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Sinonasal solitary fibrous tumour: A borderline entity with diagnostic challenges

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Abstract

Introduction: Sino nasal Solitary Fibrous Tumour (SFT) has been categorised as borderline/low-grade malignant tumours in the recent WHO classification of Head and Neck Tumours (2017). SFT have been reported in pleura and diverse extra pleural sites of which Sino nasal region accounts for <0.1%. Owing to its overlapping histopathological features with various oval/spindle cell lesions in the region, Sino nasal SFT often poses as a diagnostic dilemma.

Materials and methods: Eight cases diagnosed as Sino nasal SFT, over a period of twelve years (January 2006 - December 2017) were retrieved from the archives of Department of Pathology, Kasturba Medical College, Manipal and reviewed for clinical-morphological features.

Results: Sino nasal SFT was largely seen in males (M: F-3:1) with a median age of 54.5 years (33-74years). The predominant symptoms were nasal blockage, deviated nasal septum and occasional episodes of epistaxis. Grossly, the tumours appeared polypoidal to irregular masses, filling up the nasal cavity and extending to the nasopharynx and skull base. Microscopically, the tumours were composed of vague lobules of haphazardly arranged bland oval/spindle cells separated by collagen bundles and interspersed irregular vessels and were diffuse and strongly positive for CD34 on immunohistochemistry.

Conclusion: SFT is characterized by cytological bland spindle cells with scant cytoplasm separated by thick collagen bundles, arranged in variable architectural patterns. These features show considerable overlap with angiofibroma, leiomyoma, schwannoma and fibrous histiocytomas especially in the presence of high cellularity and hypo/ hyper cellular architecture. The diagnostic clues favouring SFT include bands of collagen and positivity for CD34 and Bcl2. SFT are tumours with borderline/ low-grade histology and can be managed by endoscopic resection. The poor prognostic indicators include old age, presence of tumour necrosis, >4 mitosis/10 HPF, and local recurrence is seen in 10-15% cases.

Keywords: Solitary fibrous tumour, Sino nasal tumour, CD34, STAT6, borderline tumour

Introduction

Solitary fibrous tumour (SFT) is a mesenchymal tumour, first described in 1942 by Stout and Murray ^[1]. World Health Organisation in 2017 revised the classification of Sino nasal tumours and Sino nasal hemangiopericytoma as SFT. These tumours were classified under the borderline/ low malignant potential tumours along with desmoid-type fibromatosis, glomangiopericytoma and hemangiopericytoma ^[2]. Primarily a tumour of the pleura, SFT is seen most commonly in the pleural and abdominal cavity, followed by extremities; head and neck SFT account for around 12% of all the cases ^[3, 4]. Sino nasal SFT are unusual and account of <0.1% of all cases and owing to their overlapping morphological features with other spindle cell mesenchymal lesions in the region, presents as a diagnostic dilemma. Most of the Sino nasal SFT behave in a benign manner; however, a few case reports have documented an increased local recurrence and metastasis associated with them ^[5]. Here we present eight cases of Sino nasal SFT with their clinicopathological features and follow up to further the understanding of these uncommon tumours.

Materials and methods:

Eight cases diagnosed as SFT in the Sino nasal region over a period of twelve years (January 2006-December 2017) were included in the study. Following permission from the institutional ethics committee, the clinical and demographic data were retrieved from the electronic medical records.

Histopathology haematoxylin & eosin and Immune histochemistry slides were retrieved from the archives of the department of pathology, Kasturba medical college, Manipal and morphological features were reviewed.

Results

Sinonasal SFT was largely seen in males (M: F-3:1) with a median age of 54.5 years (33-74years). The main presenting features of the tumour were nasal blockage (75%) and deviated nasal septum (67.5%). Other complaints included nasal discharge (12.5%), epistaxis (37.5%) and localised pain (12.5%). Three cases were seen arising from the lateral

wall of nasal cavity, two cases from the maxillary sinus, while one case each was seen arising from frontal sinus, cribriform plate and nasopharynx. The size of tumours ranged from 2.2- 6.6cm in the greatest dimension (mean size: 3.6cm). Seven cases were seen limited to the nasal cavity and paranasal sinuses while one was seen extending to the base of the skull. Five cases showed an irregular grey white growth while three were polypoidal in morphology. All cases were submitted for histopathological examination into multiple irregular pieces, which were grey-white in colour and firm in consistency (Table 1).

