

A Case of Orbital Solitary Fibrous Tumor

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Background: Solitary fibrous tumor is a spindle cell neoplasm that most commonly arises in the pleura and very rarely involves the orbit.

Case: A 38-year-old woman presented with slowly progressive proptosis of 3 months duration and optic nerve head edema in her right eye. Magnetic resonance imaging revealed a well-circumscribed, round mass lesion, which showed isointensity to the gray matter in a T1-weighted image, and variegated intensity in a T2-weighted image and contact with the optic nerve in her right orbit. The tumor was successfully removed by anterior orbitotomy.

Observations: The tumor showed a “patternless pattern” of tumor cell arrangement, alternating hypercellular and hypocellular areas, a hemangiopericytoma-like pattern, and thickened strands of collagen. Immunohistochemically, the tumor cells were positive for CD34 and vimentin, and all were negative for other markers of epithelial, neural, muscular, histiocytic, and vascular endothelial cell elements. The tumor was diagnosed as a solitary fibrous tumor, and the patient was doing well with no evidence of recurrence 15 months after surgery.

Conclusions: This case was the 19th reported case of solitary fibrous tumor in the orbital region. CD34 is a highly sensitive marker for solitary fibrous tumor. **Jpn J Ophthalmol 2001;45:412–419** © 2001 Japanese Ophthalmological Society

Key Words: Histopathological study, immunohistochemical study, magnetic resonance imaging, orbital tumor, solitary fibrous tumor.

Introduction

Solitary fibrous tumor (SFT) is a rare spindle cell neoplasm in adults. It most commonly arises in the pleura,^{1–4} but recently has been described in extra-pleural sites, such as the peritoneum,^{5,6} lung,^{3,5,7} pericardium,⁸ mediastinum,^{9,10} periosteum,¹¹ liver,¹² thyroid glands,¹³ parotid glands,¹⁴ upper respiratory tract,^{15–17} paranasal sinuses,¹⁶ intracranial meninges,¹⁸ and orbit.^{19–31} We report a rare case of orbital SFT. To diagnose SFT, researchers have utilized the pathological findings of a short fascicular, storiform, or haphazard arrangement of spindle cells exhibiting the so-called “patternless pattern,” alternating hypercellular and hypocellular areas, a hemangiopericytoma-like pattern of vascularity, and stromal

thickened strands of collagen.^{1–31} However, there are only a few pathological tumor markers for SFT. Solitary fibrous tumor is characterized by its consistently strong immunoreactivity to the antigen CD34.^{14,18,20–31} CD34 is initially a hematopoietic progenitor cell antigen, and recently has been detected in endothelial cells and vascular neoplasms as well as in primitive mesenchymal cells, mesenchymal spindle cell tumors, and certain connective tissue cells in the skin.^{20,24,25,32}

To our knowledge, there have been only 18 cases of SFT reported in the orbital region.^{19–31} We report the 19th case with the findings of magnetic resonance imaging (MRI), histopathological, and immunohistochemical studies.

Case Report

A 38-year-old Japanese woman with a 3-month history of proptosis in the right eye was referred to the Yamagata University Hospital on November 5, 1998. She had no history of trauma or sinusitis, and

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complained of no pain or vision changes. Ophthalmological examination showed that her visual acuity was RE: 1.2 and LE: 1.5. Intraocular pressure was normal in both eyes (15 mm Hg in the right eye, 16 mm Hg in the left eye). Exophthalmometry measured 17 mm in the right eye and 13 mm in the left eye (Figure 1). Ocular movement was normal. A solid mass was palpable on her right orbital medial-superior margin. The conjunctiva was not hyperemic or edematous. Pupils were symmetric, round, and reactive with no evidence of a relative afferent pupillary defect. Fundus examination with indirect ophthalmoscopy showed congestion of the optic nerve head associated with linear hemorrhage, but no choroidal folds in the right eye (Figure 2). A Goldmann visual field analyzer revealed enlargement of the Marriott scotoma and a depression in the temporal inferior site of her right eye. Critical fusion frequency used to examine the optic nerve function was 43 Hz in both eyes.

