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Case report

Malignant solitary fibrous tumor of the orbit: Spectrum of histologic features

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ABSTRACT

Purpose: Primary malignant solitary fibrous tumor (SFT) of the orbit is a rare spindle cell neoplasm that requires excisional biopsy for histopathological diagnosis. We present a clinical case using contemporary immunohistochemical stains, report on the latest World Health Organization classification, and provide a review of the literature.

Observations: Report of a single case of a 65 year old male who presented with right-sided proptosis, limited adduction, ptosis, lateral globe displacement, and cheek festooning. Neuroimaging revealed a 2.2 cm, extraconal heterogeneous mass that diffusely enhanced.

En-bloc tumor resection confirmed SFT malignancy based upon nuclear atypia, hypercellularity, and increased mitotic activity (13 mitotic figures/10 high powered fields). Ki-67 showed 2% nuclear staining in the benign tumor and 10–15% staining in the malignant counterpart. Immunohistochemical analysis revealed diffuse Stat6 positivity, CD 34 positivity with partial lack of staining within the malignant portion, S-100 positivity in the malignant portion, and overall negativity for CAM 5.2, desmin, actin, CD 31, and CD 117.

Conclusions and importance: Immunoprofiling is helpful to making the diagnosis of malignant solitary fibrous tumor of the orbit. Complete tumor resection continues to be the preferred treatment. The behavior of extrathoracic SFT is unpredictable, and patients with SFT in all locations require careful, long-term follow-up.

1. Introduction

Initially described in the pleura by Stout in 1942, solitary fibrous tumors (SFT) are rare spindle cell neoplasms of mesenchymal origin. Today, SFTs comprise a spectrum of tumors ranging from those arising from the pleura with associated paraneoplastic syndromes such as hypoglycemia, to multiple soft tissue sites and the meninges.[1] Primary malignant orbital SFT, however, is a rare entity. We report an additional case that was diagnosed based upon current histopathology and immunoprofiling techniques.

2. Case report

A 65 year old male presented with persistent swelling and discharge from the right eye for over nine months. Best corrected visual acuity was noted to be 20/40 and 20/25 in the right and left eyes, respectively. Pupils were round and reactive without afferent pupillary defect, visual fields were normal to confrontation, and intraocular pressures were normal in both eyes. On external examination, the patient had limitation on adduction of the right eye resulting in binocular horizontal diplopia on left gaze. The patient also had right upper eyelid ptosis and conjunctival injection that had been previously attributed to allergic conjunctivitis. Dilated funduscopic examination was normal without signs of disc edema, optic atrophy, or choroidal folds. Neuroimaging revealed a 2.2 cm heterogeneously enhancing right medial extraconal mass (Fig. 1).

The patient underwent a transcaruncular orbitotomy for biopsy, which revealed solitary fibrous tumor based on positive staining for CD34 and BCL2 on histopathological analysis. Subsequent en bloc orbital tumor removal revealed a malignant solitary fibrous tumor

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3. Discussion

Two percent of solitary fibrous tumors arise from soft tissue and typically affect individuals in their fifties. Hypoglycemia has been described; and ten to fifteen percent of patients have metastases at the time of diagnosis.[1] In 2013, the World Health Organization reclassified extrapleural solitary fibrous tumors to be a "ubiquitous mesenchymal tumor of fibroblastic type," which shows a prominent "branching vascular pattern," and rescinded the term, "hemangiopericytoma" (HPC).[2]

Historically, the term 'hemangiopericytoma' has been used to describe lesions with a characteristic "staghorn" branching vascular pattern. However, it appears that it may have been a misnomer; and in fact this growth pattern is shared by unrelated entities that are both benign and malignant. In 2006, Gengler and Guillou proposed categorizing these HPC-like tumors into lesions that infrequently display the characteristic features (i.e. synovial sarcoma), clearly show "myoid/pericytic differentiation" that are usually benign (i.e. glomangiopericytoma/myopericytoma, infantile myofibromatosis, and a subset of sinonasal HPCs), and those that are solitary fibrous tumors, which also includes fibrous-to-cellular lesions (i.e. giant cell angiofibromas and lipomatous HPCs).[3]

Orbital SFTs can present as unilateral proptosis, eyelid swelling, or dysmotility. Diagnostically, they are indolent lesions that are oftentimes heterogeneous with low T2 signal intensity on MRI.[1,4] Tumor excision typically reveals well circumscribed, partially encapsulated, colorless masses that are firm and multinodular. SFTs are oftentimes benign with intermediate biologic potential due to low rates of local recurrence or metastasis.[2,4] Clinical and radiological features, however, do not necessarily correlate with histological signs of malignancy.