Table 1: Clinical and demographic features of Sino nasal SFT

Case no	Age (years)	Gender	Symptoms	Site	Laterality	Local spread	Size (cm)	Clinical diagnosis
1	36	Female	NO, ND,E	Cribriform plate	Right	NC	3.3	Meningioma
2	54	Male	NO, DNS,	Lateral wall of NC	Left	NC, PNS	2.7	Sino nasal papilloma
3	55	Male	NO, DNS	Maxillary sinus	Right	NC	6.5	Sino nasal papilloma
4	33	Male	Pain	Nasopharynx	Bilateral	BOS	2.2	Angiofibroma
5	52	Male	NO, E, DNS	Maxillary sinus	Right	NC	4.3	Hemangioma
6	74	Male	NO, E, DNS	Lateral wall of NC	Right	NC, PNS	2.2	Hemangioma
7	67	Female	NO	Frontal sinus	Left	NC, PNS	3.5	Polyp
8	55	Male	DNS	Lateral wall of NC	Left	NC, PNS	4.2	Allergic polyp

NO- nasal obstruction, ND- nasal discharge, E-epistaxis, DNS- deviated nasal septum, NC- nasal cavity, PNS – paranasal sinus, BOS- base of skull.

Table 2: Immunohistochemical differentiation of SFT with the differential entities. (1)(2)(7)

Tumour	Immunohistochemistry						
	CD34	Bcl2	SMA	CK	EMA	β catenin	S100
SFT	Strong and diffuse	+	-	-	-	-/focal	-
Desmoid-type fibromatosis	-	-	+	-	-	+	-
Leiomyoma	-	-	+	-	-	-	-
Schwannoma	-	-	-	-	-	-	+
Neurofibroma	-	-	-	-	-	-	+
Meningioma (fibroblastic)	-	-	-	-	+	(focal)	-
Glomangiopericytoma	-	-	+	-	-	+	-
Synovial sarcoma	-	-	-	+	+	-	-
Biphenotypic sinonasal sarcoma	+/focal	-	+	-	-	+/focal	+

Microscopic examination of the tumours revealed a variably cellular architecture, with cell rich areas and hypo cellular stroma rich regions. The overlying epithelium was intact in all the cases and no ulceration was noted (Figure 1). The cellular areas were composed of oval to spindle cells arranged in fascicles and stori form pattern (figure 2) while hypo cellular areas showed abundant collagenised stroma with scattered spindle cells (figure 3). Individual tumour cells have oval to spindle-shaped nuclei with coarse chromatin and scant cytoplasm with minimal cellular atypia (figure 4). Mitosis was scanty, <2/10HPF in all the cases. The vascular component of the tumour consists of thin and thick-walled blood with perivascular hyalinisation and tumour cell arrangement (figure 4). No necrosis was noted in the tumour sections. All the cases showed diffuse cytoplasmic positivity for CD34 (figure 5), another positive markers were Bcl2 (3/3) and vimentin (1/3). The tumour cells were negative for SMA (0/8), desmin (0/2), S100 (0/3) and EMA (0/1). All cases were managed by endoscopic resection. Clinical follow up was available for 24 months was available for five cases, while three cases were lost to follow up. None of the five cases showed any recurrence or metastasis in the follow-up period.

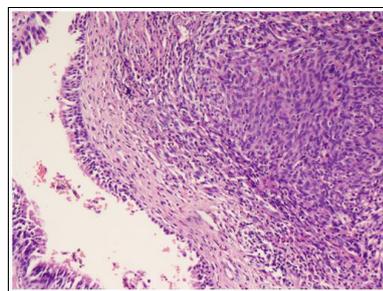


Fig 1: Oval to spindle tumour cells arranged in short fascicles. The overlying Sino nasal mucosa is intact. H&E, x100

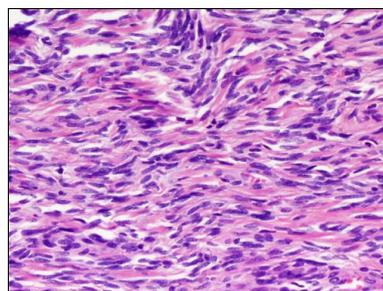


Fig 2: Spindle cells arranged in sweeping fascicles and extracellular collagen deposition. H&E, x100

