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Alveolar soft part sarcoma of the superior rectus muscle: Case report and review of literature

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ABSTRACT

Purpose: Alveolar soft part sarcoma (ASPS) is a very rare type of soft tissue sarcomas which usually occurs in the limbs and trunk.

Observations: A 25-year-old woman presented with proptosis and redness of the right eye for 8-month. She suffered from severe right upper lid edema, conjunctival chemosis, downward displacement of the globe, and proptosis. Radiological imaging was nonconclusive. Histopathological evaluations confirmed ASPS. The patient underwent exenteration as a lifesaving procedure. At 16-month follow-up, the patient is stable without any signs of recurrence or metastasis.

Conclusions and importance: We report an extremely rare case of ASPS occurring in the superior rectus muscle. Few orbital ASPS cases have been reported in the literature. A literature review of orbital ASPS was done to shed lights on the diagnosis and management of this rare tumor.

1. Introduction

Alveolar soft part sarcoma (ASPS) is a very rare type of soft tissue sarcomas that commonly occurs in the limbs and trunk of adults and head and neck of children.[1,2] ASPS accounts for less than 1% of all sarcomas and is unusual to form primarily in the orbit.[1,2] ASPS seems to affect more females and the left orbit.[1] Radiological findings and typical histopathological features can establish the diagnosis.[3] Currently, the management is mainly complete tumor resection.[1,2] Herein, we report a case of superior rectus muscle ASPS in a young female, and we review the literature.

2. Case report

A 25-year-old female presented to our oculoplastic service at Farabi eye hospital with a painless proptosis and redness of the right eye for 8-month. Her initial best-corrected visual acuity (BCVA) was counting fingers at 2 m and 20/25 in the right and left eye, respectively. External examination of the right eye showed severe ptosis, severe proptosis, downward displacement of the globe, and limitation of movement in all gazes (Fig. 1A). Slit-lamp examination revealed severe eyelid erythema and edema, conjunctival injection, and chemosis (Fig. 1B). The examination of the left eye was normal.

Orbital computed tomography (CT) scan showed a large ovoid extraconal homogenous solid mass measuring 5.2 × 2.5 cm. The lesion was in the right upper orbital cavity within the superior rectus-levator complex, causing globe indentation and optic nerve compression (Fig. 1C and D). Brain and orbital magnetic resonance imaging (MRI) showed no extension to the cranial fossa or the sinuses (Fig. 1E and F). No signs of metastasis were evident in the systemic examination or imaging.

Biopsy demonstrated foci of alveolar pattern separated by fibrous stroma (Fig. 2A). Neoplastic infiltration composed of large polygonal cells with eosinophilic granular cytoplasm containing nuclei with prominent nucleoli arranged in solid sheets were seen (Fig. 2B and C). Numerous tumoral cells cytoplasm contained Periodic acid-Schiff (PAS) positive diastase granules (Fig. 2D). The tumor was highly vascular, and mitotic figures and tumor necrosis were present. Perineural and lymphovascular invasion were noticed. Muscle markers (vimentin, desmin, and myoglobin) and non-muscle markers (S-100 and Ki67) were used for immunohistochemical (IHC) staining in our case. All markers were negative. The histopathological and immunoprofile confirmed the diagnosis of ASPS. According to the eighth edition of the American Joint Committee for Cancer Classification (AJCC), the cancer had a T3M0N0 staging at the time of diagnosis.[4]

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Abbreviations

ASPS	alveolar soft part sarcoma
BCVA	best-corrected visual acuity
CT	computed tomography
MRI	magnetic resonance imaging
PAS	periodic acid-Schiff
IHC	immunohistochemical
AJCC	American Joint Committee for Cancer Classification
EBRT	external beam radiotherapy
RECIST	Response Evaluation Criteria in Solid Tumors

