

Case Report

Myofibroblastic sarcoma of the oral cavity: a diagnostic dilemma and report of two cases

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(Received: 29 July 2021, accepted: 18 November 2021)

Keywords:
Myofibroblastic sarcoma / high grade / fibroblastic/myofibroblastic tumours / oral cavity / case report

Abstract – Introduction: Myofibroblastic sarcoma is designated as a low-grade malignancy, commonly affecting the deep soft tissue of the head and neck. Despite being classified as low-grade, myofibroblastic sarcoma with high-grade features have been reported. **Observations:** Two such cases affecting the oral cavity, which were diagnosed as different entities upon biopsy, were observed. Case 1 presented as multiple, well-circumscribed soft tissue swellings of the tongue and alveolar mucosa and was diagnosed as synovial sarcoma. Case 2 manifested as a large extensive osseous lesion of the maxilla and was diagnosed as an inflammatory myofibroblastic tumour. **Conclusion:** Myofibroblastic sarcoma with high-grade features remains a diagnostic dilemma due to its overlapping features with other spectra of fibroblastic/myofibroblastic tumours and lack of consensus regarding its classification as a separate entity. Establishing the definitive diagnosis requires adequate tumour sampling and a systematic clinicopathological approach.

Introduction

Myofibroblastic sarcoma or myofibrosarcoma is a low-grade malignancy, frequently affecting the extremities and head and neck region [1]. Despite being classified as low grade, its infiltrative behaviour has been well established [2]. This rare entity was first recognised in 1998, typically affecting adults, with a median age of 40. In the oral cavity, the tongue is a commonly affected site [2,3]. Although it has been described as a deep soft tissue neoplasm, lesions from gnathic bone have been reported. By 2019, approximately 55 cases involving the head and neck region have been published in the literature [4]. Histologically, it is a part of the fibroblastic/myofibroblastic group of tumours, which range from benign to overtly malignant neoplasms [5]. It is challenging to distinguish myofibroblastic sarcoma from other spindle cell tumours, particularly those exhibiting fibroblastic/myofibroblastic differentiation in small incisional biopsies, due to overlapping microscopic features. Assessment of the clinical features, histomorphology, coupled with a panel of immunohistochemical stains, will aid in formulating an accurate diagnosis [5,6].

In this report, two cases of myofibroblastic sarcoma of the oral cavity, with high-grade features, which were previously diagnosed as different lesions upon biopsy, are described.

