

Case Report

Primary mesenchymal chondrosarcoma of the orbit: Histopathological report of 3 pediatric cases



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Abstract

Mesenchymal chondrosarcoma (MCS) is an unusual tumor mainly found in the skeleton. Around third of the cases occur in extra-skeletal sites with the orbit being the third most common site in these cases. In previous reviews of the orbital cases, it has been concluded that orbital MCS tends to occur in women in the second or third decades of life. However, 8 cases of orbital MCS have been reported so far in the pediatric age group (age less than 18 years-old) one of which has been considered congenital MCS in a 5-days old newborn girl. We describe 3 additional pediatric cases with primary orbital MCS and they were all males. Our cases presented with proptosis and calcific orbital masses on imaging studies. Histopathological examination of the excised masses shared the typical presence of undifferentiated mesenchymal cells and immature areas of cartilage. The diagnosis of MCS was further confirmed by immunohistochemical staining. Brief review of the literature in relation to this diagnosis in the orbit is also presented.

Keywords: Mesenchymal, Chondrosarcoma, Orbit, Proptosis, Cartilage

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Introduction

Mesenchymal chondrosarcoma (MCS), is an unusual tumor first described by Lichtenstein and Bernstein.¹ It is usually found in the skeleton, but around one third of the cases may also be found in extra-skeletal sites.^{2,3} Orbital MCS was first described by Cardenas-Ramirez in 1959.⁴ Subsequently, reports of orbital involvement by this neoplasm were published reaching 28 cases mentioned in the English-written literature mostly in adults.⁵ As the orbit is a rare site of

mesenchymal chondrosarcoma, here we report 3 pediatric cases with primary orbital MCS.

Case reports

Case I

A thirty-month old healthy boy presented with progressive right eye proptosis of 1 month duration. Magnetic resonance imaging was done and revealed right orbital mass. He was

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then referred to our institution with a provisional diagnosis of rhabdomyosarcoma for further management.

At presentation, he had right eye proptosis with hypoglobus and complete restriction of extraocular movements (frozen globe). Pupils demonstrated a 4+ afferent pupillary defect in the right eye. Anterior segment examination of both eyes was unremarkable. Fundus examination of the right eye showed a healthy optic disc, macula, tortuous retinal blood vessels and choroidal folds indicating a mass effect.

Physical examination showed two café-au-lait spots on the right arm and upper right chest.

Blood investigations included complete blood count, hemoglobin levels, urea and electrolytes and blood sugar which were all within normal limits.

Computed tomography (CT) scan revealed right orbital intraconal mass of homogeneous density filling the retrobulbar space of the right orbit and extending along the optic nerve. The mass caused expansion of the bony orbit with ill-defined medial wall.

Magnetic resonance imaging (MRI) was done and showed a right partially lobulated intraconal mass with an extension to the extraconal spaces, particularly on the medial aspect with remodeling of the lamina paprecea. On T1 and T2 weighted images, the lesion demonstrated isotonic signal intensity equal to the brain grey matter. Post-contrast images showed peripheral rim enhancement. The optic nerve has been evaluated during radiological imaging but it was not identified or visible in all obtained sequenced images. However, the canalicular and intracanalicular parts of the right optic nerve maintained normal morphology and signal intensity. These findings have led to a radiological suggested diagnosis of rhabdomyosarcoma or optic nerve glioma.

The patient was booked, for tumor excisional biopsy and debulking surgery. Intraoperatively, the tumor was found to

be friable. On gross pathology, the specimen consisted of multiple, friable, pieces of tissue which aggregated to measure 55 × 30 mm in maximum dimensions.

