

ORIGINAL STUDY

Synovial sarcoma of the oral cavity: Report of 4 cases and review of the literature

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ABSTRACT

Synovial sarcoma is a rare and high-grade soft tissue tumour that rarely affects the head and neck region. Approximately 90% of synovial sarcomas are seen in the extremities. About 5 to 10% occur in the head and neck region with high incidences in the parapharyngeal space and hypopharynx. In the oral cavity, synovial sarcoma has been reported in the buccal mucosa, tongue, floor of the mouth, the retromolar region, hard and soft palates, the gingivobuccal sulcus and the mandible. In this paper, we report 4 very rare cases of monophasic synovial sarcoma of the oral cavity and highlight the need for proper diagnosis and treatment plan in the cases of synovial sarcoma. So far, around 250 cases of synovial sarcoma of head and neck have been reported in the literature. In India, on extensive literature search we could retrieve 18 cases of synovial sarcoma involving the head and neck region, of these 11 cases of primary synovial sarcoma involving the oral cavity have been reported previously. To our knowledge, this is the first series of primary synovial sarcoma of the oral cavity in the Indian literature.

KEYWORDS: monophasic synovial sarcoma, metastasis, lower alveolus, hard palate, retromolar trigone, upper alveolus.

INTRODUCTION

Synovial sarcoma is a high-grade soft tissue tumour and the fourth most common soft tissue tumour¹. Approximately 90% of synovial sarcomas are seen in extremities in young adults whose treatment involves surgical resection followed by adjuvant radiotherapy^{2,3}.

Synovial sarcoma is rare in the oral cavity, showing variable aggressiveness and slow growth⁴. The first case of synovial sarcoma of the head and neck was described by Jernstrom in 1954⁵. A review article written by Stanbouly et al. stated that, from a total of 243 cases analysed from 1950 up to 2020, the most common site for development of synovial sarcoma in the head and neck region was the neck (17.7%) followed by the oral cavity (11.5%)⁶.

According to the literatures, 5 to 10% of synovial sarcomas occurred in the head and neck region, mostly in the parapharyngeal space and hypopharynx, with pre-

dominance in the paravertebral connective tissue and the least common in the larynx⁷. In the oral cavity, incidences of synovial sarcoma in the buccal mucosa, tongue, floor of the mouth, the retromolar region, the hard and soft palates, the gingivobuccal sulcus and the mandible have been reported⁸.

Monophasic and biphasic synovial sarcomas are two histological variants delineated in the literature, the monophasic being the most common variant containing spindle cells and the biphasic variant containing both epithelioid and spindle cells⁷. We present 4 cases of primary monophasic synovial sarcoma of the oral cavity.

MATERIAL AND METHODS

Objective: To explore clinical, histopathological, immunohistochemistry (IHC) features of synovial sarcoma

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Figure 1. Clinical image of the case showing a mass in the right maxilla and the hard palate.

of the oral cavity along with the treatment, prognosis and a review of the literature.

Setting and design: Hospital-based cross-sectional study.

Methods: The data of all cases of synovial sarcoma of the oral cavity diagnosed over a period of 5 years, from January 2018 to December 2022, were retrieved. The hematoxylin and eosin (H&E) sections and IHC sections were studied. A strict histopathological and recently updated criteria were applied and patients with a confirmed diagnosis of primary synovial sarcoma of the oral cavity were included in this study. This study comprises 4 cases of primary synovial sarcoma over a period of 5 years (from Jan 2018 to Dec 2022). A literature review was conducted by searching PubMed, Google Scholar and National Cen-

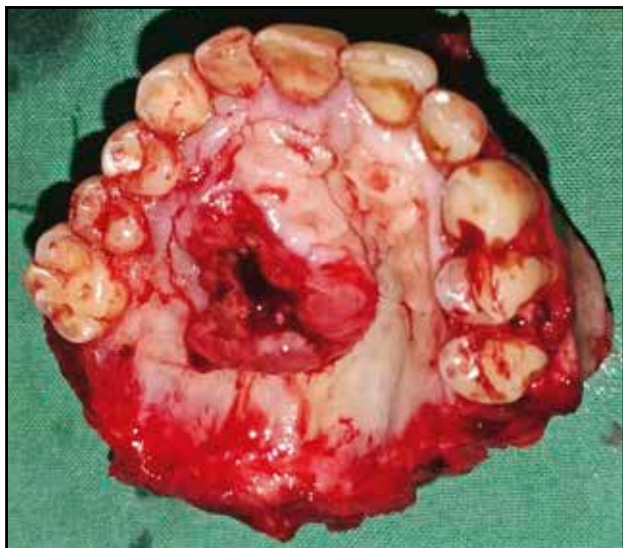


Figure 3. Gross image of the resected specimen of Case 1 showing a mass involving the right half of the hard palate.

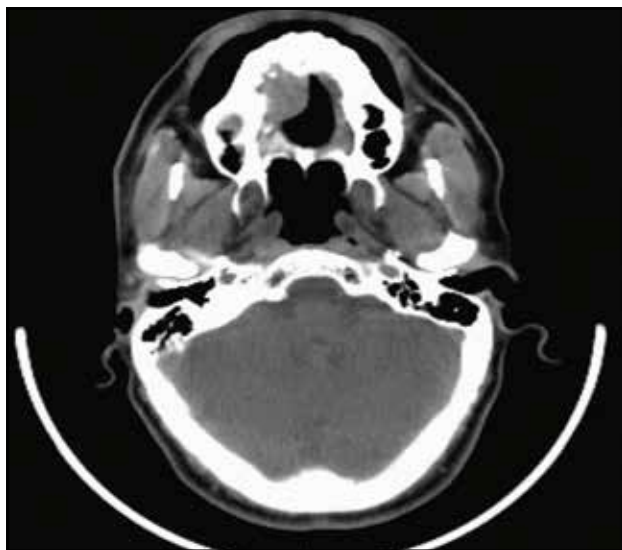


Figure 2. Crano-facial CT scan, axial cut of Case 1 showing a mass in the right maxilla and hard palate.

tre for Biotechnology Information database, using the keyword search term “Synovial sarcoma” and “Synovial sarcoma oral cavity”. All 18 case reports of synovial sarcoma involving the head and neck region from the Indian literature were included. Case reports published in a language other than English and without English language abstract were excluded.

