

## Synovial sarcoma: a rare neoplasm of paranasal sinus

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### Abstract

Synovial Sarcoma (SS) is a rare soft-tissue malignant tumour. Its presentation in the head and neck region is uncommon. Because of the complex anatomy of the head and neck region, surgery with clear margins is not achievable. In such cases, a multi-modality approach is required as there is no established standard of care. In this report, we share the case of a girl who presented with nasal obstruction. Imaging revealed a mass involving the left nasal cavity, paranasal sinuses without intracranial extension. It was diagnosed as synovial sarcoma. She underwent surgical excision and adjuvant radiation therapy (RT) to the tumour bed, followed by an incomplete course of chemotherapy. Later on, she developed systemic disease. Considering the rarity of this case and lack of guidelines for standard treatment, we report on this case to share our experience with management and treatment outcome

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### Introduction

Sarcomas are an uncommon and heterogeneous group of tumours of mesenchymal origin. They include less than 1% of all adults and 12% of paediatric malignancies.<sup>1</sup> One of the subtypes is synovial sarcoma (SS). In young adults, SS frequently presents in extremities. It occasionally presents in the head and neck region, which accounts for only 3-10% of all SS cases.<sup>1</sup> The mean age at diagnosis is 32 years and affects both males and females.<sup>1</sup>

The mainstay of the management of SS is surgical resection. The aim of surgery is to achieve a clear margin with no residual disease.<sup>2</sup> SS in the head and neck region poses difficulty in accomplishing this goal due to the

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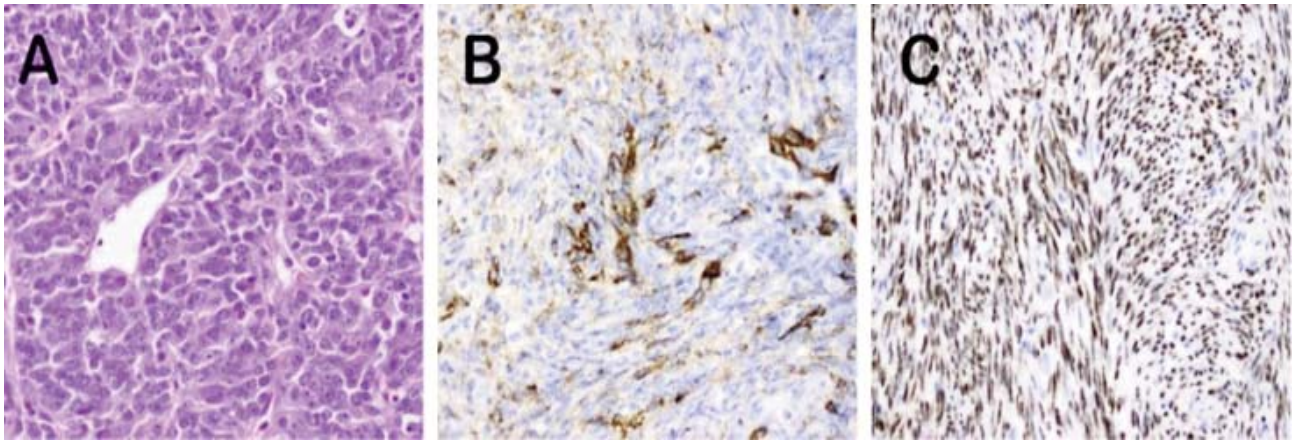
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complex anatomy of this region.<sup>2</sup> As this is a rare clinical scenario, no consensus guidelines are available for its management. Besides this, there is sparse literature available for adjuvant treatment.

### Case Report

A 22-year-old girl, with no known comorbidity, presented to Aga Khan University Hospital, Karachi, in December 2019, with the complaint of left nasal obstruction. The obstruction had worsened over one year with increasing difficulty in breathing, change in the quality of voice, and swelling over the left side of the face. Examination revealed a mass protruding out of the nasal vestibule. Magnetic Resonance Imaging (MRI) of the head and neck region showed a large left-sided mass involving the left maxillary and ethmoid sinus, extending into the left nasal cavity without orbital or intracranial extension (7.5cm in maximum transverse, 8.0cm in maximum anteroposterior and 4.0cm in maximum craniocaudal dimension). CT scan of the neck, chest and abdomen did not show regional or distant metastasis. Biopsy was performed, which revealed high grade monophasic synovial sarcoma on Haematoxylin & Eosin stains with positive immunohistochemical markers, like TLE1 (Transducin-like enhancer of split 1) in a diffuse strong distribution and EMA (Epithelial Membrane Antigen) [Figure 1]. In addition, the tumour showed positivity for other markers, i.e. CD99 (MIC2) and Bcl2, to support the diagnosis of SS. However, the tumour showed negative staining for cytokeratin (CKAE1/AE3) and desmin, which ruled out sarcomatoid carcinoma of the oral mucosa and spindle cell rhabdomyosarcoma, respectively. Although molecular translocation [X,18] confirmation is the gold standard for diagnosis of SS, this test could not be performed because of unavailability.