It is important to establish the diagnosis of malignant SFT because of their higher mortality rate. Immunohistochemical analysis continues to be the gold standard for diagnosis. Histological analysis of SFT reveals mixed hypo and hypercellular regions delineated by hyalinized collagen and thin vessels, as well as frequent myxoid changes and rare mitotic figures. Tumor cells usually stain positive for specific markers such as CD34 (90–95%) and Stat6, but variably to S-100 protein, keratin, and desmin.[2–6]

In contrast, locally aggressive or malignant SFTs can show interval increase in size, increased cell mitoses, atypia, necrosis with and without hemorrhage, and infiltration into adjacent structures. Mitotic index appears to be the best prognostic indicator to date.[2] Areas of malignancy are typically CD 34 negative, while positive for Stat6, S-100, p53, cytokeratin, and certain gene fusion variants of NAB2-STAT6 (Table 1).[1–4,6–9]

Long term follow-up is essential. Further efforts to identify signaling pathways that lead to tumor dedifferentiation and malignant transformation will likely establish prognostic indicators and targets for multimodal therapy. Currently, the identification of signaling pathways that portend poor prognosis has yet to be fully elucidated. Recent biomolecular studies suggest the potential role of the nuclear signal transducer and activator of transcription 6 (STAT6) gene, given the discovery of NGFI-A binding protein 2 (NAB2)-STAT6 as a SFT-specific fusion gene.[8,9] However, while Stat6 is a highly specific marker for SFTs, the prognostic role of various NAB2-STAT6 fusion genes in determining disease free survival remains unclear.[6,10] Future studies will continue to delineate the oncogenic cascade in malignant SFTs, and these genes may impact overall prognostication and serve as designer therapy targets.

4. Conclusions

Complete surgical resection with long term follow-up and longitudinal neuroimaging to monitor for recurrence is essential. Locally advanced, recurrent, or metastatic extrapleural SFT lesions

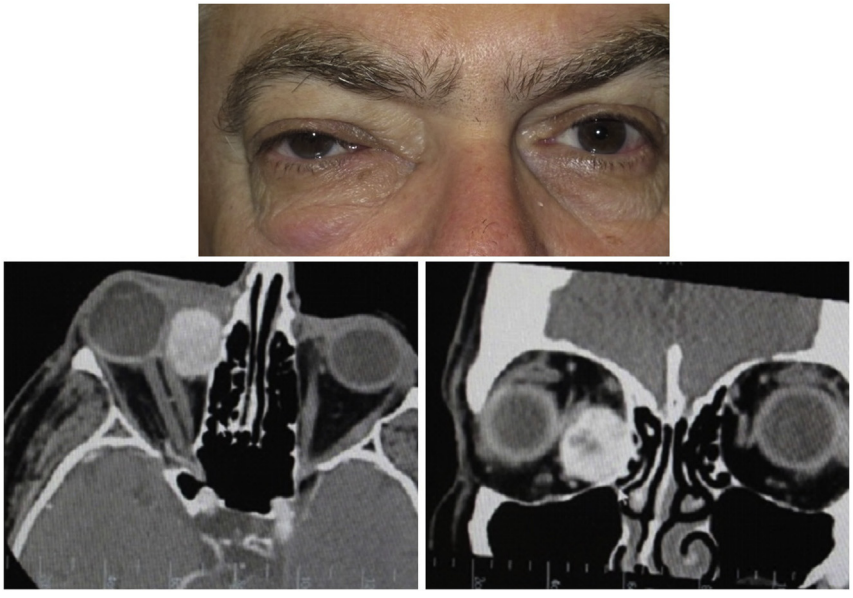

Fig. 1. Patient Characteristics: Patient presents with right-sided exophthalmos, lateral globe displacement, upper eyelid ptosis, and diminished adduction. Axial and coronal computed tomography scans reveal a large, enhancing, extraconal mass displacing the globe laterally.