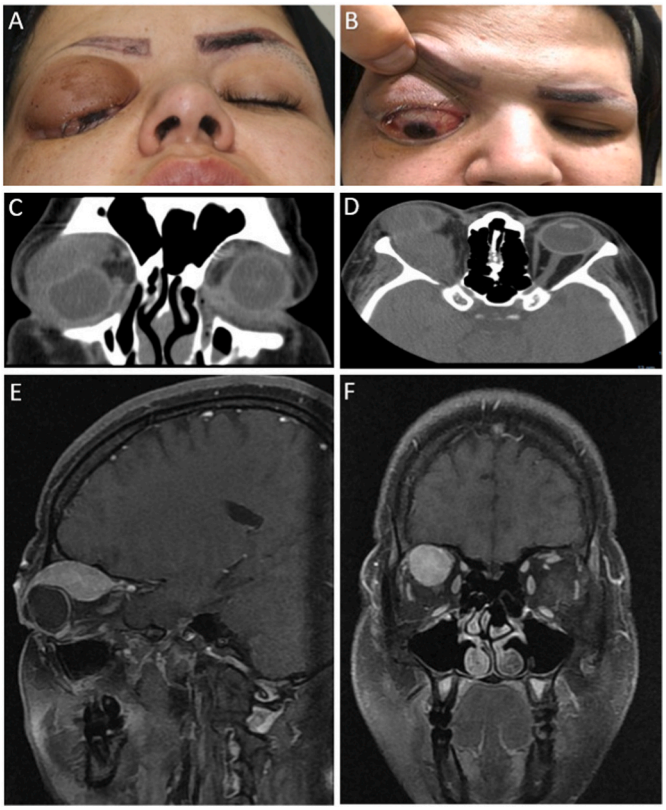

Fig. 1. A and B, External photographs of a 25-year-old woman showing severe eyelid swelling, ptosis, proptosis, downward displacement of the globe, and injection. C, Coronal orbital computed tomography (CT) scan showing isodense superior mass with globe indentation. D, Axial orbital CT scan showing the mass inside the superior rectus muscle throughout its length to apex and exhibiting optic nerve compression. E, Sagittal T1-weighted Fat Sat magnetic resonance imaging (MRI) contrast image showing hyperintense fusiform mass lesion of the superior rectus muscle sparing the origin and insertion. F, Coronal T1-weighted Fat Sat MRI contrast image showing the orbital mass with no cerebral or sinuses extension.

The patient underwent concurrent neoadjuvant chemotherapy (Doxorubicin 20 mg/m^2 weekly for 8 cycles) and external beam radiotherapy (EBRT) with a total dose of 6000 cGY in 30 fractions over 5 weeks. Unfortunately, the response to the neoadjuvant treatment was poor and would be labeled stable disease as per the Response Evaluation Criteria in Solid Tumors (RECIST 1.1) criteria.[5] Therefore, orbital exenteration was inevitable. The resected tumor measured about 5.2 cm at its largest diameter. Based on our experience, we performed a minimal reconstruction and let the granulation tissues grow in the empty space. The cut surface of the tumor showed a homogeneous, yellowish

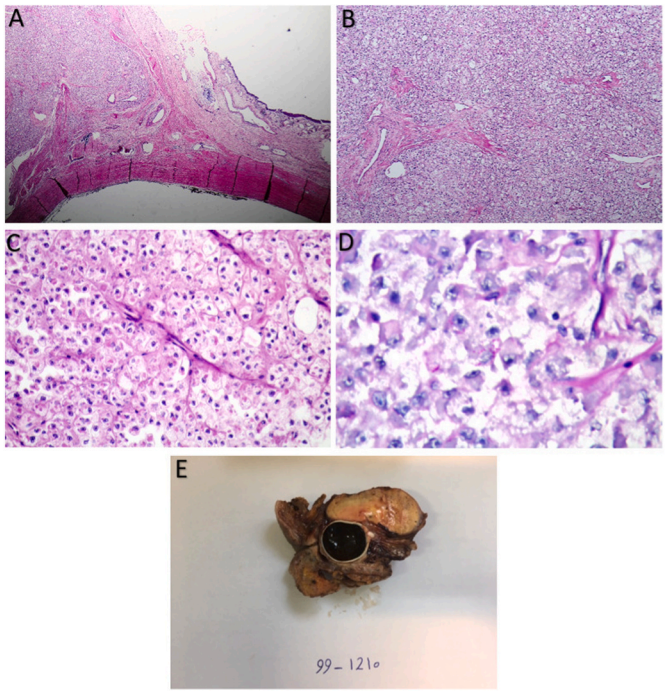

Fig. 2. A, Histopathologic examination shows a solid alveolar growth pattern separated by thick, fibrous septa near the sclera (hematoxylin-eosin [H&E], 20 ×). B and C, Low (100 ×) and high (400 ×) power view of typical alveolar soft-part sarcoma, showing an organoid, pseudoalveolar proliferation of large, eosinophilic cells and a delicate capillary network (H&E). D, Granular or needle-like crystals are seen in the cytoplasm of tumoral cells by periodic acid-Schiff (PAS) positive diastase resistant (PAS diastase, 400 ×). E, A macroscopic longitudinal section of the orbital exenteration specimen showing a partly well-defined creamy solid tumor.

appearance (Fig. 2E). The eye globe, optic nerve, and surgical margins were tumor free. Serial follow-up orbital MRIs were obtained and showed no evidence of recurrence or metastasis. At 16-month follow-up, the patient is still having complete response as per RECIST guidelines.

