CASE REPORT

Extraskelatal orbital mesenchymal chondrosarcoma: surgical approach and mini review

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SUMMARY

Extraskelatal orbital mesenchymal chondrosarcoma (MC) is an extremely rare and highly aggressive tumour. It has characteristic radiological features and pathognomic histological biphasic pattern. Radical resection with negative margins is the mainstay of treatment; role of adjuvant chemotherapy and radiotherapy is yet not well defined. We report a rare case of 18-year-old man who was diagnosed to have orbital MC. He presented with locally advanced disease with no vision in the affected eye. He underwent right orbital exenteration; a transcranial intradural approach was used to divide the optic nerve, and the temporalis muscle flap was utilised to fill the exenterated orbit. Though optic nerve involvement is rare in orbital MCs, a transcranial approach may be used effectively to avoid traction on optic chiasma and ensure margin-free resection in case of optic nerve involvement up to orbital apex. Unfortunately, prognosis remains dismal in MCs despite treatment.

BACKGROUND

Mesenchymal chondrosarcomas (MCs) are highly aggressive cartilage forming tumours.^{1 2} Extraskelatal orbital MCs are extremely rare tumours.² They have characteristic radiological features and pathognomic histological biphasic pattern. These tumours are malignant small round cell neoplasms with focal cartilaginous differentiation.^{3 4} Owing to rarity of these tumours, there are no definitive management guidelines available. Radical resection with negative margins is the primary modality of treatment; the role of adjuvant therapy is yet to be clearly defined.^{2 3 5 6} Though orbital location is associated with better survival compared to other locations, overall prognosis of MCs remains dismal.^{2 3}

CASE PRESENTATION

An 18-year-old man sought treatment for progressive proptosis and blurring of vision in right eye since 6 months. He had treatment for his present illness in another hospital where right orbitotomy and debulking of the tumour was undertaken 1 year ago; histopathological examination of the specimen confirmed MC. He was subsequently prescribed adjuvant chemotherapy but he did not go for the treatment.

Presently, his general and systemic physical examination was unremarkable. He had proptosis of the right eye with restriction of extraocular movements; even perception of light was absent in that eye. His other eye had almost normal vision (visual acuity of 6/9).

INVESTIGATIONS

CT of the head and neck region showed a 6.0×4.5 cm retrobulbar right orbital mass with marked proptosis; there were multiple cystic areas with calcification in the lesion and it was infiltrating the extraocular muscles. The tumour was also infiltrating the optic nerve, though no intracranial extension was seen. CT chest did not reveal any metastatic disease.

Contrast-enhanced MRI further revealed that there was no intracranial extension of the tumour along the optic nerve (figure 1).

TREATMENT

The patient underwent initial pterional craniotomy for intradural sectioning of the optic nerve as well as control of ophthalmic artery to prevent traction on chiasma/optic nerve; intradural optic nerve resection was performed 3 mm proximal to the optic chiasm. Subsequently, a right orbital exenteration was performed and the temporalis muscle flap was used to fill the exenterated cavity (figure 2).

OUTCOME AND FOLLOW-UP

Gross examination showed a 4×3×3 cm solid tumour; the cut surface was grey-white in colour. Microscopic examination showed a malignant tumour with an admixture of undifferentiated mesenchymal cells and islands of mature hyaline cartilage. The mesenchymal cells were ovoid to fusiform with round nuclei, finely dispersed chromatin and occasional nucleoli with sparse cytoplasm. There was moderate cellular pleomorphism. Mitotic figures were rare. No necrosis or haemorrhage was seen. On immunohistochemistry, the tumour cells were focally immunopositive for S100 protein. Ki-67 labelling index was high (~25–30%). Based on the above histological and immunohistochemical features, a diagnosis of MC was made (figure 3).

The patient had uneventful postoperative recovery. He tolerated adjuvant radiotherapy (60 Gy/30 fractions) well. He is disease-free after 2 years of regular follow-up.