Microscopic examinations showed predominantly undifferentiated mesenchymal round cells with hemangiopericytoma vascular pattern (Fig. 1A). Several areas of immature cartilage with focal calcifications were seen within a myxoid stroma (Fig. 1B). Immunohistochemical staining panel was performed. The tumor cells showed diffuse positivity for vimentin and showed focal expression of CD99, CD56 and NSE (Fig. 1C and D). S-100 stain was not performed in this case. A final diagnosis of undifferentiated malignant round cell tumor consistent with mesenchymal chondrosarcoma was made.

Case II

A 6-year-old healthy boy presented at Johns Hopkins healthcare center with his parents with a complaint that his right eye seemed bigger than the left. His vision was 20/20 in both eyes without correction. The extra-ocular motility was full. Both pupils were equal, round, and reactive to light. The right eye was displaced inferiorly by 4 mm. The anterior chamber examination was unremarkable.

Orbital ultrasound showed consistent findings with a dermoid cyst rather than a hemangioma or other vascular lesions (Fig. 2A). On CT scan, a large superior orbital mass with calcifications was identified.

The lesion was surgically excised. The gross pathology revealed a 30 × 15 × 11 mm, tan-colored mass with a smooth exterior surface. The lesion was bisected and the cut surface was firm with no evidence of cysts, hemorrhage or necrotic foci. The histopathological examination was identical in appearance to Case I with expression of CD99 by the

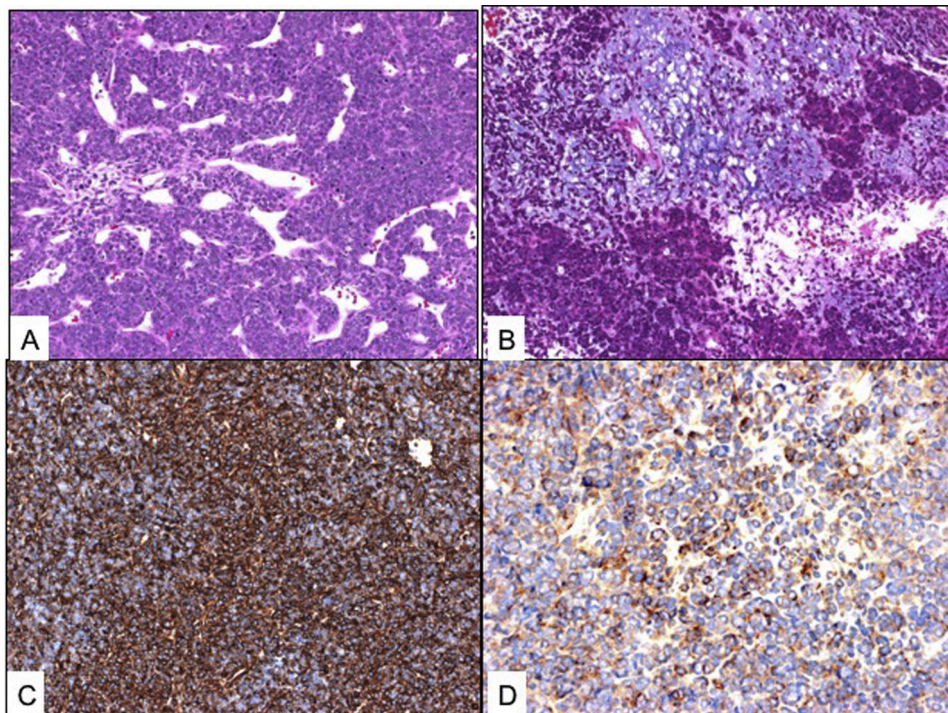


Fig. 1. (A) Tumor with hemangiopericytoma-like pattern in the first case (Original magnification x200 Hematoxylin & Eosin). (B) Areas of immature cartilage (Original magnification x200 Hematoxylin & Eosin). (C) Mesenchymal tumor cells expressing Vimentin (Original magnification x400). (D) Focal CD99 expression in noncartilaginous areas of the tumor (Original magnification x400).