3. Discussion

ASPS is an extremely rare neoplasm of soft tissues and affects mainly children and young adults. More than 15% of ASPS cases involve the orbit.[1] The high rate of relapse makes its early and correct diagnosis very crucial.[6] These tumors grow slowly without pain. We reviewed the literature in PUBMED and found only 89 cases of orbital ASPS reported worldwide from 1963 till 2021.[1–3,6–45] Table 1 summarizes the recent orbital ASPS cases reported in the literature. Our case is the second from the Middle East and North Africa region and first from Iran. The average age at diagnosis is 16.05 years with a median of 12 years (range 10 months–69 years).[1–3,6,12–18] Children less than 20 years old made up 71.25% of the cases, and 41.25% were less than 10 years. There is a slight female predilection with a female-to-male ratio of 1.32:1[1–3, 6-35, 38, 39, 41-45] and a preferential involvement of the left orbit (57.75%).[1–3,6,8,9,11–35,38,39,41–43,45] The average tumor size is 3.33 cm with a median of 3 cm (range 1.5–8.6 cm).

Using the Kaplan-Meier method, the calculated 1- and 11-year overall survival rates of reported orbital ASPS cases are 94.2% and 82.4%, respectively. Subgroup analysis for age and sex were not significant due to small sample size. Previously, Liberman et al. reported the 2- and 10-year survival rates of all ASPS to be 77% and 38%.[46] Therefore, the orbital ASPS subtype might have a better long-term survival. The average follow-up duration was 46.54 months with a median of 16 months (range 1 month–248 months). Out of the 73 patients with follow-up data, 53 (72.60%) were alive with no evidence of disease and

Table 1
Recent case reports in PubMed of orbital alveolar soft part sarcoma.

Author	Country	Number	Age (year) (median)	Sex	Eye affected	Location	Size (cm)	Management	Follow-up
Koka et al. 2021[2]	India	5	3 13 8 17 22	4 M, 1 F	3 L, 2 R	Superior extraconal; Medial extraconal and intraconal; Intraconal; Inferolateral extraconal; Orbital mass with extra-orbital extension	NM	B + S Em + S + R Em + S + C Em + S + R E + graft + R + C	11.2 m (5–15 m); 4 no Rec or M; 1 M, died
Oda et al. 2021[3]	Japan	1	29	F	L	Lateral orbit, extended to the superior orbital fissure, intra- and extraconal	3.4 × 1.9 × 2.0	S	NM
Wang et al. 2020[4]	China	3	1 12 9	2 F, 1 M	3 L	posteroinferior; intraconal; posterosuperior	3.5 × 2 × 2.5 2.4 × 2.0 × 1.5 3.8 × 2.5 × 1.6	S + R S + R S + R	3 y/Rec, free after S + R; 11 y/Rec, cerebral M, died; 8 y/Rec, free after S + R
Alghulaiga et al. 2020[11]	South Korea	1	5	M	L	lateral rectus muscle	2.5 × 1.9 × 1.7	S	51 m/no Rec or M
De Barros et al. 2019[10]	Canada	1	31	F	R	intramuscular inferior	1.6 × 1.5 × 1.4	E	2 y/no Rec or M, history of breast cancer
Nava-Castañeda et al. 2017[9]	Mexico	1	4	F	L	inferotemporal extraconal	3.5	S	6 m/no Rec or M
Hei et al. 2017[1]	China	8	19, 51, 2, 6, 2, 9, 10, 32	3 M, 5 F	3 R, 5 L	medial orbit adherent to medial rectus extending to apex; medial optic nerve and medial rectus; Inferior rectus; Between superior rectus and levator; Medial rectus; Inferolateral inferior rectus + lateral rectus + optic nerve; Lateral rectus	2.5 × 1.5 × 1.5 3.5 × 3.5 × 1.2 5.0 × 3.6 × 0.8 2.0 × 1.5 × 1.2 2.0 × 2.0 × 2.0 4.5 × 3.0 × 1.0 4.5 × 3.0 × 1.5 5.0 × 3.0 × 2.0	S + R S + E + R S S + R S + R E + R + C B + E S + R + C	6 m/no Rec or M, Lost; 2 m/Rec at 1 y, died; 61 m/no Rec or M; 49 m/no Rec or M; 13 m/no Rec or M; 13 m/no Rec or M; 3 m/no Rec or M;
Chaudhari et al. 2017[7]	India	1	22	M	R	Superior rectus + superior oblique + inferior oblique + optic nerve	5 × 4.7 × 3.7	E + R	6 m/no Rec or M
Xu et al. 2016[5]	China	1	10	F	L	Lower outer quadrant	1.5 × 2.0 × 0.8	S + C	12 m/no Rec or M
Mulay et al. 2016[6]	India	1	7	M	L	Superior quadrant	NM	S + R	NM
Kumar et al. 2016[8]	India	1	7	F	L	All orbit	8.6 × 7.5	E + C	NM (misdiagnosed and treated first as rhabdomyosarcoma

m, months; y, years; B, biopsy; S, surgical excision; E, exenteration; Em, embolization; R, radiotherapy; C, chemotherapy; Rec, recurrence; M, metastasis; NM, not mentioned.