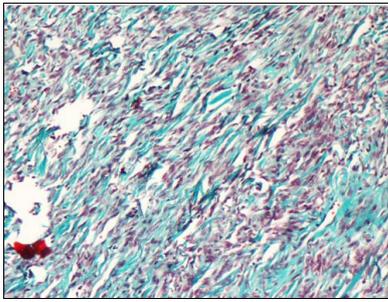


Fig 3: Tumour cells separated by collagen bundles, which are stained green on Masson's trichrome stain. MT, x100

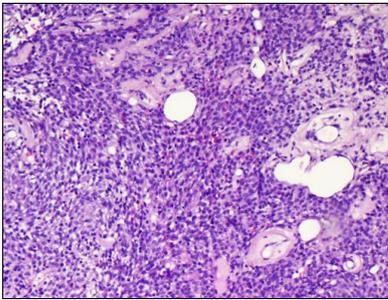


Fig 4: Tumour cells with oval cells with perivascular proliferation. Extensive hyalinisation also noted around the vessels. H&E, x100

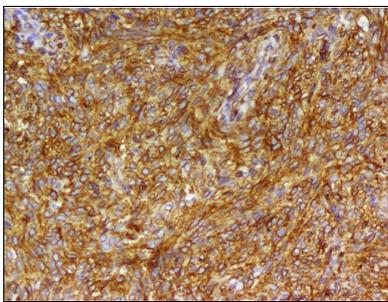


Fig 5A: Tumour cells are diffuse and strong positive for CD34, x200.

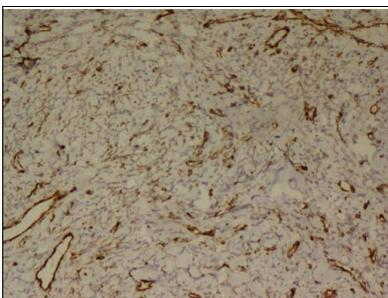


Fig 5B: SMA highlights the vascular lining. Tumour cells are negative, x100

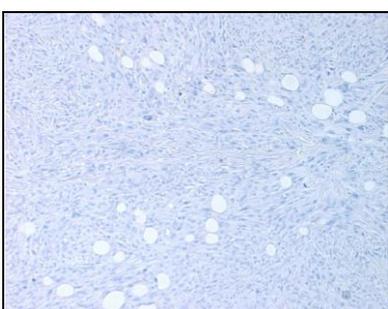


Fig 5C: Tumour cells are negative for S100 protein, x100

Discussion

Clinical presentation

Amongst the extra pleural SFT, head and neck region SFT form a sizeable number; however the prevalence in the Sino nasal region is low and is limited to case reports in the English literature. (3) (4) (6) (7) (8) (9) (10) (11) (12) (13) (14) (15) (16) (17) (18) Thompson LDR *et al* [5] reported the largest series of six cases diagnosed over a period of 10 years and provided a comprehensive review of the cases published medical literature. The age group of presentation of Sino nasal SFT is the fourth and fifth decade of life with almost equal gender predilection [1,5]. The present series also concurs with the age group however a male preponderance is seen which is similar to the findings of Thompson LDR *et al* [5]. Nasal obstruction and epistaxis are the most common presenting features of these tumours. They are usually unilateral and small in size with a mean size of 4.7cm [1, 2, 5] which was similar to the findings in the present series. The present series also observed the presence of a deviated nasal septum owing to the growth of tumour within the confined space of the nasal cavity. The local spread of tumour is usually with the nasal cavity and paranasal sinuses and reports have documented the spread to the orbit and base of the skull. WHO recognises SFT as an entity with a borderline/low malignant potential tumour, clinical features of an aggressive SFT or malignant SFT include age >55years and size >15cms and presence of metastatic disease [1, 2, 7, 19, 20].

Morphology

Sino nasal SFT is usually polypoidal and firm in consistency and managed via endoscopic resection. Surface ulceration is rare and the presence of necrosis is considered to be a feature suggestive of an aggressive course. Histological characters are similar to the classic pleural and extra pleural SFT with a variably cellular tumour. Neoplastic cells showing oval to spindle-shaped nuclei, coarse chromatin and inconspicuous nucleoli, arranged in fascicles and perivascular fashion. Large arborizing vessels are a constant feature so is the perivascular hyalinisation. The stroma rich regions show abundant collagen deposition with scanty scattered spindle cells. Mitosis is rare and a classical SFT shows only 0-2/10HPF. Presence of cellular atypia, atypical mitosis, >4 mitotic figures/10 HPF and tumour necrosis are tell-tale signs of malignant transformation or a dedifferentiated/malignant SFT [1, 19, 20, 21]. All the cases in the present study showed a typical SFT morphology and a low mitotic activity. Even with the characteristic morphology in view of a different clinical diagnosis and overlapping histology with other spindle cell neoplasms in the region, ancillary technique of immunohistochemistry was used for confirmation.