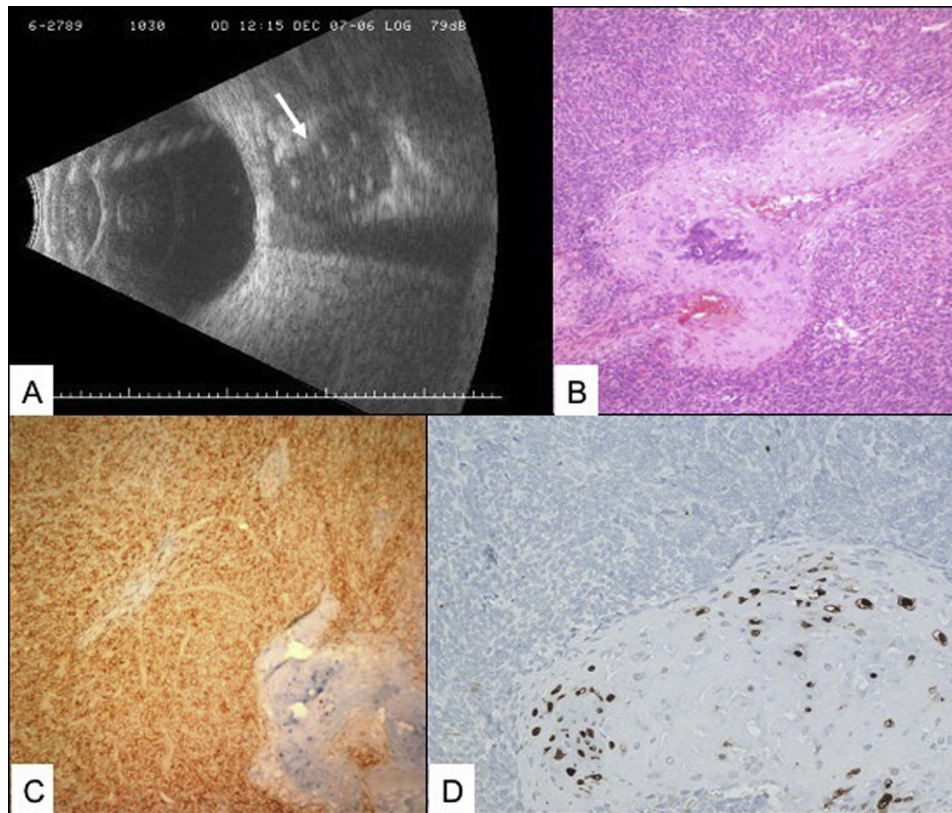


Fig. 2. (A) The bio-microscopy of the left orbit in case 2 showing a well-defined heterogeneous mass (white arrow) suggestive of a dermoid cyst. (B) The histopathological appearance of the biphasic tumor in case 2 with immature cartilage, central calcification and surrounding spindle mesenchymal cells (Original magnification x200 Hematoxylin & Eosin). (C) The mesenchymal cells in non-cartilaginous areas of the tumor expressing CD99 (Original magnification x100). (D) S-100 immunoreactivity in the chondrocytes of the mesenchymal chondrosarcoma in the same case.

mesenchymal tumor cells and S-100 in the chondroid areas (Fig. 2B–D). The vascular pattern was highlighted by CD34 stain. After an undefined period of post-operative follow up, subsequent repeated MRI and CT studies did not identify any signs of residual or recurrent tumor.

Case III

A 17-year-old known epileptic male patient, presented with a history of gradual onset of left side proptosis increasing over one year and swelling of both left upper and lower eyelids. The patient did not report any diminution of vision. Refraction was done and showed hyperopic shift measuring more than +1.5 diopters on the left side. The patient also complained that his proptosis has been progressively increasing with a degree of nocturnal lagophthalmos. His past medical history confirmed the diagnosis of partial epilepsy with secondary generalized seizures in another health care facility one year earlier. His CT scan done at the time of this diagnosis was unremarkable. The patient was also a known smoker and had family history of diabetes mellitus.