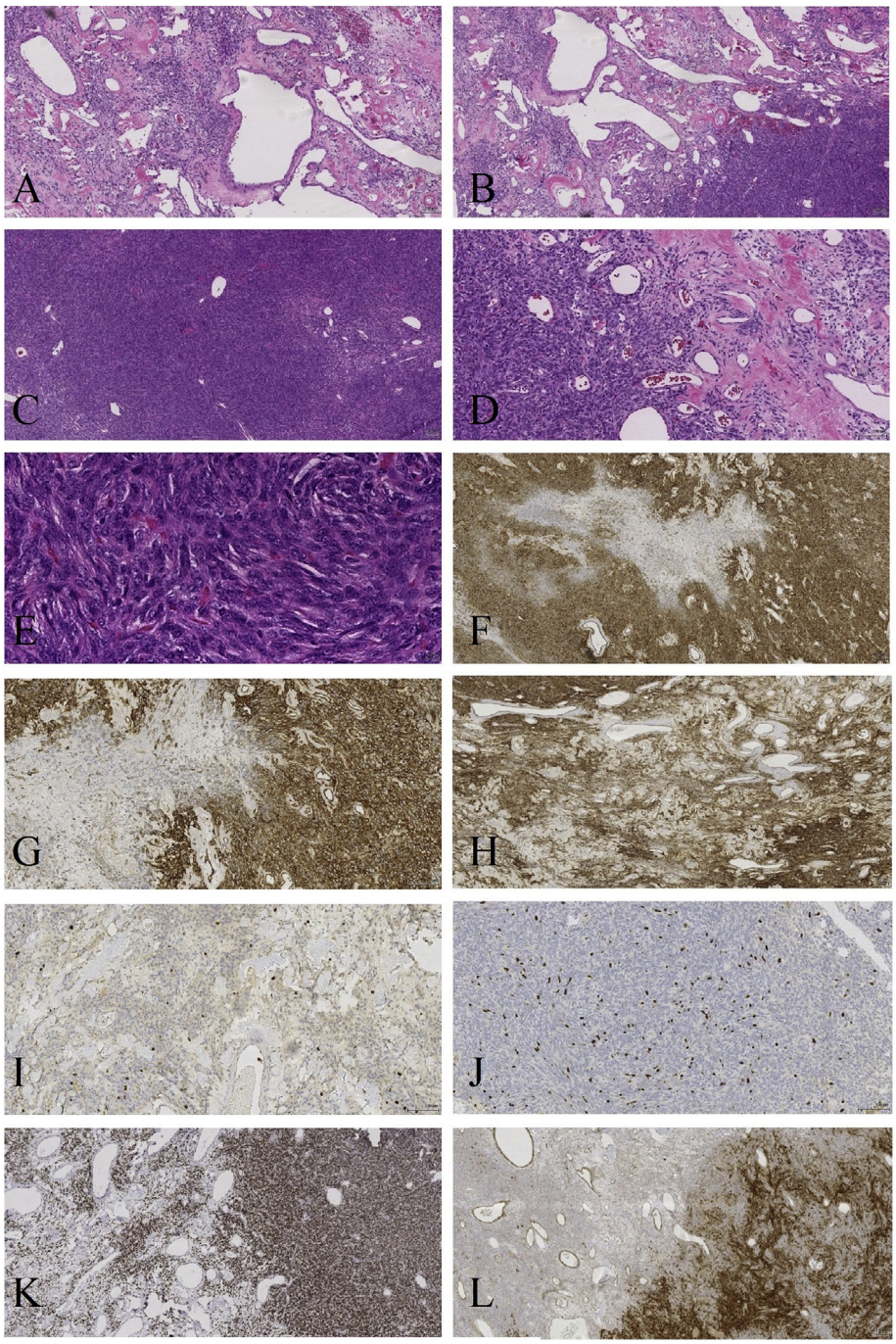

Fig. 2. Histopathological Findings: A-E. Hematoxylin and eosin (low power benign, transition, malignant zones; high power transition, malignant zones) F-H. CD-34 (low power positivity in benign, low and high power areas of decreasing staining within malignant zone) I-J. Ki-67 (high power differential staining in benign (2%) and malignant (10–15%) zones). K. Stat6 (low power diffuse positivity in benign, malignant, and transition areas). L. S-100 (low power positivity in malignant portion of transition zone).

Table 1
Radiographic and Immunohistochemical Markers of Benign vs. Malignant Solitary Fibrous Tumor.

SFTs	Ultrasound	CT	MRI	Pathology	Immunohistochemistry
Benign	Well circumscribed, homogenous, echo-lucent	Heterogeneous enhancement	Heterogeneous enhancement, isointense (T1), hypointense (T2)	Spindle cells arranged in fascicular pattern, vascular channels, +/− cysts	$CD34^{+}$ STAT6+
Malignant	+/− invasion of surrounding structures	Interval increase in size, +/− invasion of adjacent structures		Mitoses (>4 per 10 HPF), cellularity, pleomorphism, necrosis +/- hemorrhage	CD34− STAT6+ S100+ P53+ Cytokeratin+ +/− NAB2-STAT6+

*Abbreviations: CT, computed tomography; HPF, high-power fields; MRI, magnetic resonance imaging, SFT, solitary fibrous tumor.

have been treated with radiation or combination chemotherapy.[1,11,12] Due to the rarity of these tumors, the role of radiation and combination chemotherapy remains controversial.

Patient consent

Written patient consent was obtained.

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Conflict of interest

The following authors have no financial disclosures: LSE, MB, MSS, NR.

Authorship

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

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