The patient underwent left lateral rhinotomy and left medial maxillectomy along with excision of the mass. The postoperative histopathology report was consistent with SS; the pathologist did not make comments on the margins as it was a piecemeal resection. The case was discussed in site-specific head and neck multi-disciplinary tumour board meeting (MDT) and the recommendation was to offer adjuvant radiation therapy (RT) on account of piecemeal resection, followed by chemotherapy. She underwent external beam radiation therapy (EBRT) with a total dose of 66 GYs in 33 fractions with an intensity



**Figure:** (A) H&E stain slide with magnification x 400, showing High grade monophasic synovial sarcoma, (B) Tumour cells showing positivity for EMA immunostain, (C) Tumour cells showing positivity for TLE1 immunostain in a diffuse strong distribution

modulated radiation technique (IMRT). After completion of EBRT, she was advised to receive four cycles of chemotherapy. She had one cycle of Doxorubicin and Cyclophosphamide (AC) and denied receiving further cycles of chemotherapy. Follow-up MRI two months after EBRT revealed no residual disease. She was on regular follow-up for one year. On every follow-up, head and neck physical exam along with fibre optic exam of the nasal cavity and paranasal sinuses was done. She was advised to continue follow-up for five years, but she was lost to follow-up after one year of completion of treatment. She remained disease-free for one year and then re-presented with complaint of generalised body pain and dry cough. CT scan of the chest, abdomen and pelvis showed systemic disease involving lung, liver, and bone. She was advised palliative chemotherapy, but she left against medical advice and did not turn up for treatment. Patient's consent was taken for publication of this case report.

## Discussion

Head and neck sarcoma is a rare entity. There is a lack of clear guidance about its management and outcome. Synovial sarcoma is considered an uncommon malignancy of the extremity, which affects the population between 15 to 40 years of age with only 3-10% of SS occurring in the head and neck region.<sup>3</sup> From the available indexed literature, we reviewed 12 cases of paranasal synovial sarcoma, as summarised in Table 1.

Treatment of choice for SS is resection with clear surgical margins.<sup>2</sup> Complete excision is considered the main prognostic indicator for local recurrence and overall survival<sup>4</sup> and piecemeal resection is not a preferred option as it directly correlates with the treatment outcomes. However, in the head and neck region, it is

sometimes difficult to resect the tumour with safe clear margins. So, in those sarcoma cases where upfront surgery is not possible, neoadjuvant chemotherapy is an option for chemo-sensitive tumours. In our patient's case, neo-adjuvant chemotherapy would have been a better option, as synovial sarcoma is a chemo-sensitive tumour. Unfortunately, her case was not discussed before surgery and she ended up with piecemeal resection. Ideally, every case should be discussed in MDT before first treatment modality and this case is a classic example of the fact that if the primary surgeon had discussed her case in site-specific multidisciplinary tumour board, the outcome would have been different.

There may be two patterns of disease's failures: either loco-regional recurrence or the development of distant metastasis after treatment of synovial sarcoma. Therefore, an interesting question arises here regarding the necessity of adjuvant EBRT and chemotherapy for local and systemic disease control.

Literature supports incorporating adjuvant EBRT for patients with high-risk features for local disease relapse.<sup>5</sup> Nancy Lee et al, highlighted the importance of multidisciplinary approach in the treatment of SS. They reported the pattern of failure in 40 patients treated for head and neck SS in their institute. The factors which increase the risk of local recurrence after surgery are positive margins, biphasic subtype, skull base location and large tumour size.<sup>6</sup> Their team experienced that the adjuvant EBRT improved the local control, and overall and disease-specific survival rates.<sup>5</sup>

Sturgis et al, in their study, reported the treatment outcome of 25 patients of sarcoma in the head and neck region and stressed incorporation of EBRT as an adjuvant setting in high-grade sarcoma of the head and neck

