CASE REVIEW

Giant Cell Rich Solitary Fibrous Tumour (GCR SFT) of the Eyelid: An Unusual Variant.

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ABSTRACT

One rare form of solitary fibrous tumor (SFT) that mostly affects the orbital region is the giant cell-rich SFT (GCR-SFT). Dedifferentiated and fat-forming versions of SFT are among its other variations. GCR-SFT, formerly known as giant cell angiofibroma, does not carry a better prognostic significance when compared to the conventional SFT. We discuss the case of a 33-year-old man who had painless swelling of his right upper eyelid for six months. A homogenous enhancing soft tissue lesion, at the right orbit preseptal tissues, at the superomedial aspect, is visible on contrasted computed tomography imaging of the orbit. An excision biopsy revealed a circumscribed tumour measuring 20 x 15 x 8 mm with varied collagenous stroma, associated with thin-walled and branching 'staghorn' vasculature. The tumour is composed of ovoid to spindle cells that form a patternless architecture with many multinucleated giant cells interspersed. Immunohistochemistry for CD34 and STAT 6 are positive in the tumour cells. A final histopathological diagnosis of GCR-SFT was established. Since the histological appearance of SFT may not match its behaviour, complete surgical excision is crucial in its management. Awareness of this rare variant of SFT is essential for guiding in its diagnosis with appropriate ancillary tests and for further management with risk assessment.
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INTRODUCTION

The uncommon mesenchymal tumour known as solitary fibrous tumour (SFT) has fibroblastic origin. The pleura was reported to be the first site affected. According to later research, it can also arise in various extra-thoracic anatomical locations, such as the orbit, salivary glands, adrenal glands, pelvis, skin, liver, urinary bladder, and retroperitoneum (1). Orbital involvement of SFTs was first reported by Dorfman et al. 1994 and Westra et al in 1994 according to Alsaadi et al. 2022 (2). It affects mostly adults. No discernible gender preference existed although reports from various studies and in the 2020 WHO Classification of Eye and Orbit Tumours show the ratio of affected male are higher than female (1). It is classified as an intermediate (rarely metastasising tumour) in the 2020 WHO Classification of Soft Tissue and Bone Tumors. In view of the discrepancy between histological features of SFT and its behaviour, risk stratification model was suggested as an improved means of assessing prognosis in SFT, as opposed to the usual benign or malignant classic terms (3).

Strong suspicion and familiarity with the radiological and pathological features are necessary for an accurate diagnosis of SFT. A difficult diagnosis may be presented by SFT with extensive angiomatoid alterations on radiography that may resemble a vascular tumour. Due to the lesion's distinctive staghorn vasculature, the conventional (non-central nervous system (CNS)) SFT was formerly known as hemangiopericytoma. Consequently, positive STAT6 immunohistochemistry with established diagnostic criteria enables accurate diagnosis. STAT6 serves as a highly sensitive and specific substitute for NAB2-STAT6 gene fusion, a known genetic mutation that occurs in this entity (4,5).

Two microscopic variants, giant cell-rich (GCR) and fat-forming, were also found in addition to the morphological variability observed in conventional SFT. They are categorised as variants of SFT because of the clinicopathological, immunohistochemical, and genetic similarities with conventional SFT. Dedifferentiated variant and malignant SFTs were also documented in the literature as the more aggressive types (4). Although

large cystically dilated angiomatoid regions are rare in GCR-SFTs, they were previously classified as giant cell angiofibromas due to their significant vascularization. Su et al. 2024 stated that the first GCR variant of SFT in the orbital region was reported by Dei Tos et al. in 1995 (1). Extraorbital sites such the eyelids, conjunctiva, and nasolacrimal duct have also been reported ever since. In a thorough review of GCR SFT, they have found and analysed 38 GCR-SFT reports involving 66 cases that arise from different anatomical sites between 1995 and 2023. Among these cases, eyelid GCR-SFT accounts for 13.6% following orbital involvement (28.8%) (1). Histology is typically not a reliable indicator of the biological behaviour, making it difficult to predict the clinical course of SFTs. This is especially true for orbital SFTs, because they are so uncommon. Thus, it is also crucial to be aware of this variant of SFT to differentiate it from other mimickers when choosing for appropriate ancillary testing and to ensure that complete excision is achieved.