On examination, the best corrected visual acuity was 20/20 in both eyes. His intraocular pressure measured 12 mmHg on the right side and 14 mmHg on the left. His left eyelids were mildly swollen. The extra-ocular motility was full but with painful movements on the affected side. The Hertel exophthalmometer (at base of 116) measured 22 mm on the right side and 26 mm on the left with a 4-mm proptosis

(Fig. 3A). Slit lamp examination, and the optic nerves were unremarkable bilaterally. Blood investigations were all within normal limit.

CT scan revealed a well-defined intraconal mass measuring 22 × 17 mm located between the lateral rectus muscle and the optic nerve with subsequent minimal displacement of the optic nerve. Multiple areas of fine and coarse calcification were seen with minimal degree of enhancement following intravenous contrast injection. There was no evidence of bony changes and both globes and remaining recti muscles were normal (Fig. 3B).

At the time of excisional biopsy about 3 weeks later, the left globe was further displaced with obvious scleral show and 7-mm proptosis. A palpable prominent deep mass was felt at the inferior orbital rim at that time.

Grossly, the mass was gray to pink in color, well defined, and slightly lobulated without a definite capsule. Histopathology of the specimen showed islands of immature cartilaginous tissue with central areas of calcification and other larger areas of small round oval to spindle-shaped mesenchymal cells constituting the stroma between the islands of the immature cartilage (Fig. 3C). Delicate vascular channels with hemangiopericytoma-like pattern were seen. The diagnosis of mesenchymal chondrosarcoma was confirmed with further expression of CD99 by spindle cells on non-chondroid origin and S-100 protein by the cartilaginous cells. The patient had repeated CT scan 2 years post-operatively, which showed very tiny calcifications and no recurrence.

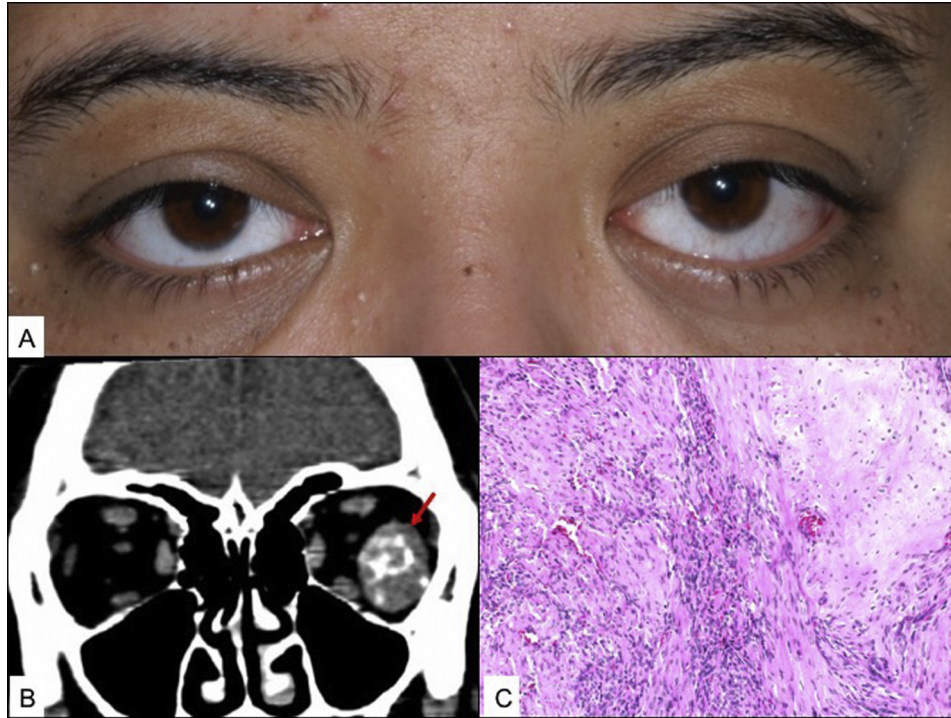


Fig. 3. (A) The clinical appearance in the 17-year old boy (Case 3) with left proptosis and scleral show. (B) Coronal computerized tomography scan showing the left intraconal calcific well-defined round mass (Red arrow). (C) The typical mesenchymal chondrosarcoma tumor in case 3 showing biphasic spindle cells and immature chondroid islands (Original magnification x200 Hematoxylin & Eosin).