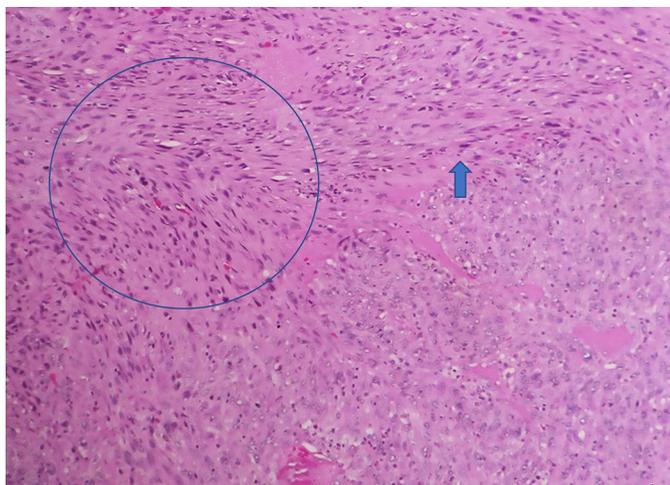
Observation

Case 1

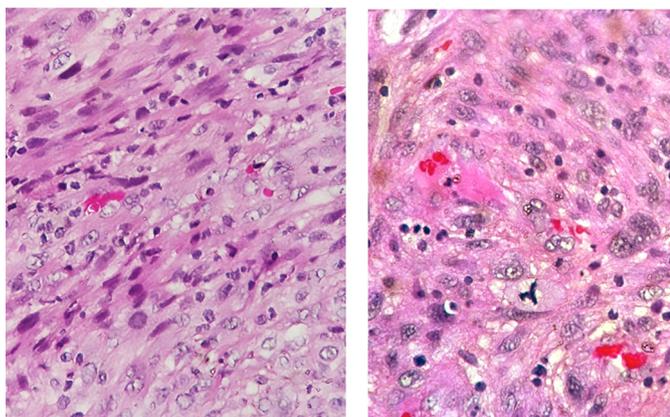
A 73-year-old man, a known case of prostate carcinoma, bronchial asthma, and gastritis, was referred from another hospital for gradually enlarging swellings of the tongue and alveolar mucosa over the past six months. An incisional biopsy had been performed, and the lesions were reported as synovial sarcoma. The patient had no other symptoms and did not experience any appetite or weight loss. Intraoral examination showed two pedunculated, non-ulcerated nodular swellings located on the right lateral border of tongue and right mandibular posterior alveolar mucosa, measuring 4 cm x 1 cm, and 2 cm x 1 cm, respectively. The lesions were neither tender, nor indurated on palpation. The cervical lymph nodes were not enlarged. The patient was edentulous, and panoramic radiograph showed no evidence of bone involvement. Preoperative computerised tomography (CT) showed no evidence of metastatic lesions to the brain, head and neck, lungs, abdomen, or pelvis.

The swellings were subsequently excised and sent for histopathological examination. Both lesions showed similar histopathological features comprising infiltrative proliferation

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(a)



(b)

(c)

Fig. 1. Case 1. Histopathological examination of haematoxylin-eosin stained specimen. Myofibroblastic tumour cells showing fascicular pattern (blue arrow) and vague storiform pattern (blue circle) (a); Tumour cells ranges from tapering to ovoid with plump vesicular nuclei, prominent nucleoli and pale cytoplasm (b); Bizarre, atypical cells and aberrant mitosis (c) (a,100×; b and c, 400×).

of spindle cells exhibiting fascicular and vague storiform patterns. The tumour cells exhibited tapered to ovoid plump vesicular nuclei, prominent nucleoli, and pale cytoplasm. Focal areas were predominated by large bizarre, binucleated, multinucleated and pleomorphic cells. Mitoses, including aberrant forms, were frequent, ranging from 6 to 12 mitotic figures per 10 high power fields (HPF) (Fig. 1). The background stroma was collagenous, with focal hyaline changes and numerous interspersing thin-walled capillaries. The tumour cells showed positivity for vimentin, smooth muscle actin (SMA), and CD68. Focal positivity was noted for desmin, S100, epithelial membrane antigen (EMA), and pan-cytokeratin (AE1/AE3). The tumour cells were negative for CD34, caldesmon, myogenin, cytokeratin 7 (CK7), HMB45 and anaplastic lymphoma kinase (ALK) protein. Transducin-like

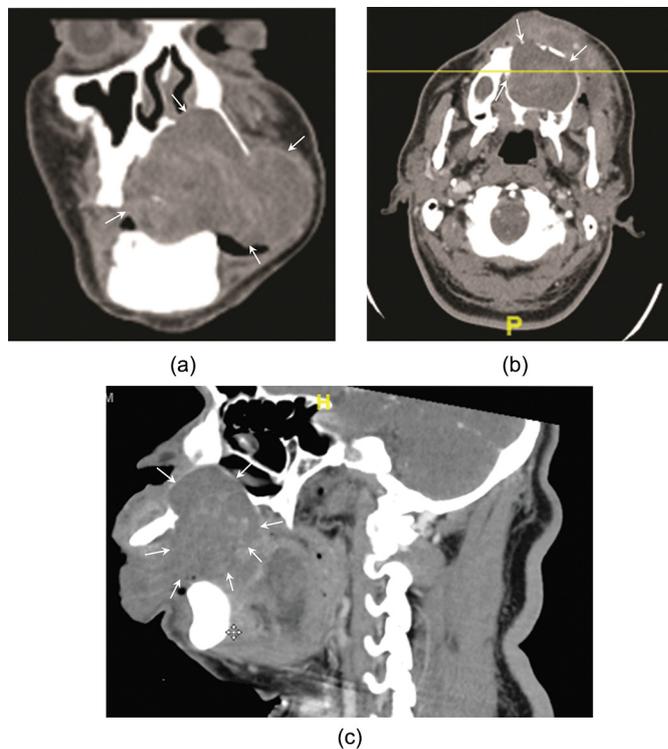


Fig. 2. Case 2. Coronal (a), axial (b), sagittal (c) images of computed tomography scan. Well defined, large expansile mass at the left maxilla with extension into the maxillary antrum, nasal cavity and surrounding soft tissues (white arrows).

enhancer of split 1 (TLE1) and CD99 showed scattered faint nuclear positivity. The excision margins were free of tumour.