CASE REPORT

A 33-year-old man had 6-month history of painless swelling in his right upper eyelid. There was neither visual impairment nor past trauma. Contrasted computed tomography of the orbit revealed a homogenous enhancing soft tissue lesion at the right orbit preseptal tissues on the upper medial aspect. The lesion measures 2.0 x 1.7 x 1.2cm. There was no intralesional fat or calcification. The lesion appears to abut the superior medial aspect of the right cornea and conjunctiva. Extension beyond the layers into the anterior chamber or globe or intranasal extension was not evident. The lesion was excised. A firm, homogenous tumour measuring 20 x 15 x 8 mm with a brownish cut surface was obtained. The tumour was circumscribed and, under the microscope, consists of spindle to ovoid cells that create a patternless architecture in association with a variable collagenous stroma that includes thin walled, widely branching "staghorn" vasculature (Fig. 1A). Intermingled with the tumour cells are several multinucleated giant cells (Fig. 1B). There are mostly foreign body type and occasional floret type multinucleated giant cells observed. Storiform architecture was not seen. Mitosis was rarely seen (1 per 10 high power fields (hpf)). A clear resection margin was attained, and there was no tumour necrosis.

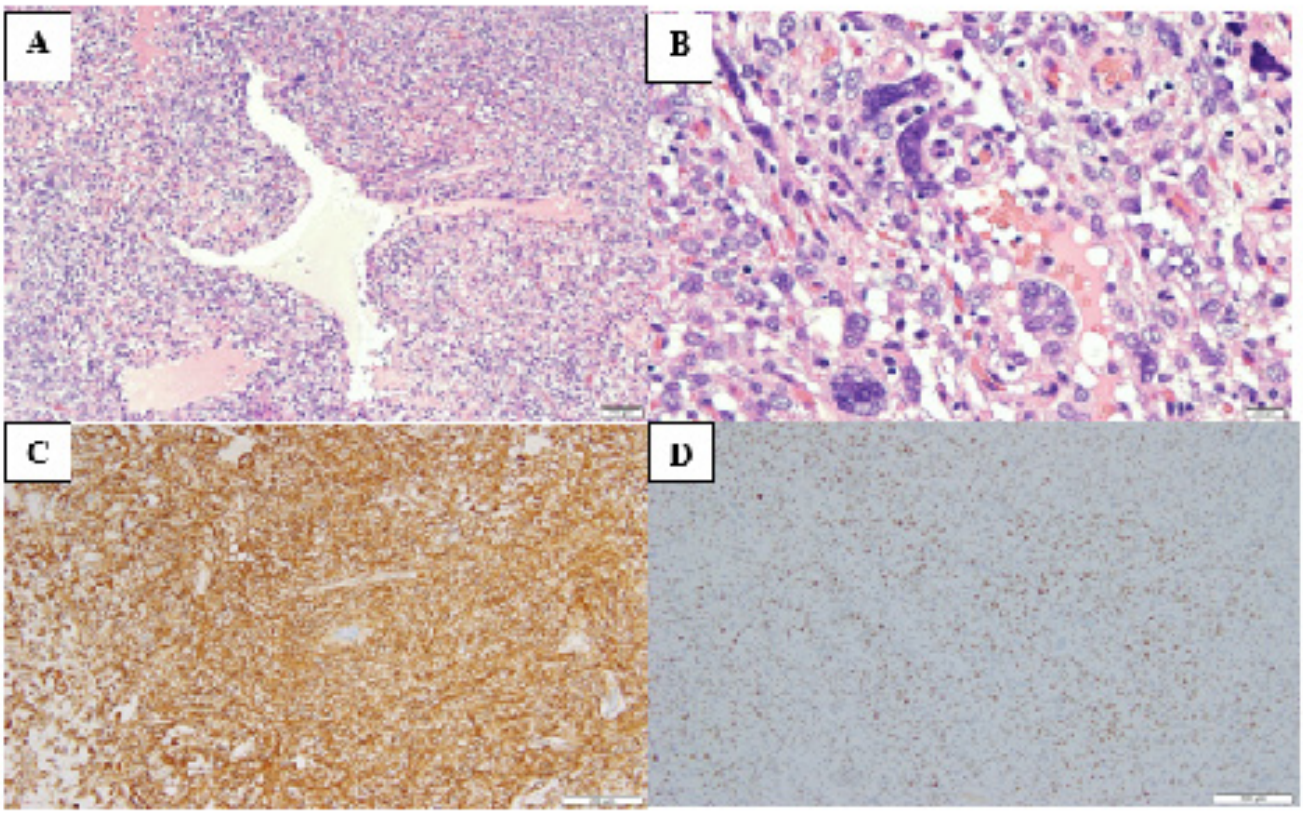

Fig. 1: A. Tumour composed of ovoid to spindle cell in patternless architecture associated with thin-walled branching 'staghorn' vasculature (x100, H&E).
B. Multinucleated giant cells among the ovoid tumour cells (x400, H&E).
C. Positive CD34 immunohistochemistry shows membranous and cytoplasmic brownish staining.
D. STAT 6 immunohistochemistry is positive indicated by brownish nuclear staining (C,D: x 100, immunohistochemistry).