PERSONAL EXPERIENCE

CASE 1

A 50-year-old male patient presented to our hospital with complaint of a swelling in the hard palate

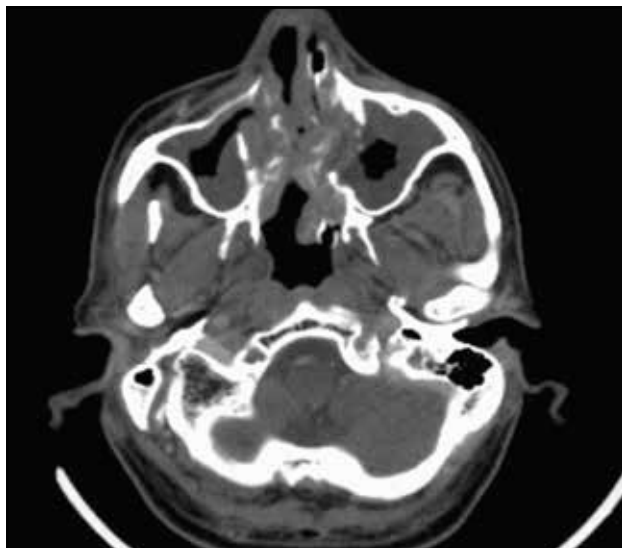


Figure 4. Crano-facial CT scan, axial cut, showing local recurrence in Case 1 involving the nasal cavity and bilateral maxillary sinuses.

region in the last 5 months. Initially, the swelling was small and gradually increased to the present size that caused difficulty in feeding. On examination, a mass measuring 4×3 cm was seen from the right side of the anterior maxilla, crossing the midline and involving the hard palate. The overlying mucosa was stretched, ulcerated and erythematous. On palpation, the swelling was firm to hard in consistency and tender (Figure 1). There was no evidence of cervical adenopathy. Past medical history was unremarkable. Routine blood investigations were within normal limits.

Contrast-enhanced cranio-facial CT scan revealed a large irregular mass on the right side of the anterior maxilla in the midline, measuring about 4.7×2.8×2.8 cm, involving the upper alveolus and extending posteriorly to the palate, causing erosion and bony perforation of the palate on the right side (Figure 2). Our clinical diagnosis was a malignant tumour, possibly a carcinoma. So, we did an incisional biopsy under local anaesthesia and histopathology revealed a malignant tumour with predominantly spindle cell morphology.

We performed a bilateral maxillectomy through transoral approach and the postoperative recovery was uneventful. Grossly, an ulcerative tumour measuring 4.5×2.8 cm was seen involving the right half of the hard palate, extending to the right upper alveolar mucosa (Figure 3). The defect was reconstructed with a split-thickness skin graft.

Histopathologic examination of the resected tumour revealed a malignant spindle cell tumour without any evidence of keratinisation. So, we considered possibilities of sarcomatoid squamous cell carcinoma and other spindle cell sarcomas like angiosarcoma and synovial sarcoma. Hence, immunohistochemistry (IHC) was done for a precise diagnosis. On IHC, the tumour cells were positive for

CK, EMA, BCL2, CD99, Calponin, TLE1, and negative for p63, p40 and CD34. With this typical immune profile, we made a diagnosis of monophasic synovial sarcoma.

The patient received adjuvant radiotherapy which consisted of 30 fractions of 60Gy IMRT. 3 months after treatment, the contrast cranio-facial CT scan revealed that there was evidence of recurrence in the nasal cavity and bilateral maxillary sinuses (Figure 4). The patient was given three cycles of chemotherapy for recurrence. At his 2-month follow-up visit, the patient complained of generalised back pain and vomiting in the last 20 days. The abdominal ultrasonography revealed liver metastasis. The patient refused to take any further treatment and died within 7 days.

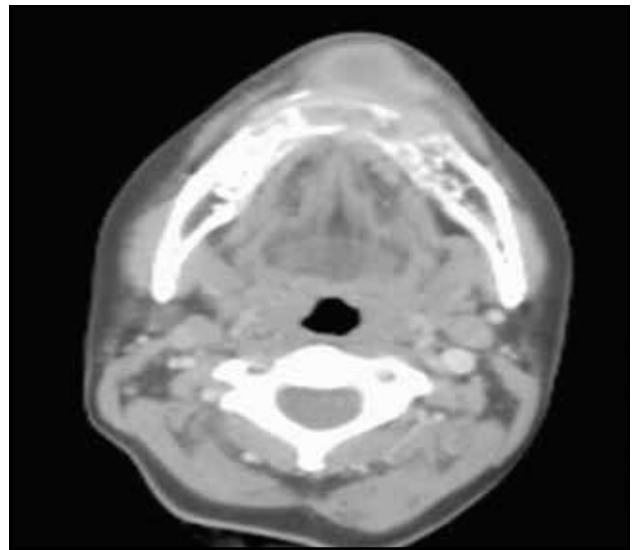


Figure 5. Cranio-facial CT scan, axial cut of Case 2 showing advanced mass in the central arch of mandible.