DISCUSSION

Soft tissue sarcomas account for <1% of the overall burden of malignant tumours.⁷ Chondrosarcoma is a rare histological subtype and constitutes 1% of all soft tissue sarcomas. Conventional type is the most common; other rare histological variants are clear cell, mesenchymal, dedifferentiated chondrosarcomas.^{8 9} The pathogenesis of extraskelatal MC is unknown.³

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Figure 1 CT and MRI. Axial contrast-enhanced CT image (A) showing large lobulated heterogeneously enhancing intraconal orbital mass on right side with few calcifications, causing proptosis. Underlying bones appear grossly normal, except for mild pressure erosion of lamina papyracea on the right side. Axial and sagittal postcontrast T1 weighted fat saturation MRI (B and C) showing intensely enhancing lobulated intraconal orbital mass on the right side. The mass is encasing the right optic nerve (black arrow).

MC is a rare and highly malignant cartilage forming tumour which was first described by Lichtenstein and Bernstein in skeletal system in 1959.¹ Dowling first described extraskeletal MC in 1964.¹⁰ MC constitutes 1% of all chondrosarcomas and it can occur in skeletal and extraskeletal locations.¹¹ In one of the largest case series of MC, Nakashima *et al*² reported that 35% MCs were located in the extraskeletal system; the common locations were the meninges and lower extremity. Both Salvador *et al* and Nakashima *et al* reported only one patient of extraskeletal orbital MC each in their series of 30 and 111 patients, respectively.^{2 12} In one of the early case series Jacobs *et al*⁵ reported three cases of orbital MC with review of the literature and showed that optimal outcomes can be achieved with good quality controlled surgery. Font *et al*¹³ reviewed the literature and reported 26 cases of MC treated between 1969 and 2009 and highlighted the importance of multimodality management.

A PubMed search using MESH words 'orbital neoplasm' [Mesh] and 'chondrosarcoma, mesenchymal' [Mesh] was conducted on 17 July 2016; filters like humans, English and from 1 January 1990 to 31 December 2015 were applied to refine the search and identify the recent literature. A total of 18 articles were identified and further manual search of PubMed was performed, which yielded six more relevant articles. Most of the reviews focus on clinical presentations, radiological and pathological features. In this review we focused mainly on surgical

Figure 3 (A) Cellular tumour composed of undifferentiated oval to spindle-shaped mesenchymal cells containing islands of moderately well-differentiated cartilage (arrow) (x400; H&E). (B) The tumour cells are mildly pleomorphic with round nuclei, finely dispersed chromatin, occasional prominent nucleoli and scant cytoplasm (x400; H&E). (C) Tumour cells are focally immunopositive for S100 (x400). (D) Ki-67 labelling index is high (x400).

approaches, multimodality management options, relapse patterns and survival outcomes (table 1).

Orbital MCs affect patients in their second or third decades of life, with a female preponderance. Common presentations are proptosis of eye ball with decreased visual acuity, pain in eye, headache and restriction of eyeball movements. Distant metastasis is exceptional at presentation.^{3 5 6 13} Radiological examination is usually warranted for diagnosis and anatomical localisation to access operability. The characteristic CT findings are a well-defined, enhancing lobulated mass with multiple areas of fine and coarse calcification. MRI is superior for delineation of lesion and it provides better visualisation of tumour extension, especially when there is neurological involvement. Marked contrast enhancement and type III time-intensity curve on MRI is highly suspicious for MC.¹⁴ The pathognomic histopathological appearance of MC is a biphasic pattern composed of mesenchymal and chondrocytic components; there are undifferentiated, round or spindle-shaped mesenchymal cells and areas of cartilaginous tissue often presenting central calcifications and even ossification. Vimentin and CD-99 immunostaining is positive in undifferentiated cells, and S-100 in the chondroid areas. The histological differential diagnosis for MCs includes Ewings sarcoma, lymphoma, neuroblastoma, desmoplastic small round-cell tumours and small cell osteosarcoma.^{2 4}