**Table-1:** Case reports of Paranasal synovial sarcoma

Study	Age/sex	Clinical presentation	Radiology	Tumour nature	Location	Histology	Treatment	Outcome/Follow up
Trible et al. 1970. <sup>11</sup>	24/F	Headache, abducen nerve paralysis radiating to left eye, ptosis of left eye lid, decreased visual acuity	Homogeneous density in left sphenoid sinus, destruction of the floor of sella	Metastasis	Sphenoid sinus	NA	Surgery and RT	Died due to disease/2 years
Cihak et al. 1997. <sup>12</sup>	25/M	NA	CT: mass in left supraorbital rim and maxillary sinus	Recurrence	Maxillary sinus	MFSS	Multiple resection, chemo and RT	Recurrence after 2 years and underwent wide excision
Rangheardet al. 2001. <sup>13</sup>	12/M	NA	NA	Primary	Maxillary sinus	NA	Surgery, chemo and RT	No evidence of disease / 10years
Kartha & Bumpous, 2002. <sup>14</sup>	24/F	Pain and proptosis	6-cm ethmoid sinus mass	Primary	ethmoid sinus	MFSS	Surgery, RT (8600 cGy), chemo after recurrence	Died due to disease / 9 months Metastasis to lung and meninges
Bettio et al.2004. <sup>15</sup>	36/M	Progressive right eye visual impairment	Cranial base tumour (5 cm) invading the sella, sphenoid sinus, orbit and optic chiasm	Primary	Sphenoid sinus	MFSS	Surgery	Died 1 week after surgery
Gallia et al.2005. <sup>16</sup>	44/M	Right-sided proptosis	Expansive mass (3.3 cm) involving right frontal sinus and extending to right ethmoid sinus	Primary	Frontal sinus	MFSS	Surgery, RT (6120 cGy IMRT) and chemo	No evidence of disease /2 months
A. Jain et al. 2018. <sup>17</sup>	36/F	left nasal obstruction and epistaxis	2× 2 × 2.5 cm in left posterior part of nasal cavity extending up to olfactory fossa	Primary	Ethmoid	MFSS	Surgery and RT	No evidence of disease /6 months
Yildirim et al.2005. <sup>18</sup>	52/ F	Progressive enlarging nasal mass (1 year)	No CT done. Rhinoscopy: 1.5-cm solitary, pink tumour, originating from the nasal septum, filling the vestibule	Primary	Nasalseptum	MFSS	Local excision	No evidence of disease /18 months
Subramania et al. 2012. <sup>19</sup>	45/M	epistaxis and blurred vision	3.3-cm mass in sphenoid sinus extended to clivus, prepontine cistern and right cavernous sinus	Primary	Sphenoid	PDSS	Surgery (biopsy) + Chemotherapy	NR
Salcedo-Hernandez et al.2013. <sup>20</sup>	26/M	NR	4 cm size (radiology retains NR)	Primary	Maxillary	NR	Surgery	Died because of disease (119 months)
Wong et al. 2014. <sup>21</sup>	80/ F	epistaxis	Not reported	Primary	Ethmoid	MPSS	Surgery	Died because of disease /9 months Metastasis to brain and lymph nodes
Shin Saito et al. 2018. <sup>22</sup>	53/ M	Nasal obstruction	Mass in left maxillary sinus, expanding into common nasal meatus	Primary	Maxillary	BPSS	Surgery +RT(6600 cGy/33) and chemo(PI)	No evidence of disease (12 months)
Present case	22/ F	Nasal obstruction	7.5 x 8.0 x 4.0 cm mass involving left maxillary and ethmoid sinus, extending into the left nasal cavity	Primary	Maxillary+ Ethmoid	MPSS	Surgery RT+Chemo (1 cycle)	Disease free till 12 months/Metastatic disease

MPSS = monophasic synovial sarcoma; BPSS = Biphasic synovial sarcoma; PDSS= poorly differentiated synovial sarcoma; RT = Radiation therapy

region.<sup>6</sup> Moreover, Mamelle et al, also reviewed four cases and concluded the same management. The same study reported 29% of mortality at three years, with an overall mortality reported to be 43%. The development of pulmonary metastases causes the patient's death.<sup>7</sup>

The other debate over the management of SS is the utilisation and efficacy of chemotherapy as an adjuvant treatment after surgery. Only one retrospective study by Mattavelli D et al, studied the clinicopathological prognostic factors of head and neck soft tissue sarcoma. Tumour size and grade are the independent prognostic factors for disease specific mortality. The study also stated that the local recurrence was affected by the tumour size, while distant metastasis was affected by grade and tumour location.<sup>8</sup>

A. Italiano et al studied the predictive value of grade for benefit from adjuvant chemotherapy (Doxorubicin and Cyclophosphamide, AC) in a large cohort-based analysis. The long-term follow-up revealed that patients with grade 3 disease may benefit from AC. On multivariate analysis, AC was significantly associated with improved metastasis-free survival (MFS) and overall survival in grade 3 patients.<sup>9</sup> Andrea Ferrari et al established the importance of systemic therapy in a retrospective analysis. They reported five-year MFS rate of 60% with chemotherapy and 48% without chemotherapy.<sup>10</sup>

Hence, the literature advocates RT and chemotherapy in all patients with high-risk features for loco-regional and distant relapse like positive surgical margins, high grade, tumour size and location.

Our patient was in compliant to chemotherapy, hence she presented with disease relapse in lungs, liver and bones. Financial constraints, treatment related toxicity and increased numbers of visits are considered a limitation for patient's compliance with the treatment. As literature related to the disease is scarce and inadequate, reporting of similar cases should be encouraged to further understand the behaviour of the disease to adjuvant treatment.

## Conclusion

Synovial sarcoma is a rare entity in the head and neck region. Few case reports have been published in literature with synovial sarcoma in the paranasal region. Our patient presented with nasal obstruction. Workup revealed left nasal mass involving left maxillary and ethmoid sinus. She underwent surgery after biopsy. The postoperative histopathology report was consistent with SS. Surgery remains the mainstay of treatment and there is a lack of clear guidance about the adjuvant treatment. She was

offered adjuvant radiation and chemotherapy. She remained non-compliant with chemotherapy and re-presented with systemic disease relapse.

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