A computed tomography (CT) scan revealed a sharply defined soft tissue density mass, which was



Figure 1. (top) and (bottom). Proptosis is observed in right eye.

uniformly well-enhanced in the retrobulbar and medial sides of the right orbit. There was no evidence of calcification or bone destruction (Figure 3). Magnetic resonance imaging showed that a well-circumscribed, round mass had contact with the optic nerve. The lesion showed isointensity to the gray matter in a T1-weighted image, and iso- and hypointensity in the central area, and hyperintensity at the tumor's edge in a T2-weighted image. The lesion revealed good homogeneous enhancement on postcontrast using a gadolinium diethylenetriamine pentaacetic acid (Gd-DTPA) T1-weighted image (Figure 4). There were no systemic abnormalities.

The patient underwent excision of the lesion by anterior orbitotomy. As the tumor lay in the orbital fatty tissue and did not adhere to the adjacent structures, it could be totally excised. There was no evidence during the operation that the tumor had adhered to or invaded the optic nerve.

Postoperative visual acuity and ocular movement remained intact. Proptosis and optic disk edema of her right eye fully resolved. Visual field abnormalities, including enlargement of the Marriott scotoma and a depression in the temporal inferior site of her right eye, also resolved completely. Fifteen months after surgery, the patient was doing well with no evidence of recurrence.

Histological Examination/Materials and Methods

The surgical specimen was fixed in 10% buffered formaldehyde and embedded in paraffin. The tissue sections were stained with hematoxylin-eosin and examined by light microscopy. Immunohistochemical studies were performed on the formaldehyde-fixed paraffin-embedded tissues by the peroxidase-antiperoxidase technique, using antibodies to CD34, vimentin, S-100 protein, cytokeratin, desmin, smooth muscle actin, Factor VIII, and α -antichymotrypsin.

Results

Gross Pathology

The tumor was well-circumscribed and appeared encapsulated, elastic hard, and reddish in color. It had a solid appearance and pinkish-white color at the cut surface. It measured 22 \times 15 \times 15 mm (Figure 5).

Microscopic Pathology

Sections of the tumor showed alternating hypercellular and hypocellular areas. The hypercellular area was composed of spindle cells that were arranged haphazardly or in part were arranged in a storiform pattern

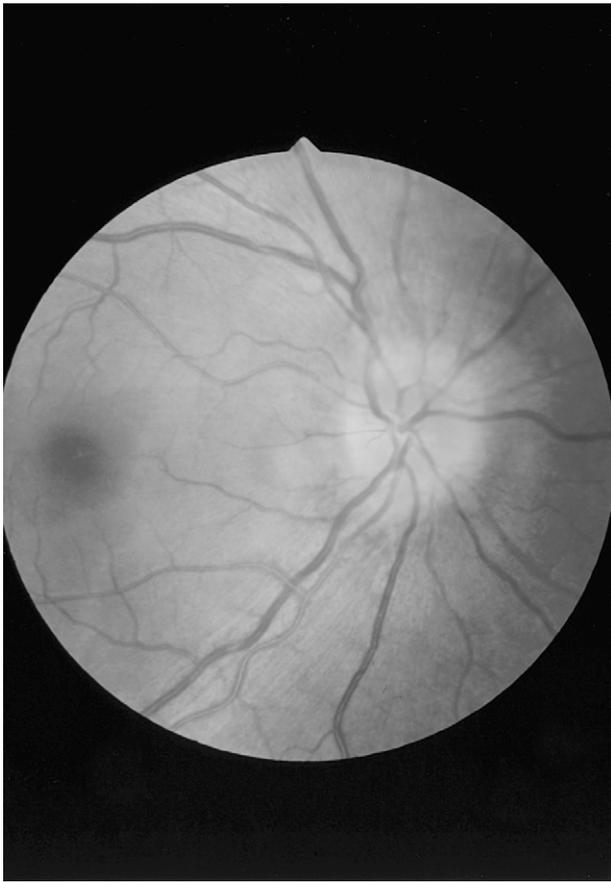


Figure 2. (left) Right eye. Optic nerve head is congested, and associated with linear hemorrhage at inferior edge (right) Left eye. No abnormal findings.

with short interlacing fascicles (Figure 6A). The hypocellular area was a less cellular sclerotic region in which tumor cells were interspersed with dense bundles of collagen (Figure 6 top right). In part, tumor cells were

seen around dilated staghorn-shaped vessels, creating a hemangiopericytoma-like pattern (Figure 6 bottom left). The tumor cells had uniform, oval, vesicular nuclei with finely dispersed chromatin and inconspicuous



Figure 3. Axial view by orbital computed tomography, (left) not enhanced, (right) contrast enhanced. Well-circumscribed, soft tissue density mass was seen in retrobulbar and medial sides of right orbit. Lesion was uniformly well-enhanced.