The patient was reviewed weekly for one month, and the surgical sites were healing well. About two-months post-operatively, the patient presented to another hospital with difficulty breathing and expired shortly after, due to old age.

Case 2

A 55-year-old man presented with a one-year history of painless diffuse swelling involving the left palate, with an extensive buccolingual expansion of the posterior maxillary arch. It was slow-growing and associated with bleeding and halitosis. The swelling measured approximately 7 cm × 6 cm, with surface ulceration, and not associated with any discharge. Upon palpation, the swelling was tender and soft in consistency. Left submandibular lymphadenopathy was present.

Panoramic imaging showed ill-defined radiolucency on the partially edentulous left maxillary alveolar ridge with loss of normal bony trabeculations and involvement of the left maxillary antrum. Subsequent CT scan revealed a well-defined expansile mass with heterogenous enhancement of the left maxilla measuring 7.1 × 4.9 × 5.4 cm, with erosion of the left alveolar process and extension into the left maxillary sinus and

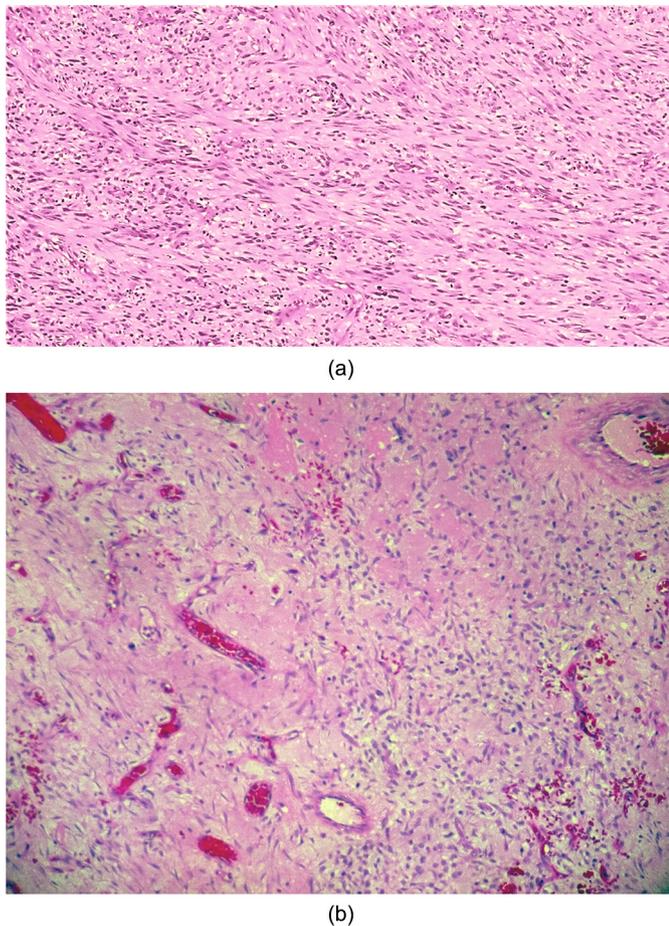


Fig. 3. Case 2. Histopathological examination of the haematoxylin-eosin stained specimen. Proliferation of tapered spindle cells resembling myofibroblast in long fascicular pattern, alternating with haphazard pattern arrangement (a); Scattered capillaries are also seen (b) (a and b, 100×).

nasal cavity (Fig. 2). Multiple level II and III lymph nodes were seen bilaterally, with the largest, measuring 1.2 × 1.2 cm, noted on the left side. There was no evidence of distant metastasis to the brain, thorax, abdomen, or pelvis.