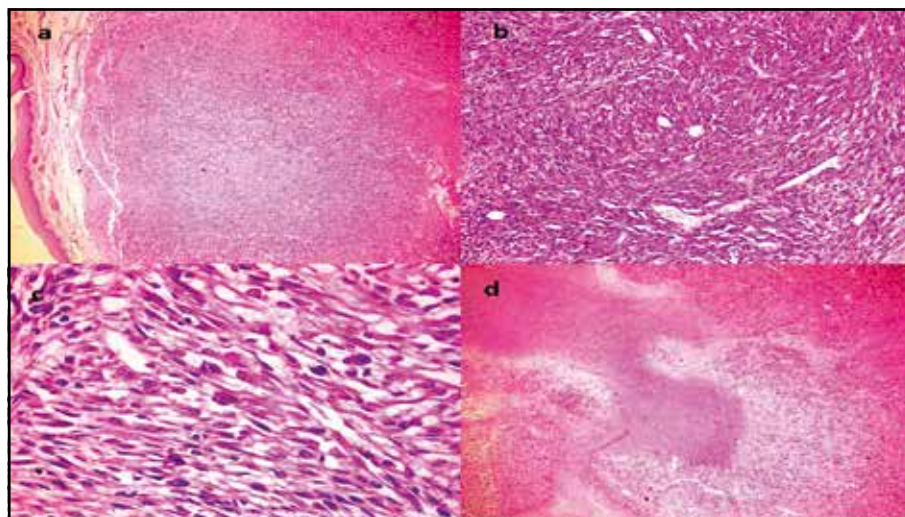


Figure 6. Microscopic images from Case 2 showing: (a) Subepithelial spindle cell neoplasm in the alveolar mucosa (b) With hemangiopericytomas vascular pattern (c) Nuclear atypia with increased mitosis and (d) Foci of tumour necrosis (H&E a and dx40, b×100, c×400).

CASE 2

A 35-year-old female patient reported to our hospital with complaint of swelling in the lower anterior region of the jaw for 6 months. She had complaints of difficulty in swallowing and speech. On examination, an ulcero-proliferative growth measuring approximately 5×4 cm was seen in the lower anterior region of the alveolar mucosa, involving the lower gingivobuccal sulcus (GBS) and the lower lip mucosa and crossing the midline, extending towards the contralateral side. On palpation, the growth was firm in consistency and tender. Level 1b lymph node was non tender, hard and mobile. All vitals and routine blood investigations were within normal limits.

Contrast cranio-facial CT scan revealed a locally advanced mass arising from the alveolar arch of the symphysis menti along the central inferior GBS. There was

significant osteolysis of involved bone with neoplastic tissue into the medullary canal of the mandible and multiple enlarged nodes in the bilateral submandibular space and level II lymph nodes (Figure 5). Our clinical diagnosis was a carcinoma of the lower anterior alveolus, so we did incisional biopsy and histopathology revealed a diagnosis of malignant spindle cell tumour.

We performed near total mandibulectomy with bilateral supraomohyoid neck dissection (SOHND) and the defect was reconstructed with an anterolateral thigh (ALT) flap. The histopathology showed a subepithelial spindle cell neoplasm with nuclear atypia with increased mitosis, foci of tumour necrosis and a hemangiopericytoma pattern (Figure 6). Immunohistochemistry revealed that tumour cells were positive for CK, EMA, BCL2, TLE1, SMA, CK7, CD99, Calponin and negative for p63,

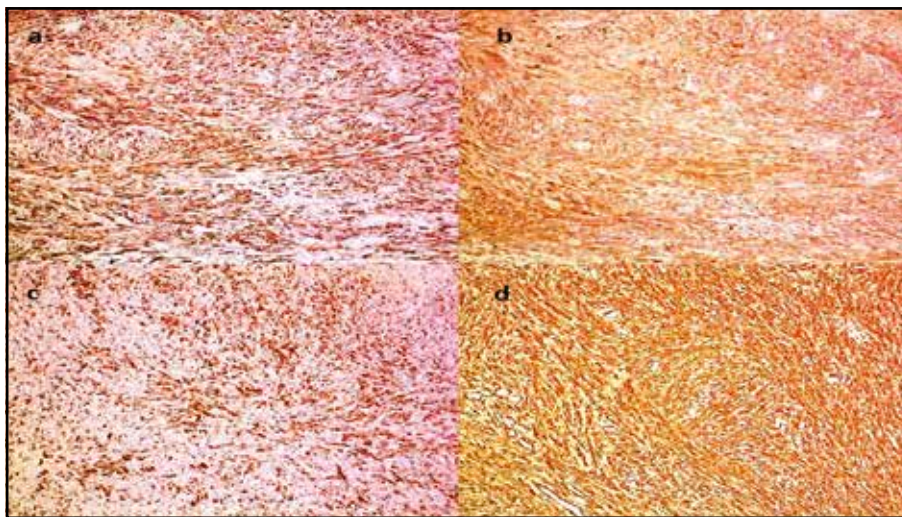


Figure 7. Immunohistochemistry images from Case no 2 with tumour cells showing expression of a) CK, b) EMA, c) CK 7 and d) Vimentin (IHC a, b, c, d×100).

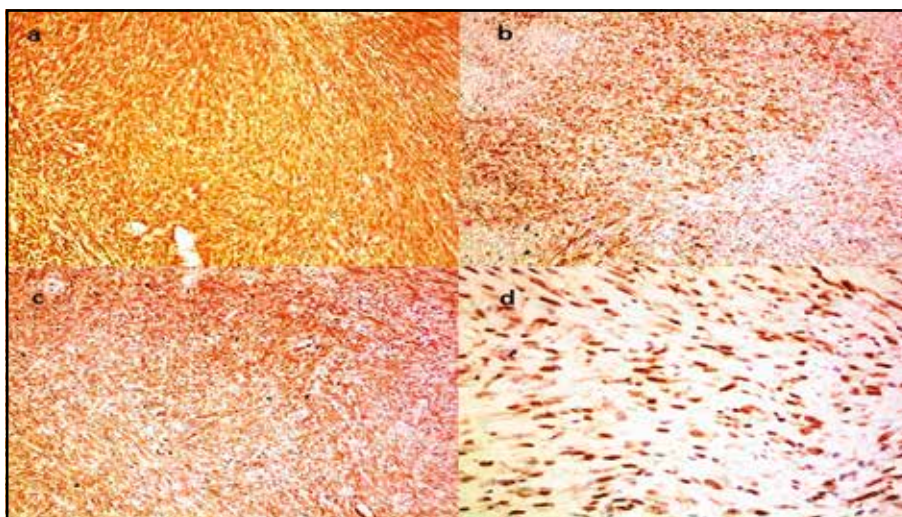


Figure 8. Immunohistochemistry image from Case no 2 with tumour cells showing expression of a) CD 99, b) BCL 2, c) Calponin, d) Nuclear expression of TLE 1 (IHC a, b, c × 100, d×400).