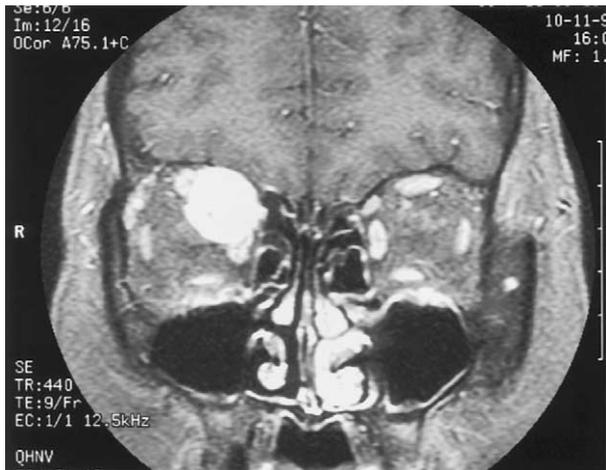
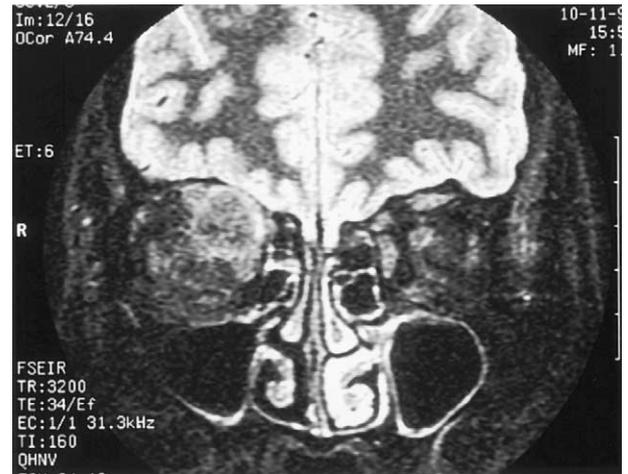
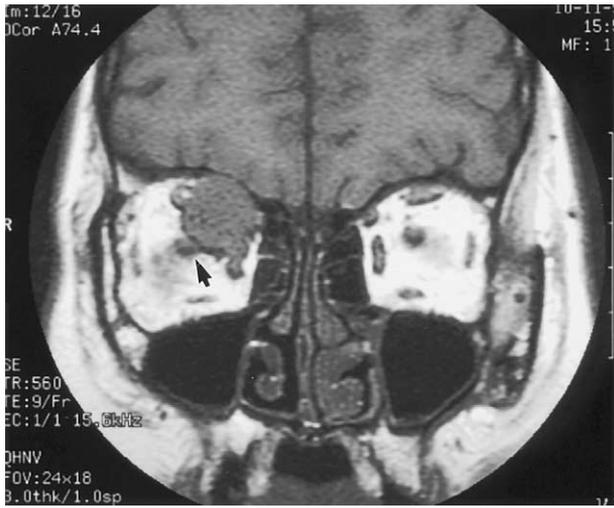


Figure 4. Coronal view by orbital magnetic resonance imaging, (top left) T1-weighted image, (top right) T2-weighted image, (bottom) postcontrast by gadolinium diethylenetriamine pentaacetic acid T1-weighted image. Lesion shows isointensity to gray matter in T1-weighted image, and iso- and hypointensity in central area, and hyperintensity at tumor's edge in T2-weighted image. Lesion shows homogeneous enhancement. Lesion is in contact with optic nerve (Arrow).



Figure 5. (left) Tumor was encapsulated, elastic hard, and reddish in color. (right) Solid appearance and pinkish-white color at cut surface.