Discussion

Mesenchymal chondrosarcoma (MCS) is a rare subtype of chondrosarcoma accounting for around 2–3% of cases.⁶ Extra-skeletal mesenchymal chondrosarcoma is unusual accounting for one third of the total MCS cases. The orbit is the third most common extra-skeletal site following the meninges and lower extremities.^{2,3} Unlike skeletal mesenchymal chondrosarcoma, orbital lesions tend to be predominant in females, and affects the age group of second and third decades.^{2,7} However, this was not evident in our three cases, where our patients were all males; and were in the pediatric age group (Table 1). Congenital MCS has been reported in two studies, one of which was orbital.^{8,9} On the other hand, the neoplasm has been reported in an 84-year-old lady by Shimo-Oku in 1980.¹⁰ The mean duration of symptoms before the diagnosis was 6 months ranging from 2 weeks to 19 months.⁷ Clinically, orbital chondrosarcoma patients mainly present with progressive proptosis often developing over months to years, as seen generally in our patients.^{5,7}

Less frequent symptoms include: pain of variable severity, diplopia and impaired vision while ptosis, lacrimation and nasal obstruction were less consistently described.^{5,7,11} One of our patients described painful eye movements as shown in Table 1. Optic nerve edema can also be noted but in advanced lesions.¹¹ Metastases at presentation are not mentioned in the literature, but subsequent dissemination has been reported.^{7,12}

Radiological studies are helpful as a guide towards accurate diagnosis. On CT scan, the lesion has been reported to be well-defined, heterogeneously enhancing and mainly located within the intraconal space.^{13,14} Bone destruction is usually not encountered but some may show widening of the orbital bone indicating slowly-growing lesions. Areas of mottled and fine calcification are seen within the mass and are crucial to reach to the diagnosis, which were noted in all our cases. On MRI, the tumor on T1-weighted scans have low to intermediate signal intensity and isotense to brain on T2-weighted scans, with moderate enhancement after gadolinium administration. Calcifications are noted as low

Table 1. Summary of the demographics and clinical signs and symptoms of our 3 cases.

Case No.	Age	Gender	Location	Duration of symptoms	Clinical symptoms	Examination
I	2.5 years	Male	Right eye	1 month	Proptosis	Proptosis (not measured) Hypoglobus, Frozen globe + 4 Afferent Pupillary Defect Café-au-lait spots
II	6 years	Male	Right eye	Not known	Proptosis	Proptosis 4 mm
III	17 years	Male	Left eye	1 year	Proptosis Eyelids swelling, Lagophthalmos	Proptosis (4 mm) Hyperopia, Mild eyelids swelling Painful eye movements

Table 2. Radiological and pathological findings in the 3 cases.