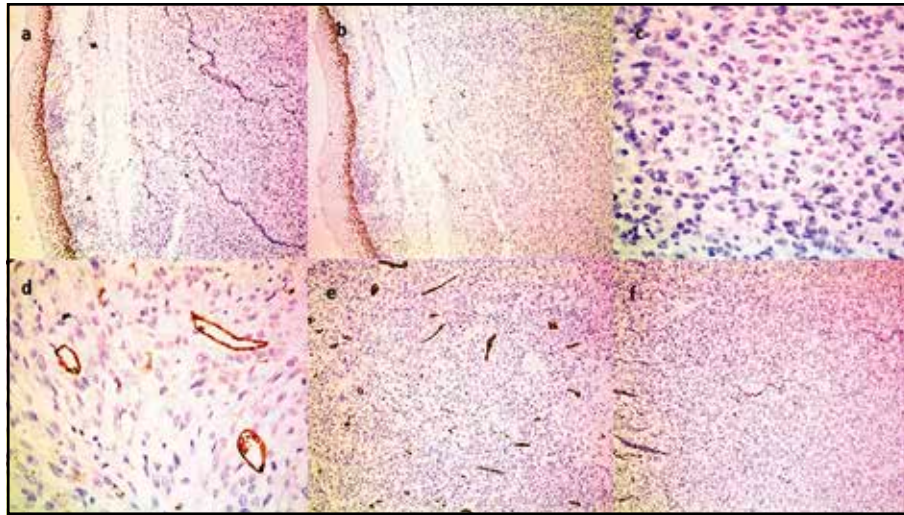


Figure 9. Immunohistochemistry images from Case no 2: the tumour cells are negative for a) p63, b) p40, c) S-100, d) CD 31, e) CD 34 and f) Desmin (IHC a, b, e, f $\times 100$, c and d $\times 400$).

p40, CK20, CD34 and S 100 (Figures 7-9). Hence, we made a diagnosis of monophasic synovial sarcoma.

The patient received adjuvant radiotherapy which consisted of 30 fractions of 60 Gy IMRT. 3 months after treatment, the contrast chest CT scan showed multiple nodular lesions in the lungs suggestive of metastatic deposits (Figure 10). The patient was advised chemotherapy. But the patient refused to take chemotherapy and died within a month.

CASE 3

A 55-year-old male patient reported to our hospital with complaint of swelling in the upper anterior region of the jaw in the past 2 months. He had complaints of pain in the same region. On examination, there was a bony hard, tender swelling in the upper anterior alveolus. The overlying mucosa was ulcerative and erythematous. There was no evidence of cervical adenopathy. Past



Figure 10. Chest CT scan of Case 2 showing metastatic deposits in lungs.

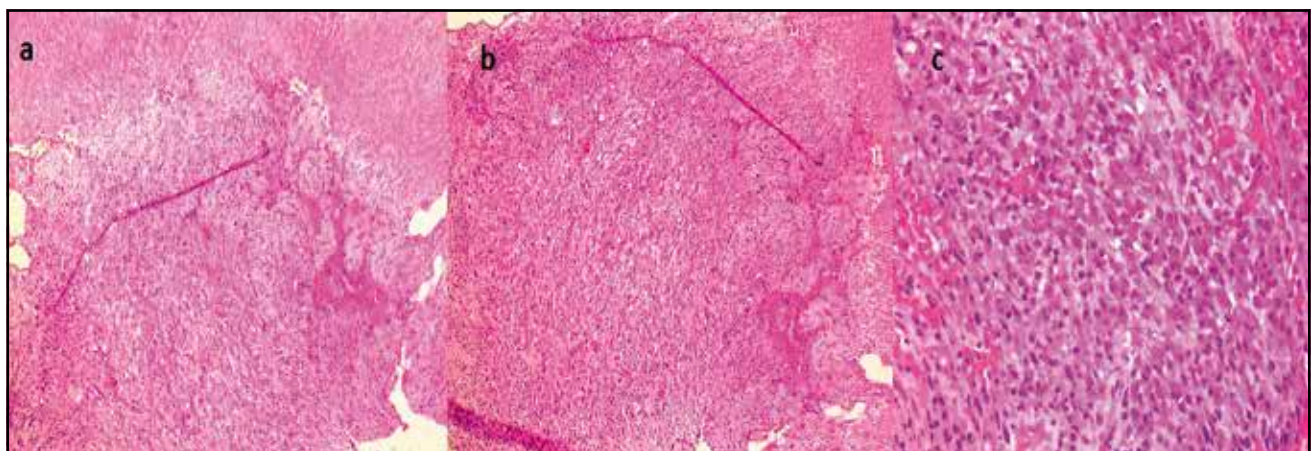


Figure 11. Hematoxylin and eosin images of Case 3 showing: a) tumour covered by an ulcerated epithelium; b) & c) a malignant spindle cell tumour without any evidence of differentiation (H&E a $\times 100$, b $\times 100$, c $\times 400$).