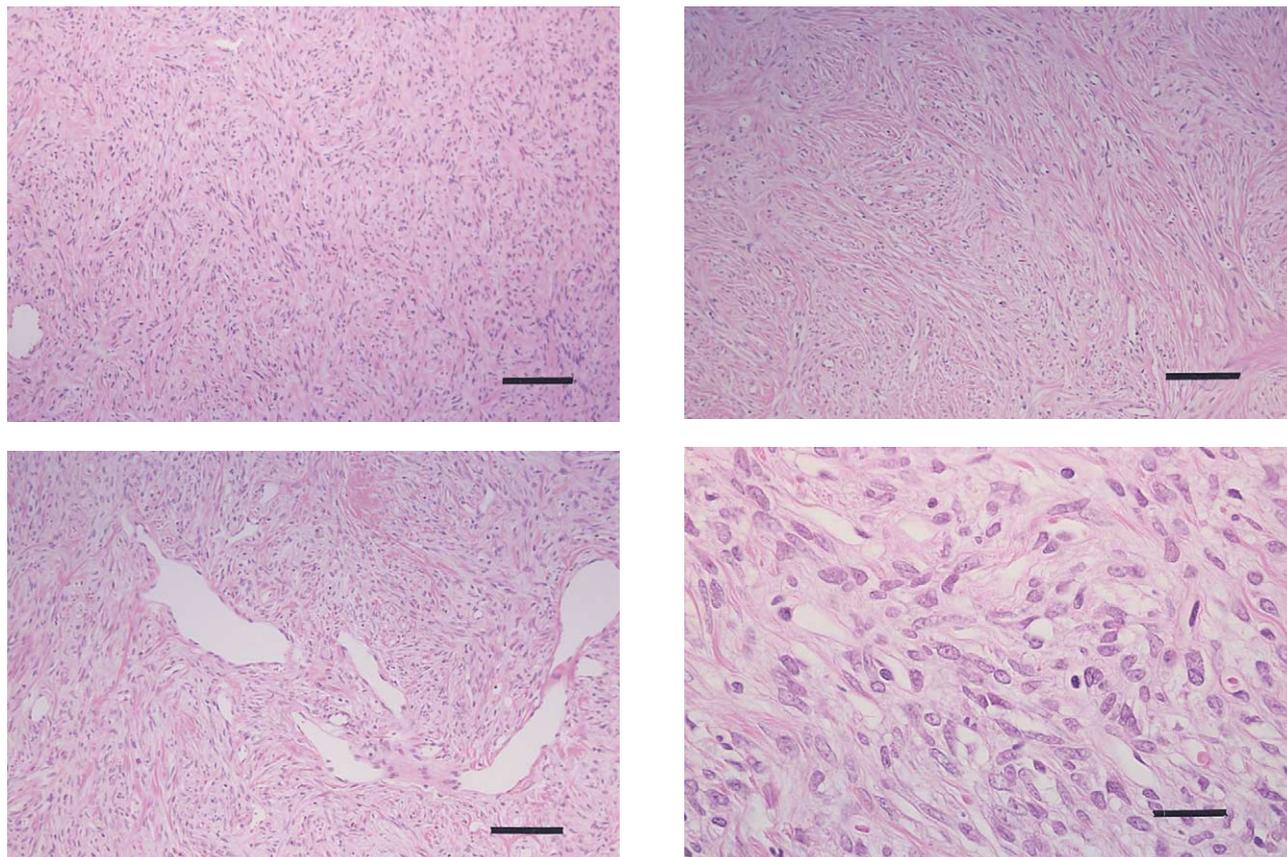


Figure 6. Microscopic findings with hematoxylin-eosin staining. (**top left**) Hypercellular area: many spindle cells are arranged haphazardly. Bar = 100 μm ; (**top right**) Hypocellular area: tumor cells are interspersed with dense bundles of collagen. Bar = 100 μm ; (**bottom left**) Dilated staghorn-shaped vessels are creating hemangiopericytoma-like pattern. Bar = 100 μm . (**bottom right**) Tumor cells have oval, vesicular nuclei with finely dispersed chromatin and inconspicuous nucleoli. Bar = 25 μm .

nucleoli. Mitotic count was low and areas of necrosis or hemorrhage were not seen (Figure 6 bottom right).

Immunohistochemically, the tumor cells were strongly positive for CD34 and vimentin. They were uniformly negative for S-100 protein, cytokeratin, desmin, smooth muscle actin, Factor VIII, and α -1-antichymotrypsin. These immunohistochemical findings are typical of SFT (Figure 7).