Immunohistochemistry

SFT show strong and diffuse immunoreactivity for CD34 and Bcl2, patchy positivity is seen for CD99. STAT6 is a new marker, which shows strong nuclear positivity in SFT with a sensitivity of 95%. The tumour cells are non-reactive for desmin, smooth muscle actin, s100, Cytokeratin and β catenin [1, 2, 7]. In the present study, all cases were positive for CD34, Bcl2 was positive in three cases where it was done. SMA, S100 were consistently negative.

Genetics

Recent studies have brought into light the presence of NAB2-STAT6 fusion gene in SFT. Such a fusion gene product leads to activation of ERG1, which is an initiator for the formation of SFT. This fusion production can be detected by real-time polymerase chain reaction and tissue microarrays, which help in the molecular diagnosis of SFT. STAT6 immunohistochemistry is a good surrogate for the presence of this fusion protein in SFT. Other mutations like overexpression of PDGF α , P53 and TERT promoter mutations are indicators of malignant transformation of SFT. [1, 2, 22].

Differential diagnosis

The morphological features of SFT show a considerable overlap with many entities encompassing fibrohistiocytic, myomatous, neural tumours and even low-grade sarcomas. The fascicular arrangement of bland spindle cell along with vascular elements in stroma present diagnostic overlap with angiofibroma while the cellular areas simulate a desmoid-like fibromatosis and leiomyoma. Subtle histological clues like the presence of ectatic vessels and expression of SMA by tumour cells help in differentiation of angiofibroma, while β catenin and SMA help to exclude desmoid like fibromatosis and leiomyoma respectively [1, 7]. Smooth muscle tumours of uncertain malignant potential although extremely rare in the nasal cavity can mimic an SFT owing to their architecture and locally aggressive behaviour; however, a careful mitotic count and immunoreactivity for SMA help in their differentiation [23]. The hyper-hypocellular architecture and spindle-shaped nuclei can arise suspicion of neural tumour namely a neurofibroma or schwannoma, in such cases, S100 positivity helps to document a neural differentiation. Fibroblastic meningioma forms a differential for the tumour arising from the cribriform plate and rich in collagenous stroma along with spindle cells, positive staining with EMA points towards a diagnosis of meningioma over SFT [5, 7]. Glomangiopericytomas are tumours of myoid origin and classified together with the SFT in the sinonasal region. They show a vascular component along with perivascular hyalinisation or a hemangiopericytomatous pattern. These can be differentiated from SFT by their reactivity for SMA and β catenin [2]. Low-grade sarcomas, like synovial sarcoma can be differentiated by its positivity for CK and EMA while biphenotypic sinonasal sarcoma shows positivity for SMA, S100 owing to their myoid and neural origin [1, 7]. Table 2 summarises the main immunohistochemical reactivities for the main differential entities of SFT.

Management and Prognostic factors: The most favoured plan of management is surgical resection of the tumour. Complete resection of tumours pose a difficulty owing to the accessibility of the region and the tumour is removed in a piecemeal fashion [1, 2, 5]. Assessment of margins and leftover tumour also poses similar difficulties. The prognostic factors for sinonasal SFT have not been well document, WHO in the revised classification of head and neck tumours laid down a few indicators which could be used for prognostication. Age >55 years, tumour size >15 cm, tumour necrosis, high cellularity, cellular atypia, increased mitosis (>4/10HPF) can be used as gross and microscopic indicators and their presence in the tumour indicated a poorer outcome. Local recurrence and metastasis

are rare but documented in the English literature with the latter more commonly seen with the malignant SFT [2, 3, 19, 21].

Conclusion

Sinonasal SFT is an unusual mesenchymal tumour with a unique NAB2-STAT6 fusion gene signature. The architectural heterogeneity and overlapping histology with other tumours make it a diagnostic dilemma for surgical pathologists. The immunopositivity for CD34 helps to a great extent to point towards SFT. The difficult surgical accessibility of the region warrants a thorough examination of microscopic features which are imperative in prognostication of the tumour and predicting its behaviour. The present series in the largest documenting SFT in the sinonasal region so far and corroborated with the existing literature to append our understanding about this enigmatic entity.

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