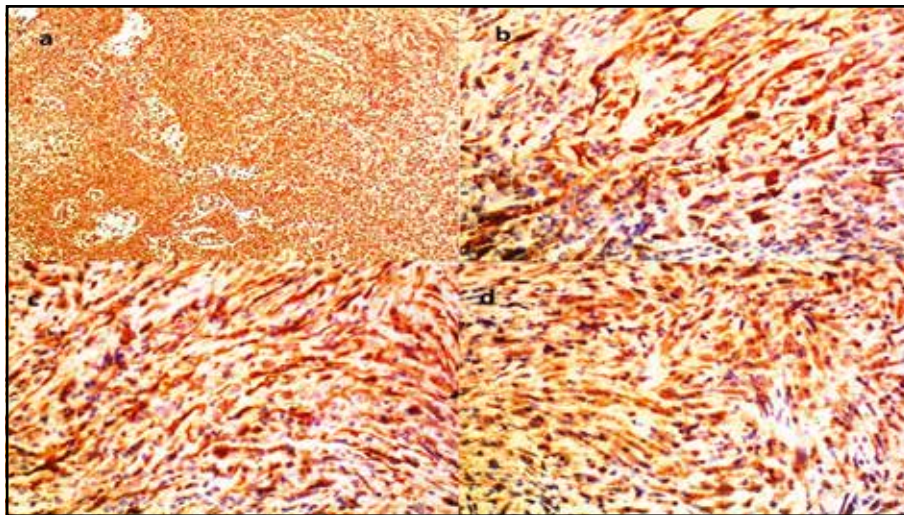


Figure 12. Immunohistochemistry images of Case 3 showing tumour cells expressing a) Vimentin, b) CK, c) EMA and d) CD 99 (IHC a x100, b, c and d x400).

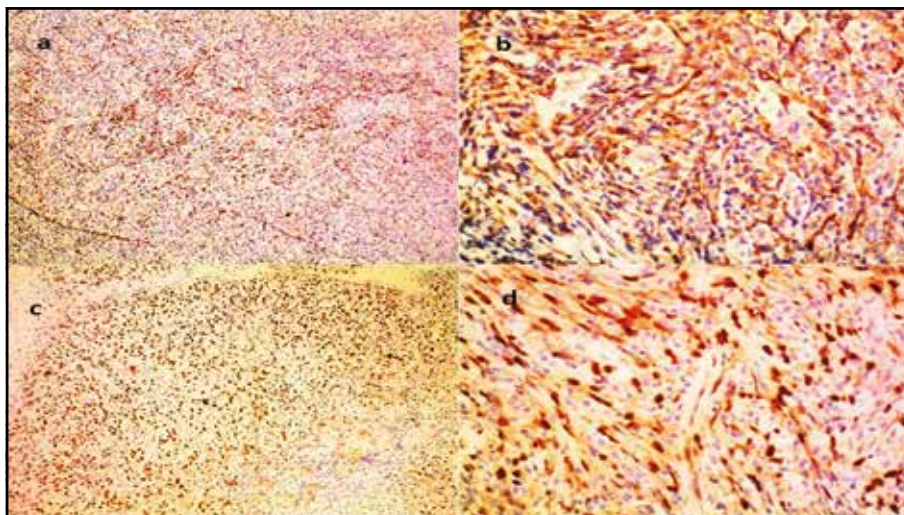


Figure 13. Immunohistochemistry images of Case 3 showing tumour cells expressing a) BCL 2, b) Calponin, c) and d) The tumour cells show bright nuclear expression of TLE 1 (IHC a and c x100, b and d x400).

medical history was unremarkable. All vitals were within normal limits. A contrast cranio-facial CT scan revealed a destructive mass in the upper anterior alveolus measuring 4×3.5×2.8 cm. The clinical diagnosis was a carcinoma of the upper anterior alveolus.

We did an incisional biopsy under local anaesthesia. The microscopic examination showed a malignant spindle cell tumour; no evidence of differentiation was noted (Figure 11). Since it lacked any differentiation, we considered possibilities of sarcomatoid carcinoma and other soft tissue spindle cell sarcomas. Hence, we performed IHC. On IHC, the tumour cells were positive for CK, EMA, CD 99, TLE1, calponin, and negative for BCL2, p63, p40 and CD34 (Figures 12-14). Hence, we confirmed a diagnosis of monophasic synovial sarcoma.

We performed maxillectomy and a splint was

placed. The patient refused to take further treatment. 2 months post-surgery, the chest radiograph revealed metastases to the lung and the patient succumbed to the disease within a month.

CASE 4

A 49-year-old male patient reported to our hospital with complaint of a 6-month old ulcerative lesion in the left retromolar trigone (RMT). On examination, an ulcerative lesion measuring approximately 4×3 cm was seen in the left RMT region. There were no other head and neck abnormalities detected and no evidence of cervical adenopathy. Past medical history was unremarkable. A contrast cranio-facial CT scan revealed an infiltrative and destructive mass involving in the left RMT, measuring 4×2.5×1.5 cm.

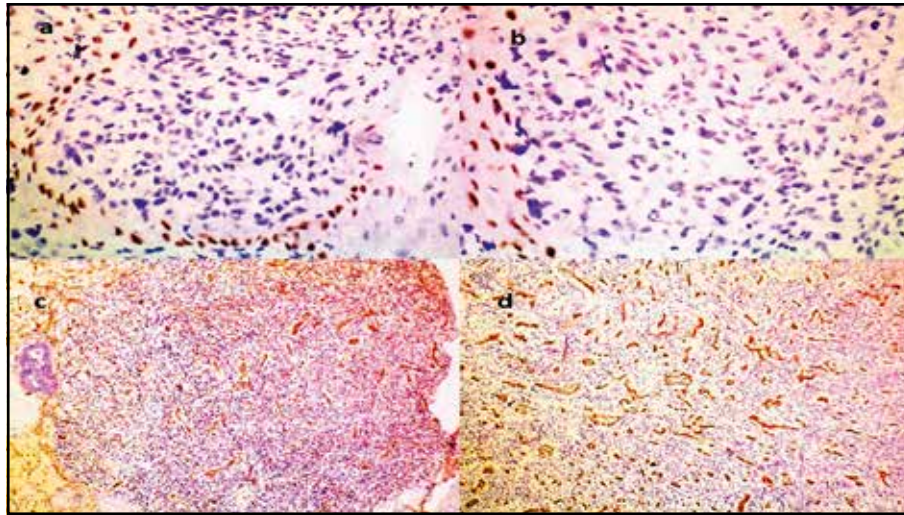


Figure 14. Immunohistochemistry images of Case 3 showing tumour cells are negative for a) p63, b) p40, c) CD 31, d) CD 34 (IHC a and b $\times 400$, c and d $\times 100$).