Discussion

Diagnosis

Solitary fibrous tumor was first described as a localized fibrous mesothelioma in the pleura by Klemperer and Rabin in 1931.¹ It was once thought to be of mesothelial origin and was called benign or localized fibrous mesothelioma.^{1,3,6,7,8,12} However, evidence of mesothelial differentiation has not been found by light microscopy or electron microscopy, or in the consistent negative immunoreactivity of epi-

thelial markers, or in the subsequent identification of this tumor in extrapleural sites not usually associated with serosal surfaces, including the thyroid glands,¹³ parotid glands,¹⁴ nasal cavity,^{16,17,22} and paranasal sinuses.¹⁶ This supports a mesenchymal, possibly fibroblastic/myofibroblastic origin for SFT.^{3-8,10,11,13,14,16-28,30}

The classic histologic features of SFT are a short fascicular, storiform, or haphazard arrangement of spindle cells exhibiting the so-called "patternless pattern," alternating hypercellular and hypocellular areas, a hemangiopericytoma-like pattern of vascularity, and stromal thickened strands of collagen.¹⁻³¹ In addition, synovial sarcoma-like areas and neural-type palisades have been described.² The present case showed these typical histologic features of SFT, including the "patternless pattern" of tumor cell arrangement, alternating hypercellular and hypocellular areas, a hemangiopericytoma-like pattern, and thickened strands of collagen.

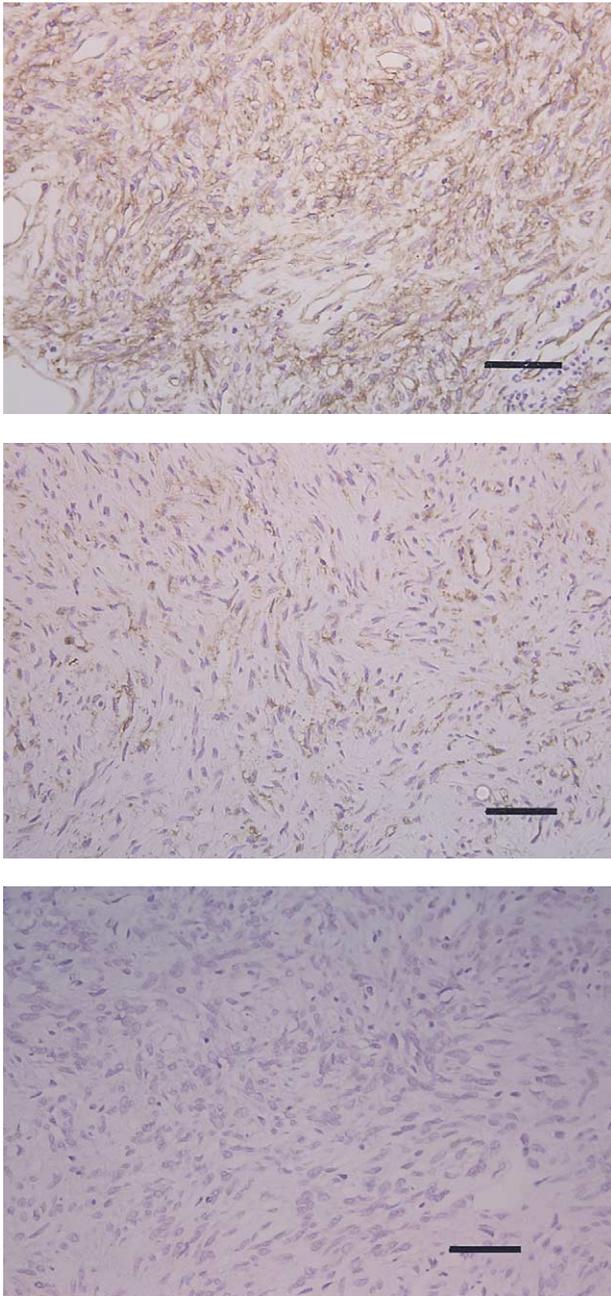


Figure 7. Immunohistochemical findings: Tumor cells are strongly positive for (top) CD34 and (middle) vimentin, and negative for (bottom) S-100 protein. Bars = 50 μ m.