Surgical resection is the mainstay of therapy. The aim of surgery is to achieve R0 resection.^{2 3 5 13} Our patient presented with a locally advanced disease with complete loss of the vision in the affected eye and the tumour involved the optic nerve up to the orbital apex. Though optic nerve involvement is not typical for orbital MC five cases in the literature have shown its involvement. In three cases the optic nerve was involved up to the orbital apex only and in remaining two cases intracranial extension was present.¹⁵⁻¹⁹ Difficulties are encountered during surgery in advanced tumours reaching up to the orbital apex and lateral approaches are recommended for such tumours.²⁰ We did not attempt intraorbital division of the optic nerve as it might have resulted in positive margin; moreover, it might also have caused traction injury to the optic chiasma resulting in loss of vision in the other unaffected eye. Therefore, we used a

Figure 2 (A) Preoperative: Exophytic, fleshy right orbital mass. (B) Intraoperative: Transcranial intradural approach for optic nerve division, (C) Preserved temporalis muscle (in hand) and tumour (covered in gauze piece), (D) Post-tumour resection cavity filled with temporalis muscle.

Table 1 Surgical approaches, treatment details, relapse patterns and survival outcomes in patients with mesenchymal chondrosarcoma of orbit

Number	Author and year	Age/sex	Surgery	Neoadjuvant/adjuvant treatment details	Relapse	Follow-up	Status last visit
1	Hanakita <i>et al</i> 2012	20/F	Exenteration with rectus muscle graft	No	No	6 years	Disease-free
2	Szumera Ciekiewicz A <i>et al</i> 2012	31/F	Partial excision	4 cycles NACT ¹ (DDP ² +VP 16 ³)	No	10 months	Disease-free
		29/F	Enucleation	Adjuvant RT ⁴	Local	3.5 years	Alive with disease
3	Patel R <i>et al</i> 2012	50/M	Inferior orbitotomy and excision	No	No	NA ⁵	NA
4	Yang BT <i>et al</i> 2012	Six cases 11–37 years M:F 5:1	Surgery (details not provided)	NA	2 local	0.5–8 years	4 disease free 2 alive with disease
5	Liu M <i>et al</i> 2010	26/F	Lateral orbitotomy and excision	Adjuvant RT (50 Gy)	No	18 months	Disease-free
6	Bonavalonta P <i>et al</i> 2010	23/M	Trans-septal orbitotomy and excision	No	No	3 years	Disease-free
7	Razak AR <i>et al</i> 2010	22/M	Exenteration	NACT 6 cycles (VIDE ⁶) and adjuvant RT (60 Gy)	No	2 years	Disease-free
8	Font RL <i>et al</i> 2009	24/F	Exenteration	Adjuvant CT 4 cycles (AI) and adjuvant RT (60 Gy)	No	8 years	Disease-free
9	Kaur A <i>et al</i> 2008	25/F	Lateral orbitotomy and excision. Followed by exenteration after 10 months for local recurrence	Adjuvant CT (VAC ⁷) 6 cycles and adjuvant RT (48.6 Gy)	No	2 years	Disease-free
		27/M	Exenteration	Adjuvant CT (VAC) 6 cycles and adjuvant RT (41.4 Gy)	No	2 years	Disease-free
10	Odashiro AN 2009	14/M	Lateral canthotomy and excision (R2 resection)	Adjuvant CT (Details—NA)	No	2 months	Disease-free
11	Angotti-Neto H <i>et al</i> 2006	21/F	Anterior orbitotomy and excision (piecemeal)	Adjuvant RT	No	6 months	Disease-free
12	Tuncer S <i>et al</i> 2004	5 months/F	Exenteration	NACT+RT (1 VAC+3 IEC ⁸ +41.4 Gy RT) followed by 3 IEC adjuvant CT	No	4 years	Disease-free
13	Khouja N <i>et al</i> 1999	27/M	Subfrontal epidural approach and excision twice followed by exenteration after second recurrence	Adjuvant RT (65 Gy)	Yes	2 years	Alive with disease
14	Koeller <i>et al</i> 1999	Review article—No new case reported					
15	Shinaver <i>et al</i> 1997	18/M	Lateral orbitotomy and piecemeal excision (R2 resection)	No	NA	NA	Lost to follow-up
16	Sugiyama k <i>et al</i> 1995	16/M	Craniofacial resection	NA	NA	NA	NA
17	Lauer <i>et al</i> 1995	NA	Resection	Adjuvant CT-RT ⁹ (details—NA)	NO	30 months	Disease-free
18	Bumpous <i>et al</i> 1995	Transorbital approaches to cranial base—no new case reported					
19	Herrera A <i>et al</i> 2012	52/M	Exenteration	Adjuvant VAC-IE ¹⁰ +66 Gy RT	No	NA	Disease-free
20	Looi A <i>et al</i> 2006	7/M	Lid sparing exenteration, temporalis transfer and dermis fat graft	Adjuvant 8 cycles VAC-IE	No	15 months	Disease-Free
21	Kashyap S <i>et al</i> 2001	45/M	Biopsy only	NA	NA	NA	NA
22	Jacobs <i>et al</i> 1994	13/F	Kronlein orbitotomy and excision	No	No	18.5 years	Disease-free
		10/F	Lateral orbitotomy and excision	No	No	16 years	Disease-free
		11/F	Anterior craniotomy and excision (R2 resection)	Adjuvant VAC for 9 weeks and 60.6 Gy RT	No	6 months	Dead
23	Bagchi M <i>et al</i> 1993	28/F	Lateral orbitotomy and excision (piecemeal)	NA	No	2 years	Disease-free
24	Khuteta A <i>et al</i> 1992	10/F	Exenteration	NA	NA	NA	NA