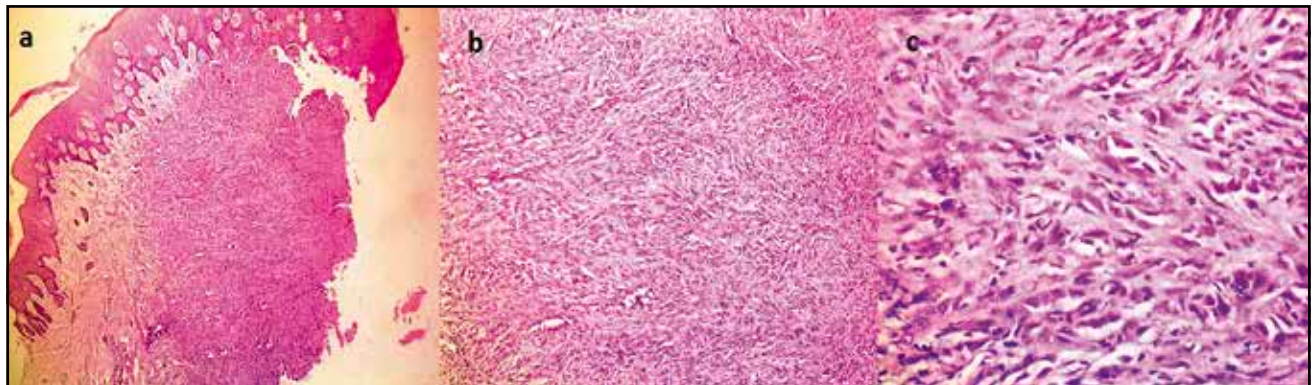


Figure 15. Hematoxylin and eosin images of Case 4 showing: a) tumour covered by intact squamous epithelium, b) and c). Malignant spindle cell tumour without any evidence of differentiation (H&E a $\times 40$, b $\times 100$, c $\times 400$).

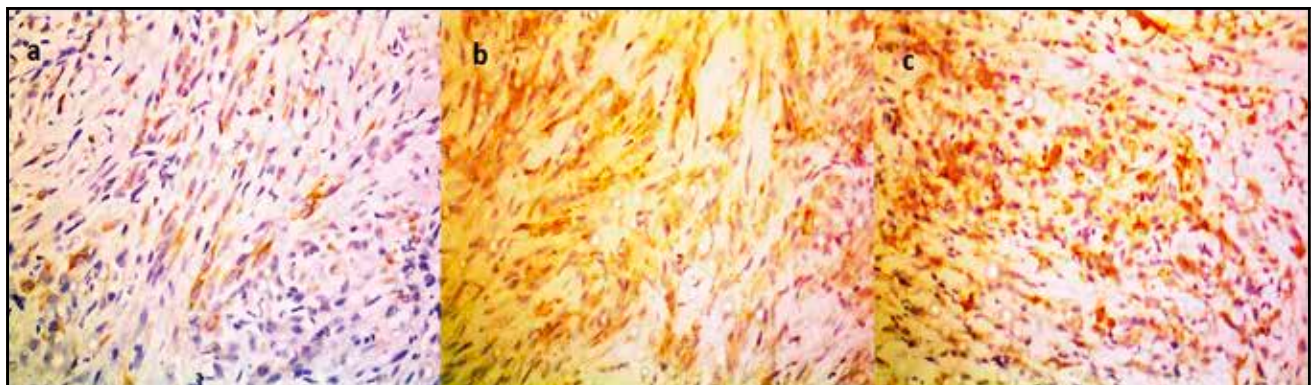


Figure 16. Immunohistochemistry images of Case 4 showing tumour cells expressing a) CK, b) EMA, c) CD 99 (IHC a, b and c $\times 400$).

We performed diagnostic incisional biopsy and the histopathology examination revealed malignant spindle cell tumour (Figure 15). Differential diagnosis in this case included a sarcomatoid carcinoma, other

spindle cell sarcomas and malignant melanoma. On IHC, the tumour cells were positive for vimentin, CK, EMA, BCL2, calponin, and TLE1 and negative for desmin, CD31, CD34, S-100, p63, p40 and HMB 45