Immunohistochemical Observation

Immunohistochemically, the tumor cells have been reported to express a strong diffuse immunoreactivity to CD34 antigen.^{14,18,20-31} In addition, vimentin (a marker of mesenchymal origin)^{2,3,5-17,19,21-25,27,28,30,31} is usually positive, and KP-1 (a marker of mesenchymal

and histiocytic elements: CD68) is occasionally positive.²¹ Immunohistochemical staining is negative for epithelial markers (cytokeratin,^{2,3,5-19,21-23,25,27} epithelial membrane antigen,^{2,3,5,7,11,12,15,18,19,21-23,25,27,28,30} carcinoembryonic antigen),^{3,9,22} neural markers (S-100 protein,^{2,3,5,7,10,11,13-19,21-23,25,27-31} glial fibrillary acidic protein,^{19,22,27} Leu-7,¹⁹ neurofilament),^{3,13,16,19,22} muscle element markers (desmin,^{2,5-7,11-16,18,21-24,27} smooth muscle actin,^{14,18,21,22,28,30} muscle-specific actin,^{14,21-23,30} myoglobin,²² actin),^{2,6,15-17,25} histiocytic markers (α -1-antitrypsin,^{13,19} α -1-antichymotrypsin),^{13,19,30} and vascular endothelial cell markers (Factor VIII).^{3,6,19,22,30} The present case showed that CD34 antigen and vimentin were positive, and other markers of the epithelial element, neural element, muscular element, histiocytic element, and vascular endothelial cell element were all negative.

CD34 monoclonal antibodies recognize a single-chain transmembrane glycoprotein of 115 kDa. CD34 antigen is selectively expressed in human hemopoietic progenitor cells and the vascular endothelium.³² The diagnostic utility of CD34 immunoreactivity is not limited to leukemia or vascular neoplasms, but includes primitive mesenchymal cells, mesenchymal spindle cell tumors, and tumors of the outer root sheath of hair follicles.^{20,24} Westra et al²⁰ described that SFT and dermatofibrosarcoma protuberans demonstrated a strong and generalized CD34 positivity; in contrast, neurofibroma, schwannoma, and hemangiopericytoma showed weak positivity for CD34. CD34 immunoreactivity was not observed in mesothelioma, synovial sarcoma, fibrosarcoma, and spindle-cell thymoma. This evidence suggests that SFT may arise from primitive mesenchymal cells and that CD34 immunoreactivity can be a highly sensitive marker of SFT.

Differential Diagnosis

Because SFT has a variety of morphological patterns that overlap with those of other spindle cell tumors, and because a wide range of mesenchymal tumors can occur in the orbit, the differential diagnosis of orbital SFT includes fibrous histiocytoma, rare fibroblastic tumors, as well as other uncommon spindle cell tumors such as hemangiopericytoma, meningioma, and nerve sheath tumors. Fibrous histiocytoma, which is the most common mesenchymal orbital tumor in adults, is composed of fibroblastic and histiocytic cells including histiocyte-like giant cells, and typically shows a uniform storiform pattern.^{19,21,25,30} In SFT, there may be a focal storiform pattern but it is not present throughout the tumor, and histiocyte-

like giant cells are not seen.^{19,30} Other benign fibrous tumors of the orbit, such as fibromatosis, show homogeneous, dense collagenous fibrous tissues with minimum vascularity and without a storiform pattern.¹⁹ Fibromatosis has an infiltrative nature that is different from the circumscribed nature of SFT.²¹ Hemangiopericytoma is composed of oval to fusiform cells, characteristically surrounding variably sized branching, so-called “staghorn-shaped” vessels.^{19,33} In hemangiopericytoma, abundant stromal banded collagen is rarely seen,^{19,21,22} and CD34 immunoreactivity is weaker than in SFT. In meningioma of the orbit, tumor cells are arranged in nests, whorls, commonly with psammoma bodies. Particularly in fibroblastic meningioma, a storiform pattern is prominent. Tumor cells in meningioma are immunoreactive for EMA and keratin proteins,^{19,30} markers which are usually negative in SFT. Schwannoma of the orbit has Antoni A (palisading pattern and Verocay bodies) and Antoni B areas, and unlike SFT, these tumor cells are immunoreactive to nerve sheath differentiation markers, such as S-100 protein.^{19,21,22,24,30}

Recently, giant cell angiofibroma, because of its morphological features with a richly vascularized and patternless proliferation of spindle-shaped cells and its immunoreactivity to CD34 and vimentin, has been reported to most closely resemble SFT.³⁴ However, giant cell angiofibroma has multinucleated giant cells and pseudovascular spaces which are not features of SFT. Moreover, giant cell angiofibroma is mainly lo-

cated in the eyelid in contrast to SFT, which is likely to be situated in a deeper portion of the orbit.