Case No.	CT scan findings	MRI findings	Tumor size	Gross pathology	Microscopic findings	IHC staining
I	Right orbital intraconal mass of homogeneous density filling the retrobulbar space, extending along the optic nerve. Expansion of the bony orbit with ill-defined medial wall	Partially lobulated intraconal mass extending to extraconal space. Isotonic signal intensity equal to the brain grey matter on T1 & T2. Peripheral rim enhancement with contrast. The optic nerve could not be identified	55 × 30 mm	Multiple friable pieces of tissue	Undifferentiated round cells with hemangiopericytoma-vascular pattern. Focal myxoid stroma and immature cartilage areas	Mesenchymal cells expressing Vimentin and CD99 Focal expression of CD56 and NSE
II	Large right superior orbital mass with calcifications		30 × 15 × 11 mm	Tan-white mass, smooth exterior surface, firm interior	Biphasic tumor in with immature cartilage, central calcification and surrounding spindle mesenchymal cells	Mesenchymal cells expressing CD99 Chondroid area cells staining with S-100 highlighted vascular pattern by CD34
III	Well-defined left intraconal mass, minimal displacement on the optic nerve. Areas of fine and coarse calcification minimal enhancement with contrast injection		22 × 17 mm	Gray to pink in color, well defined, and slightly lobulated without a definite capsule	Islands of cartilaginous tissue with central areas of calcification and other larger areas of small round oval to spindle-shaped mesenchymal cells constituting the stroma between the islands of the immature cartilage. Delicate vascular channels with hemangiopericytoma-like vascular pattern	Mesenchymal cells expressing CD99 Chondroid area cells staining with S-100

signals in both T1- and T2-weighted scans. However, mild enhancement is seen even within the calcified component on contrast-enhanced MRI.^{14,15}

Since the tumor is well-defined with moderate contrast enhancement, the diagnosis is often delayed and can be mistaken with more common lesions such as neural tumors (meningioma, schwannoma, and neurofibroma), vascular lesions (sclerosing hemangioma), fibrous tumors (solitary fibrous tumor and fibrous histiocytoma), and rhabdomyosarcoma in younger age groups.^{13–15} Our cases were consistent with those mentioned in the literature regarding radiological and histopathological examination (Table 2). Grossly, the tumor appears to be lobulated, soft to firm, grey-white to reddish tan focally calcified or cartilaginous and often vascular.^{2,3,13} On microscopic examination, the MCS show two basic histopathological cellular features: the undifferentiated, round, spindle-shaped mesenchymal cells arranged in sheets or small clusters and the areas of cartilaginous tissue. This cartilaginous differentiation is crucial to reach the diagnosis of MCS.^{3,16} It consists of endochondral ossification with bone formation, coarse calcification or a loosely arranged mature hyaline cartilage. Some tumors may show vascular spaces with a hemangiopericytic pattern. The mesenchymal cells are undifferentiated with round or elongated hyperchromatic nuclei and scanty cytoplasm. While the spindle cells are usually more pleomorphic with atypical islands of well-differentiated hyaline cartilage.^{2,3,13,16} Immunohistochemistry can be done in cases of doubt to differentiate MCS from Ewing's sarcoma and soft-tissue chondroma. The tumor cells express positivity for S-100 protein in the cartilaginous area and CD99 and vimentin in the cellular component, which was observed in our cases as shown in Table 2.^{16,17} Type II collagen is expressed by the extracellular matrix of the neoplasm in the chondroid islands as well as the non-chondroid areas.¹⁶

The mainstay treatment of MCS is surgical. Radical surgical excision with wide margins of resection is known to be the most effective modality. Radiotherapy and chemotherapy are considered in cases where the tumor cannot be resected or appears histologically aggressive.^{2,7,13} The prognosis of MCS is highly variable. When considering all sites, the prognosis is generally poor. Local recurrence and distant metastasis can occur after more than 20 years, thus a long-term follow up is essential. However, despite the small number of cases reported, orbital MCS have a higher survival rate than MCS in other locations.^{2,7}

Conclusions

Extra-skeletal mesenchymal chondrosarcoma is a rare neoplasm with isolated case reports of orbital primary involvement including a single case of congenital MCS and few cases in the pediatric age group. Here we are reporting 3 cases in children, and all were males in contrary to what has been concluded in the orbit. Although rare, it should be considered in calcified lesions affecting children and young adults. Complete removal of the neoplasm is the primary management with long-term follow up.

Conflict of interest

The authors declare that there is no conflict of interest.

Acknowledgment

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