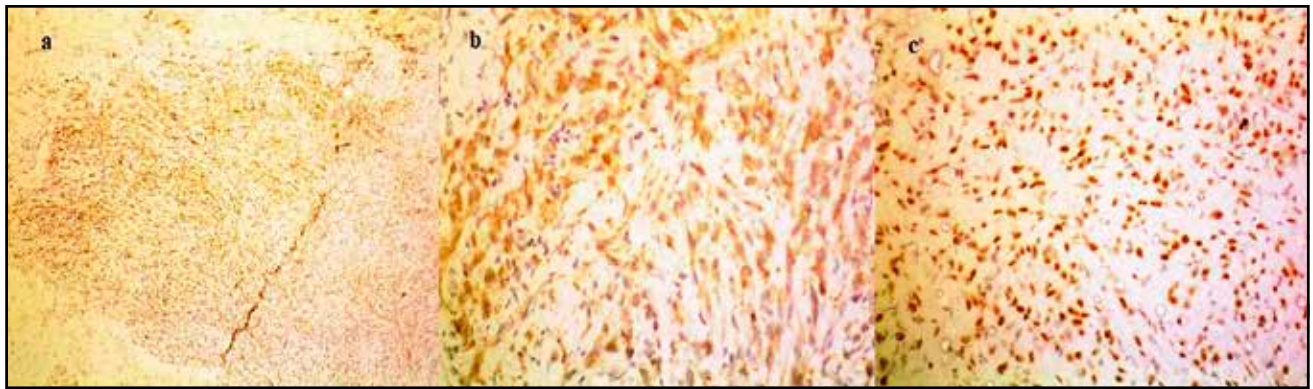


Figure 17. Immunohistochemistry images of Case 4 showing tumour cells expressing a) BCL 2, b) Calponin and c) nuclear expression of TLE (IHC a $\times 100$, b and c $\times 400$).

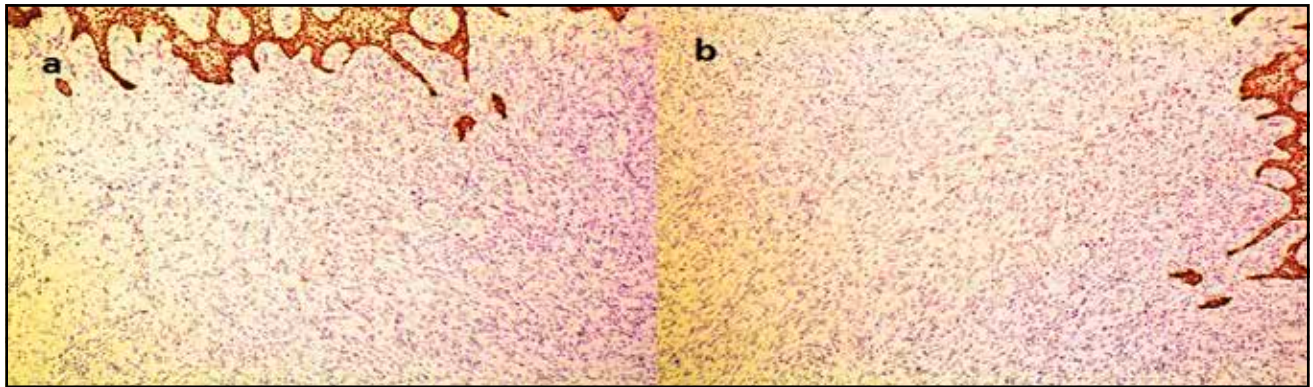


Figure 18. Immunohistochemistry images of Case 4 showing tumour cells are negative for a) p63 and b) p40 (IHC a, b $\times 100$).

(Figures 16-18). Hence, a diagnosis of monophasic synovial sarcoma was made.

The patient refused the surgical treatment and underwent 3 cycles of neoadjuvant chemotherapy and discontinued it after 3 cycles. The patient did not return for follow-up.

LITERATURE RESEARCH AND DISCUSSIONS

In 1865, synovial sarcoma was originally described by Simon who stated that, "it is a well-defined clinical and morphological entity", and was so named in 1934 by Sabrazes et al⁹. Synovial sarcoma is a malignant tumour of mesenchymal origin that occurs most commonly in the extremities of young adults and adolescents^{2,9}. This tumour type can be found at any age group range of 15-40 years and both genders are similarly affected². Of the 4 cases presented here, 3 occurred in men and 1 in a woman. The patient age ranged between 35 to 55 years.

About 5 to 10 cases of synovial sarcoma occur in the head and neck region, mostly in the parapharyngeal space and hyopharynx⁷. In the oral cavity, the posterior tongue is the most frequent site described in the litera-

tures followed by buccal mucosa, the soft palate, RMT and floor of the mouth¹⁰. On extensive search of the literature, about 250 cases of synovial sarcoma are reported in the head and neck region. There have been only 18 cases of synovial sarcoma reported in the head and neck region from the Indian literature, of which 11 are in the oral cavity (Table 1). All these are single case reports; so, this is the first Indian case series of synovial sarcoma of the oral cavity. In the presented series, tumours were located in the hard palate, lower anterior alveolus, upper anterior alveolus and retromolar trigone.

The common clinical feature of this tumour is a slowly enlarging, deeply located, palpable mass with pain in 50% of the cases. The tumours were firm, rubbery and comparatively well demarcated, with focal areas of infiltration. Some tumours were pedunculated or polypoid, with ulcerated areas and spontaneous haemorrhage¹⁰. In our all 4 cases, the presence of a slowly growing swelling before clinical presentation was seen.

Tumours arising from the head and neck region mainly present as a dysphagia, hoarseness, dysphonia, and headache, depending on origin and plane of spread of tumour²⁵. In other parts of the body, the tumour presents as a palpable slowly growing mass simulating a benign course²⁶. Tumours range from 2 cm to

Table 1. Analysis of reported cases of synovial sarcoma of the head and neck region from the Indian literature, including the current 4 cases.