Comparison with Previous Cases

Eighteen cases of orbital SFT have been described (Table 1).^{19–31} The ages of the patients ranged from 19 to 76 years. Eight cases were men and 10 were women. The clinical sign in 12 of the 18 cases was proptosis. The prominent location of the tumor was on the medial site of the orbit. Expression of CD34 and vimentin was seen in all cases that were examined for these markers. Treatment in all cases was surgical excision. Twelve cases had no evidence of recurrence. Only 1 case has documented recurrence and this recurrence happened twice.¹⁹

The MRI findings of SFT described that the mass lesion was isointense or hypointense to gray matter in a T1-weighted image.^{11,18,23,27,29,31} In a T2-weighted image, the lesion showed hypointensity,²³ or hyperintensity,²⁷ or variegated intensity.^{11,29,31} Using Gd-DTPA, the lesion showed homogeneous enhancement,^{18,27,29} or variable enhancement with central areas of less enhancement.^{23,31} In the current case, the mass lesion had isointensity to the gray matter in T1, variegated intensity in a T2-weighted image and homogeneous enhancement. The variable findings of MRI were considered to be due to the tumor's diversified pathological components including cellularity, rich collagenous fibers, and vascularity in the hemangiopericytoma-like pattern.

Table 1. Summary of Clinical Findings of Orbital Solitary Fibrous Tumor

Patient No.	Age (year)	Sex	Presentation	Laterality	Location	Size of Tumor (mm)	Immunoreactivity		Treatment	Outcome
							CD34	Vimentin		
1 ¹⁹	44	Male	Proptosis	Right	medial	30	ND	+	Excision	NED, 18 months
2 ¹⁹	65	Female	Proptosis	Left	medial	15	ND	+	Excision	NED, 12 years
3 ¹⁹	69	Female	Proptosis	Right		15	ND	+	Excision	Recurrence at 4 and 6 years
4 ²⁰	60	Male	Orbital mass	NR		NR	+	ND	NR	NR
5 ²⁰	63	Female	Orbital mass	NR		NR	+	ND	NR	NR
6 ²⁰	40	Female	Proptosis	Left	superolateral	32×26×15	+	+	Excision	NED, 18 months
7 ²⁰	20	Female	Tumor palpable	Left	anteromedial	30×20×20	+	+	Excision	NED, 23 months
8 ²¹	19	Female	Tumor palpable	Right	lower anterior	25×13×10	+	+	Excision	NED, 6 years
9 ²²	21	Male	Proptosis	Left	medial	45×20×20	+	+	Excision	NED, 22 months
10 ²³	75	Male	Proptosis	Left	retrobulbar	NR	+	+	Excision	NED, 1 month
11 ²⁴	43	Female	Proptosis	Left	superolateral	40×30×20	+	+	Excision	NED
12 ²⁵	76	Male	Proptosis	Left	superolateral	15	+	+	Excision	NED, 1 year
13 ²⁶	48	Female	Proptosis	Left	superomedial	35	+	ND	Excision	NR
14 ²⁷	23	Male	Proptosis	Right	superomedial	25	+	+	Excision	NED, 9 months
15 ²⁸	23	Female	Palpebral swelling	Left	medial	22×13×10	+	+	Excision	NR
16 ²⁹	32	Female	Proptosis	Left	lateral	20×15×8	+	ND	Excision	NR
17 ³⁰	48	Male	Proptosis	Left	medial	35×30×25	+	+	Excision	NED
18 ³¹	27	Male	Tumor palpable	Right	medial	19×19	+	+	Excision	NED, 3 months
This case	38	Female	Proptosis	Right	medial	22×15×15	+	+	Excision	NED, 15 months

ND: not done, NED: no evidence of disease, NR: not reported.

Orbital SFT generally pursues a benign, nonaggressive course and is usually cured by simple excision,¹⁹⁻³¹ which is similar to SFT in other sites. It is reported that 13–23% of SFT in the pleura have a tendency to behave in an aggressive manner.^{3,21} It is also reported that tumors with aggressive histopathological features, including hypercellularity, high mitotic counts (at least four mitoses/10 high-power fields), and cellular pleomorphism, and with the macroscopic findings of tumor necrosis and large tumor size, are likely to manifest invasion of adjacent tissue, recurrence, or distant metastases.^{19,22,24–26,28,30} Although the present case has been free from recurrence for 15 months after operation, careful follow-up is mandatory.

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