A panel of immunohistochemistry was done to assist in the diagnosis and differentiate for other differentials such as deep benign fibrous histiocytoma and giant fibroblastoma. Immunohistochemistry for CD34 shows strong membranous brownish expression, while diffuse nuclear brownish expression of STAT6 was present (Fig. 1C, 1D). Myogenic marker like Desmin showed negative brownish expression. Other immunohistochemistry panels including Bcl-2, EMA, and CD-99 which were non-specific for SFT were also positive with brownish nuclear (Bcl-2) and membranous (EMA, CD99) expression. The final diagnosis of GCR-SFT was made, and the tumour was categorised as low-risk for metastasis. According to the modified four-variable risk stratification model by Demicco et al. 2017, the total score for this case is 1 which is within the low-risk category score of 0 to 3. This is based on the age (<55 = score 0), tumour size (<5cm = score 0), mitoses (1/10hpf = score 1) and necrosis (<10% = score 0) (3). There has been no tumour recurrence during the patient's follow-up of over a year and a half after the initial diagnosis.

DISCUSSION

Solitary fibrous tumour represents a minority of mesenchymal neoplasms, with approximately 0.4 per million incidences for extrameningeal (non-CNS) tumour (5). Typically, they demonstrate a benign clinical course, often the presenting symptoms were attributable to the mass effect. Preoperative diagnosis by imaging of SFTs is challenging because the findings are nonspecific. In the 2020 WHO Classification of Soft Tissue and Bone Tumours, they belong to the fibroblastic neoplasms exhibiting rarely metastasizing behaviour. Diagnosis of SFT commonly occurs in individuals aged between the fifth and seventh decade of life, with no apparent gender predilection, although slight inclination towards male predominance is seen (1). Notably, SFTs that developed in deep organs and subcutaneous soft tissue, typically had larger diameters than those that developed in regions like the orbit and eyelid. It is found that the risk assessment standards positively associate increased tumour sizes with higher risk of metastasis (1,3).

By morphology, SFT can have variable appearances and can evolve in an unforeseen way. Conventional SFT are often well-defined masses with a solid, multinodular, white cut surface. Haemorrhage and myxoid alterations are observed in some cases. Malignant and locally aggressive tumours can exhibit signs of necrosis with uneven margins of infiltration. Histologically, typical SFT demonstrates a patternless architecture characterized by alternating hypocellular and hypercellular regions separated by thick collagenous bundles and branching vessels. Tumour cells typically appear oval to spindle-shaped with scant cytoplasm and vesicular nuclei. Cellular atypia is generally minimal, and mitosis is typically sparse. Previously known as giant cell angiofibroma, GCR-SFT is a variant of SFT characterized by a large number of multinucleated stromal giant cells that are organized around pseudovascular spaces (1,2,5).

Many soft tissue tumours, particularly those referred to as fibrohistiocytic tumors and myofibroblastic tumours, like benign fibrous histiocytoma (deep) and giant cell fibroblastoma, are included in the differential diagnosis of GCR-SFT. Deep benign fibrous histiocytoma usually appears as isolated, slowly growing nodules with branching arteries resembling SFT. It primarily affects deep soft tissue or subcutaneous tissue. It is composed of polymorphous spindle cells arranged in short fascicles and typical storiform pattern with peripheral collagen trapping and negative expression of STAT 6 immunohistochemistry (4). Giant cell fibroblastoma (GCF) is also a histologically similar intermediate soft tissue tumour. Although a few adult cases have been described, giant cell fibroblastomas usually affect children and often occur in the subcutis. It is composed of floret-like multinucleated giant cells that frequently line larger, irregularly distributed lacunar or sinusoidal pseudovascular spaces, and elongated, wavy configurations of spindle cells dispersed in a mucinous-like or collagenous stroma. Even if these tumours can be immunohistochemically CD34 positive, STAT6 nuclear expression is not present. On the other hand, a few additional mesenchymal tumours, such as nodular fasciitis, undifferentiated pleomorphic sarcoma, and dedifferentiated liposarcoma, also express STAT6 to some extent, their morphology however, differ greatly from SFT's (1). Nodular fasciitis display spindle stellate cells with a loose fascicular to storiform pattern and tissue culture-like growth without the increase in vascularity unlike SFTs. Both undifferentiated sarcoma and dedifferentiated liposarcoma show areas of marked nuclear pleomorphism and abnormal mitoses which are mostly absent in GCR-SFT.

