for better differentiated tumours (2). However, other authors are sceptical about chemotherapy and have stated that only radical surgery can improve survival (16). Some researchers reported a case of pleural MC that did not respond to chemotherapy (15). In general, MC has poor prognosis. The 5 and 10 years survival rates are 54.6% and 27.3%, respectively (17).

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Conflict of interest

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Conception and design, analysis and interpretation of the data, drafting of the article, collection and assembly of data: DVN
Critical revision of the article for the important intellectual content: YY, SM

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