Incisional biopsy was performed twice and was reported as an inflammatory myofibroblastic tumour (IMT) on both occasions. Fine-needle aspiration cytology (FNAC) of the enlarged left submandibular lymph node revealed reactive lymphadenitis. Subsequently, left subtotal maxillectomy without neck dissection was performed with preservation of the left infraorbital margin. Reconstruction plates were placed at the site of the defect.

Histopathological examination revealed an ulcerated tumour mass, composed of variably cellular spindle cells arranged in long fascicles, broad sheets, and haphazard pattern, within a myxomatous, collagenous, and hyalinised background (Fig. 3). The tumour cells exhibited variable morphology, ranging from tapered myofibroblast-like nuclei with eosinophilic cytoplasm, wavy nuclei with fine to coarse chromatin, bland spindle-shaped cells with indistinct

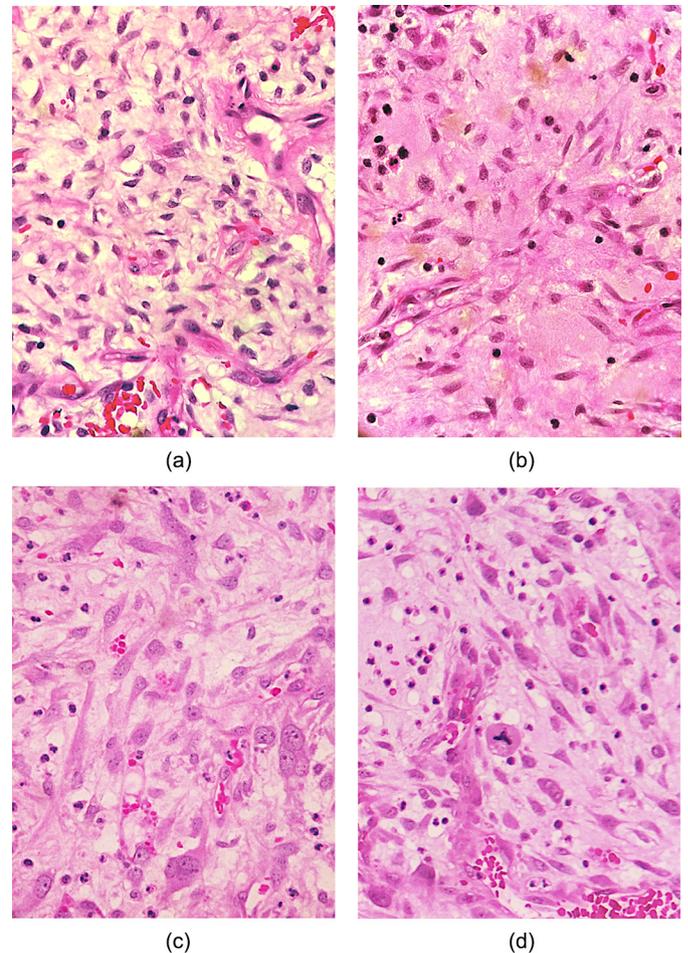


Fig. 4. Case 2. Histopathological examination of the haematoxylin-eosin stained specimen. Tapered myofibroblast like cells with eosinophilic cytoplasm, wavy nuclei, fine to coarse chromatin (a); More hyalinised less cellular areas observed (b); pleomorphic tumour cells appear larger with multiple nuclei (c); Aberrant mitotic figures noted (d) (a–d, 400×).

cytoplasmic border, and multinucleated cells. Although parts of the tumour appear bland, there were areas predominated by pleomorphic cells with few atypical mitotic figures (Fig. 4). The tumour was partly circumscribed, and diffusely infiltrating skeletal muscle fibres in other areas. Thin-walled capillaries with no specific pattern as well as areas of haemorrhage and necrosis were also evident. The tumour cells were focally positive for SMA, and negative for pan-cytokeratin (AE1/AE3), desmin, CD34 and caldesmon.