Sr. no	Reference	Age/Sex	Site	Dimension	Histologic Type	Follow-up (Months)
1	Wadhwan et al. (2011) ⁸	28/M	Mandible	4×3 cm	B	Alive (12)
2	Dhawan et al. (2012) ¹¹	26/F	Infra-temporal fossa (ITF)	3.2×3.2 cm	B	Alive (36)
3	Mahesh et al. (2013) ⁹	24/M	Buccal Mucosa	12×10 cm	Poorly differentiate	Dead (12)
4	Aparna et al. (2014) ¹²	21/M	Maxilla	3×2 cm	M	Alive (12)
5	Nanjundappa et al. (2015) ¹³	12/F	Floor of the mouth (FOM)	4×4 cm	-	Alive (36)
6	Dudani et al. (2015) ¹⁴	74/F	Tongue	5×4 cm	M	Alive (4)
7	Nath et al. (2016) ¹⁵	25/M	Larynx	4×4 cm	M	Alive (24)
8	Nath et al. (2016) ¹⁵	20/M	Parotid	7×6 cm	M	Alive (24)
9	Kashyap et al. (2016) ¹⁶	40/F	Mandible	-	Poorly differentiate	-
10	Dabholkar et al. (2017) ¹⁷	16/M	Hypopharynx	5×5 cm	B	Dead (12)
11	Narayanan et al. (2017) ¹⁸	48/M	Larynx	2×2 cm	-	Alive (36)
12	Dholaria et al. (2017) ¹⁹	33/M	Mandible	1.5×1 cm	-	-
13	Sharma et al. (2019) ²⁰	74/F	Tongue	5×2 cm	M	Alive (24)
14	Sharma et al. (2019) ²¹	17/M	Mandible	6×5 cm	M	-
15	Dhiman et al. (2021) ²²	43/F	Ethmoid sinus	-	-	Alive (12)
16	Dhiman et al. (2021) ²²	82/F	Ethmoid sinus	2×4 cm	-	Dead (2)
17	Kandoi et al. (2021) ²³	23/F	Buccal Mucosa	3×4 cm	B	Alive (2)
18	Ojha et al. (2022) ²⁴	50/F	Buccal Mucosa	-	-	Alive (12)
19	Present series	50/M	Hard palate	4×3cm	M	Dead (3)
20	Present series	35/F	Lower anterior alveolus	5×4cm	M	Dead (4)
21	Present series	55/M	Upper anterior alveolus	4 x 3.5 cm	M	Dead (3)
22	Present series	49/M	Retromolar trigone (RMT)	4×3cm	M	Lost to follow-up

Table 2. Royal Marsden Hospital (RMH) staging system⁹.

Prognostic Group	Low Grade	Intermediate Grade	High Grade	Node Metastasis	Distant Metastasis
Stage IA	< 5cm	-	-	-	-
Stage IB	5-10 cm	<5 cm	-	-	-
Stage IIA	10-15 cm	5-10 cm	< 5 cm	-	-
Stage IIB	>15 cm	10-15 cm	5-10 cm	-	-
Stage IIIA	-	>15 cm	10-15 cm	-	-
Stage IIIB	-	-	>15 cm	-	-
Stage IVA	-	-	-	+	-
Stage IVB	-	-	-	+	+

15 cm; the superficial tumours may be smaller and detected earlier, while deeper tumours quite larger and undiagnosed for a longer time²⁷.

According to Royal Marsden Hospital (RMH) staging system, all low-grade tumours <15 cm and high-grade tumours <10 cm were staged below III⁹. All tumours with nodal metastasis were staged as stage IVA and with distant metastasis were staged as stage IVB⁹ (Table 2). In the present study, cases 1, 2 and 3 were staged as stage IVB as all had distant metastasis and case 4 was staged as stage IIA. Monophasic tumours, monophasic epithelial tumours, biphasic tumours and poorly differentiated tumours are four subtypes described in the literature; the monophasic is the most common variant containing spindle cells, followed by the biphasic form containing both epithelioid and spindle cells^{7,28}. In the present study, we reported all 4 cases as monophasic synovial sarcoma of the oral cavity.

Immunohistochemistry is a useful method for diagnosis of synovial sarcoma and helps to differentiate it from other spindle cell neoplasms. According to the literature, 97% of synovial sarcomas are positive for cytokeratin and 69% of synovial sarcomas are positive for EMA^{29,30}. The BCL2 protein is a characteristic marker of synovial sarcoma, useful to distinguish synovial sarcoma from other spindle cell sarcomas³¹. Approximately 67% of synovial sarcomas are positive for CD99, the product of MIC2 gene³². In addition, 90% of synovial sarcomas are reactive for TLE1 antibody nuclear stain³³. Typically, synovial sarcomas are negative for actin, desmin, CD34, myoglobin or S 100³³; in our series, all 4 cases showed typical immunoprofile, with expression of CK, EMA, BCL2, calponin, TLE1.

Surgical resection with oncological safe margins is the mainstay treatment option for synovial sarcoma of the head and neck region. Due to the complex anatomy, a complete resection of intraoral tumours is not always feasible; a combined treatment modality consisting of extensive radical resection, adjuvant radiotherapy, and chemotherapy is frequently advised⁹. In the present study, 2 cases underwent wide surgical resection followed by postoperative radiotherapy and chemotherapy and one case underwent only wide surgical resection and one case who refused surgery was offered chemotherapy only.

Synovial sarcoma of the head and neck region has metastatic potential of 29.2% and recurrence rate of 20.8%, which is lower than other sites of synovial sarcoma³⁴. Synovial sarcoma is most frequently metastasized to the lung, lymph nodes and bone marrow¹⁰. Tumour recurrence is commonly seen in the first 2 years after the initial treatment, but it was also reported after 20 years. Synovial sarcoma is an aggressive tumour with poor prognosis (5-year survival rate, 55%)⁹. The prognosis of the tumour is adversely affected by the following factors: male gender, size of tumour more than 5 cm, tumour site, high-grade tumour, positive margins and presence of metastasis³.

In the present study, out of 4 cases 3 patients died within a year after diagnosis and 1 patient has been lost to follow-up.

CONCLUSIONS

Synovial sarcoma is a rare tumour in the head and neck region and it is best confirmed by histopathological, immunohistochemical and molecular studies. According to most authorities, synovial sarcoma of the oral cavity is aggressive in nature and it has tendency to metastasise to other sites. Tumour recurrence is very common in the first two years after the initial treatment. This underlines the need for early diagnosis and aggressive treatment of synovial sarcoma.

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