Often, a panel comprising CD34, CD99, and BCL-2 was used for immunohistochemistry in the diagnosis of SFTs. Although the immunoexpression in this panel is both strong and diffuse, it is not specific. For the NAB2-STAT6 gene fusion that takes place in SFTs, STAT6 serves as a very sensitive and specific substitute. Immunohistochemical staining with STAT6 usually shows strong and diffuse nuclear positivity. The paracentric inversion on chromosome 12q, which results in the fusion of the NAB2 and STAT6 genes, is the unique genetic abnormality that defines SFT (4,5).

Some SFTs can progress even when their histology appears benign. Several risk stratification models have been developed to improve prognostic accuracy. These models include multiple prognostic indicators, mainly clinical and histological characteristics, to predict each patient's probability of metastasis or recurrence (3). Tumours with high mitotic count, hypercellularity, atypia (round cell and anaplastic

morphology, nuclear pleomorphism) and necrosis have been termed malignant (3,5). The modified four-variable risk stratification model according to the 2020 WHO Classification of Soft Tissue and Bone Tumour are based on the age at diagnosis, tumour size, mitotic count and necrosis (3). Age scores for patients were 0 if they were < 55 and 1 if they were > 55. Mitotic activity was scored with 0 for <1 mitotic figure/10 hpf, 1 for 1-3 mitotic figures/10 hpf, or 2 for >4/10 hpf. The size of the tumour was evaluated as follows: 0 for <5 cm, 1 for 5 to <10 cm, 2 for 10 to <15 cm, or 3 for >15 cm. Less than 10% necrosis is considered to be 0, whereas >10% necrosis is assigned a score of 1. The total scores were then added up. A score of 0–3 indicated low risk of metastasis, a score of 4–5 indicated intermediate risk, and a score of 6–7 indicated high risk. The total sum of score in our case was 1 and classified as low risk progression for metastasis. Complete surgical excision with negative resection margin is crucial to lower the possibility of both malignant transformation and local recurrences. After receiving follow-up care, the patient had no local recurrence or metastases as of yet. Long-term monitoring is still required, though, because of the tumour location and the unpredictable nature of SFTs.

CONCLUSION

Giant cell rich - solitary fibrous tumour emerges as an uncommon type of SFT, frequently localized to the orbital region. GCR-SFT should be considered when making a differential diagnosis of spindle cell lesions containing multinucleated giant cells of the eyelid. Immunohistochemistry for STAT6 can help distinguish this tumour from other mesenchymal neoplasms. Surgical resection with complete margin remains the gold standard of treatment to prevent local recurrence and malignant transformation. Proper management of patients with this diagnosis would be aided by the knowledge of this variant of SFT and its propensity to arise in the orbital region. While they behave like a benign lesions, they may be classified in the higher risk category based on the risk stratification model.

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REFERENCES

1. Su Z, Wei J, Yuan X. Giant cell-rich solitary fibrous tumour of the urinary bladder: case report of an unusual histological variant and literature review. Diagn Pathol. 2024;19(1):20. doi:10.1186/s13000-024-01442-z
2. Alsaadi KA, Alwohaib M, Pinto K, Ali RH. Giant cell-rich solitary fibrous tumour of the lacrimal gland with prominent angiomatoid cystic changes and an underlying NAB2ex3-STAT6ex18 fusion. BMJ Case Rep. 2022;15(2):e247141. doi:10.1136/bcr-2021-247141
3. Demicco EG, Wagner MJ, Maki RG, et al. Risk assessment in solitary fibrous tumors: validation and refinement of a risk stratification model. Mod Pathol. 2017;30(10):1433-1442. doi:10.1038/modpathol.2017.54
4. Tariq MU, Din NU, Abdul-Ghafar J, Park YK. The many faces of solitary fibrous tumor; diversity of histological features, differential diagnosis and role of molecular studies and surrogate markers in avoiding misdiagnosis and predicting the behavior. Diagn Pathol. 2021;16(1):32. doi:10.1186/s13000-021-01095-2
5. Janik AM, Terlecka A, Spałek MJ, et al. Diagnostics and Treatment of Extrameningeal Solitary Fibrous Tumors. Cancers (Basel). 2023;15(24):5854. doi:10.3390/cancers15245854