The posterior palatal margin was positive for the tumour. However, the patient refused to undergo postoperative radiotherapy. The weekly post-surgical review for up to 6 weeks was uneventful, with the surgical site healing well. However, the patient complained of lower-left midface paraesthesia, inability to close his left eye, and mild left facial muscle weakness. He developed facial cellulitis and surgical site wound breakdown at seven weeks of follow-up. The reconstruction plates were subsequently removed, and an upper oral obturator

was constructed for the defect. A CT scan at 12 weeks follow-up showed no evidence of tumour recurrence or distant metastasis. Regular monthly follow-up was continued until one year after surgery, followed by a review at three-monthly intervals.

At 27 months review, a localised fiery red mass resembling pyogenic granuloma, measuring 1 cm × 1 cm, was noted protruding from the left palate, beneath the obturator. A CT scan showed a soft tissue lesion at the left posterolateral palate with surrounding bone erosion. The neck, nasopharynx, thorax, abdomen, and pelvis were clear. Histopathological examination of the excised lesion reported an inflammatory polyp with no evidence of malignancy. The surgical site was healing well at one-week review, and the patient was continuously monitored at three monthly intervals, with no recurrences to date.

Discussion

Spindle cell neoplasms, particularly those with fibroblastic/myofibroblastic differentiation, pose a significant challenge to pathologists due to their morphologic heterogeneity. Head and neck spindle cell tumours are even rarer entities, making them even more difficult to diagnose, especially in biopsied samples. Myofibroblastic sarcoma or myofibrosarcoma is an uncommon low-grade sarcoma showing fibromatosis-like features [2,7]. It has a slight male predilection and can occur at any age, with a peak incidence in the fourth decade of life. In the head and neck, it has a propensity for the oral cavity, especially the tongue, although lesions of the nasal cavity, paranasal sinuses and jawbones have been reported. Myofibroblastic sarcoma can manifest as a painless, slow-growing submucosal or deep-seated swelling. Metastasis is rare, consistent with its low-grade designation [2,7].

Microscopically, the tumour may exhibit fascicles, sheets, or storiform patterns. The tumour cells resemble tapered myofibroblast with fusiform nuclei, fine chromatin, and ill-defined, pale eosinophilic cytoplasm. The cells may also show plump, more rounded vesicular nuclei with small nucleoli [7]. Mitotic activity is low, necrosis is typically absent, and moderate nuclear atypia and hyperchromasia may be observed focally. The stroma is collagenous to myxoid, with scant inflammatory cell infiltrate, and may show hyaline changes. Numerous capillaries may be present, with no specific architecture of the vascular network [2,7]. Diffuse infiltration of adjacent skeletal muscles by tumour cells frequently gives rise to a checkerboard pattern, although well-circumscribed pushing margins have also been reported [3]. The neoplastic cells express variable myofibroblastic immunophenotype for actin and desmin, as seen in our cases (Case 1: SMA-positive/desmin-positive, Case 2: SMA-positive/desmin-negative). Other suggested markers include calponin, CD34 and beta-catenin [2,7].

Myofibroblastic sarcoma is synonymous with low-grade myofibroblastic sarcoma in the 2020 version of the WHO classification of soft tissue and bone tumours [7]. There has yet to be a consensus on whether myofibroblastic sarcoma with

high-grade histological features should be classified as a specific entity or grouped with other high-grade sarcomas such as undifferentiated pleomorphic sarcoma (UPS) [8,9]. The distinction is important, however, as 'myofibroblastic' UPS exhibiting widespread SMA positivity, have a less favourable prognosis than non-myofibroblastic UPS [10]. The presence of necrosis, and mitotic figures of more than 6 per 10 HPF are reportedly indications of a high-grade myofibroblastic sarcoma [11]. These features, in addition to marked atypia, were observed in our two cases, and contributed to the establishment of a high-grade myofibroblastic sarcoma diagnosis, as well as consideration of other sarcomas presenting with pleomorphic features. Other microscopic differential diagnoses include IMT, leiomyosarcoma, malignant peripheral nerve sheath tumour (MPNST) and synovial sarcoma.