8 (10.96%) were alive with local recurrence.[1–3,6,12–18] Six (8.22%) patients had lung metastasis, with one of these patients also exhibited brain metastasis and another liver metastasis.[2,6,9–11] Six (8.22%) patients died due to ASPS recurrence or metastasis,[1,2,6,8,9] and 3 (4.11%) patients died due to unrelated causes.[8,9] A total of 9 patients were lost to follow-up.

The most common reported clinical findings are exophthalmos (81%), eyelid swelling (30%), and conjunctival congestion (20%).[17] Pain, diplopia, and tearing are less frequent complaints. Decreased vision can be expected in case of optic nerve compression.[6] Font et al. reported the median duration of symptoms to be 4 months (range 2 weeks–7 years).[9] The symptoms are detected earlier in orbital ASPS cases—leading to a shorter disease course and smaller tumor size in comparison to non-orbital cases.[1] The median age at diagnosis of

non-orbital cases is above 30 years.[1] Orbital involvement can be primary or secondary due to invasion from paranasal sinuses.[9]

It is postulated that the determining prognostic factors of ASPS are the presence of metastasis at diagnosis, large tumor size, and older age.[1,2] Our patient was 25-year-old with large tumor size of 5.2 cm but no evidence of metastasis. The surgical margins were tumor free, and currently the patient exhibits no sign of recurrence 16-month postop. She was previously healthy. She underwent orbital exenteration, which is currently the best life-saving option.[1,9,17] The survival rate of young patients less than 20 years is remarkably higher. Local recurrence may occur in 1/5 to 1/2 of orbital ASPS. Furthermore, metastasis is not uncommon even in late course.[6] Hence, long-term follow-up is recommended.

Several differential diagnoses should be considered including rhabdomyosarcoma, hemangioma, melanoma, hibernoma, granular cell tumor, and metastasis.[6] Histopathology, IHC, and genetic tests are sensitive techniques for diagnosis, whereas imaging shows unspecific findings. CT scan usually reveals a homogeneous, well-defined, isointense soft-tissue mass that enhances with contrast. MRI shows hyperintense signal intensity on T1 and T2-weighted images, and intense enhancement with contrast. ASPS can be highly vascular, which exhibits flow voids on MRI.[2] Previous reports suggested that ASPS is of myogenic origin.[1] In addition to our patient, we counted 29 patients from the literature whose tumors had been associated with extraocular muscles. Histologically, ASPS demonstrates round to polygonal tumor cells arranged in alveolar pattern and separated by fibrous septa. The abundant eosinophilic cytoplasm shows PAS-positive diastase-resistant granules in 80% of patients.[1] ICH markers also help in the differential diagnosis. Positive nuclear staining of TFE3 is reported in up to 90% of ASPS cases.[10] As seen in our patient, the Ki67 proliferative index is generally low indicating a slow growing tumor. Other ICH markers are usually negative or nonspecific.

The choice of surgical plan is controversial. Complete surgical removal of small tumors and saving the globe is ideal. Although recurrence is seldom if the tumor has been completely resected, adhesion to other structures such as extraocular muscles and achievement of free margins are challenging. Many cases of orbital ASPS require exenteration or aggressive surgical resection. Exenteration was done for 26.5% of the reported cases. ASPS has a resistant nature to chemotherapy and radiotherapy. Current chemo- and radiotherapy regimens do not improve the survival rate of ASPS. Though, adjuvant radiotherapy is associated with lower local recurrence rate.[1,47] Resection of pulmonary metastasis is believed to prolong the survival rates of ASPS patients.[9,46] Nevertheless, due to the young age of our patient and the large tumor size, a course of neoadjuvant chemoradiotherapy was done to achieve the most success rate. Our patient had poor response to doxorubicin, an anthracycline. Treatment with vincristine and cyclophosphamide have inconsistent results.[17,48] Recent studies show ASPS sensitivity toward vascular endothelial growth factor receptor-tyrosine kinase inhibitors such as sunitinib, pazopanib, and cediranib.[48] Preoperative embolization was suggested to facilitate a smooth tumor excision with minimal intraoperative bleeding.[2,11]

4. Conclusions

In conclusion, orbital ASPS is a rare entity with no distinct clinical or radiological features. Histological and ICH are necessary for diagnosis. Neoadjuvant chemo- and radiotherapy are not effective. Total surgical resection is the current best option. Orbital ASPS has a better survival rate than ASPS in other locations. However, long-term follow-up is recommended due to potential recurrence. Future investigations are advised to delineate the best treatment protocol.

Patient consent

This report was prepared in accordance with the Declaration of Helsinki. The patient's consent for the publication of identifiable photographs was also obtained.

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Declaration of competing interest

None.

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