*Search details—serial number 1–18 (PubMed search using MESH words “orbital neoplasm” [Mesh] and “chondrosarcoma, mesenchymal” [Mesh]. Further manual PubMed search revealed six more articles (serial number 19–24).

†NACT¹—Neoadjuvant chemotherapy, DDP²—Cisplatin, VP 16³—Etoposide, RT⁴—Radiotherapy, NA⁵—Not available, VIDE⁶—Vincristine, ifosfamide, adriamycin, etoposide, VAC⁷—Vincristine, actinomycin D, cyclophosphamide, IEC⁸—Ifosfamide, epirubicin, cisplatin, CT-RT⁹—Chemo-radiotherapy, VAC-IE¹⁰—Vincristine, adriamycin, cyclophosphamide, ifosfamide, etoposide.

transcranial intradural approach to divide the optic nerve and ophthalmic artery to prevent traction injury to the chiasma and ensure margin free resection.

Most MCs are resistant to chemotherapy and radiotherapy. However, if the tumour is surgically unresectable or histologically highly aggressive, preoperative chemotherapy and radiation therapy may be considered.^{3 16 21} Adjuvant radiation can be considered in case of incomplete resection, close margins and recurrent tumours.^{5 6 13 21–23} Adjuvant chemotherapy may be considered in cases with aggressive behaviour and high-grade lesions. MC may be treated according to Ewing's sarcoma protocol, Vincristine, Dactinomycin, Cyclophosphamide and Doxorubicin (VACD) alone or alternating with Ifosfamide and Etoposide (VACD-IE).^{5 13 23 24} Details of various surgical approaches, neoadjuvant and adjuvant treatment protocols are summarised in table 1.

Overall, MC has a dismal prognosis and the overall 5-year and 10-year survival for MC, considering all sites, is 55% and 27%, respectively.² The prognosis is relatively better in head and neck (including orbit) MC in view of early detection and treatment.³ Details of relapse patterns and survival outcome are summarised in table 1.

Learning points

- ▶ Extraskeletal orbital mesenchymal chondrosarcomas (MC) is an extremely rare tumour.
- ▶ Radical surgery offers a best chance of cure.
- ▶ Optic nerve involvement is rare in orbital MCs. Transcranial approach may be used effectively to avoid traction on optic chiasma and ensure margin-free resection in case of optic nerve involvement up to the orbital apex.
- ▶ Excellent outcomes can be achieved with good quality controlled surgery and additional chemotherapy and radiotherapy in incomplete resection and aggressive recurrent tumours.

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