IMT is a rare, borderline malignant neoplasm and usually occurs in the viscera and soft tissue of children and young adults. Around 150–200 people have been affected annually, as reported by the United States National Cancer Institute [12]. About 15% of cases occur in the head and neck, and adults are typically affected. Oral cavity IMTs are very rare, with a tendency for local recurrence [5]. It is composed of myofibroblastic and fibroblastic proliferation resembling myofibroblastic sarcoma, has a heterogeneous histopathological presentation, and may present with cytological atypia and increased mitoses. However, atypical mitoses are absent, necrosis is rare, and the tumour cells are usually accompanied by a prominent lymphoplasmacytic infiltrate [5,13]. Although IMT is variably immunoreactive to SMA and desmin, they essentially express ALK, which is negative in myofibroblastic sarcoma [13,14].

Leiomyosarcoma typically affects the lower extremities and is rarely seen in the oral cavity [15]. However, oral and maxillofacial leiomyosarcoma has been reported in several sites, including the mandible, tongue, and buccal mucosa, in patients aged between seven to 67 years. Soft tissue lesions present as pedunculated soft tissue mass [16]. The tumour cells exhibit blunt-ended cigar nuclei, deeply eosinophilic fibrillary cytoplasm, and perinuclear vacuoles, arranged in a fascicular pattern [17]. Leiomyosarcoma exhibits diffuse SMA immunoreactivity in contrast to the tram-track staining pattern observed in myofibroblastic sarcoma. In addition to SMA and desmin, leiomyosarcoma is also immunoreactive to caldesmon, which is negative in myofibroblastic sarcoma [10,17].

MPNST accounts for 5 to 10% of soft tissue sarcomas, with around 20% arising in the head and neck. Neurofibromatosis type 1 and previous radiation exposure are known risk factors for its development, which were absent in both of our cases [18]. Nevertheless, its clinical and histological features show some overlap with myofibroblastic sarcoma, as it is more common in adults, and the spindle cells are arranged in fascicles. In addition, the nuclei are tapered, wavy, or comma-shaped, with indistinct lightly-stained cytoplasm. In contrast to myofibroblastic sarcoma, MPNSTs are negative for myoid markers and positive for S100 and SOX10 [18].

The head and neck is the second most common site for synovial sarcoma, after the extremities. It is most prevalent in children and young adults, and very rare in patients above the age of 50 [19]. The spindle cells in monophasic fibrous type may exhibit similar morphology to fibrosarcoma and arranged in sheets or vague fascicles. These histomorphological features, coupled with the immunohistochemical findings, could have led to the initial biopsy diagnosis of synovial sarcoma in Case 1. Besides occurring in an elderly patient, the lesion observed lacked the typical hemangiopericytomatous vascular pattern of synovial sarcoma. Poorly differentiated synovial sarcoma typically exhibits a rather rounded, hyperchromatic nuclei morphology rather than the bizarre, pleomorphic forms observed in the present case. Additionally, synovial sarcomas are strongly positive for TLE1 protein, with variable positivity towards CD99, as opposed to the faint reactivity observed in the lesion [20].

Conclusion

Myofibroblastic sarcoma is a rare mesenchymal neoplasm and shares similar histopathological features with other fibroblastic/myofibroblastic tumours. It is a challenge to diagnose, especially in small incisional biopsies from a heterogeneous tumour mass. Further uncertainty remains in reporting tumours with high-grade features, due to lack of agreement regarding its classification. Adequate tumour sampling and a systematic approach are required to establish the diagnosis.

Conflict of interest

The authors have no conflicts of interest to declare.

Funding

This work did not receive any specific source of funding from agencies in the public, commercial, or not for profit sectors.

Ethical approval

The ethical approval was obtained from the Human Research Ethics Committee Universiti Sains Malaysia (USM/ JEPeM/21050386). This work conformed to the principles of the Helsinki Declaration of 1975 and 1983.

Consent

Informed consent was obtained prior to the preparation of the case report, and the author/s endeavoured all effort to ensure anonymity.

Authors contributions

N. A. Rahman: Conceptualisation, Data acquisition, Writing original and final draft. M. H. Harun: Data acquisition, Writing – Reviewing and Editing. S. E. T. Sharif: Data interpretation and Critical revision.

Acknowledgements. The authors would like to gratefully acknowledge the Director of the Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan, members of Oral & Maxillofacial Surgery unit, staff of the Medical Records Department Hospital USM and Oral Pathology Laboratory, School of Dental Sciences USM for their help.

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