High-Grade Myofibroblastic Sarcoma of the Buccal Mucosa: A Rare Oral Malignancy with Rapid Fatal Progression.

Abstract:

Myofibroblastic Sarcoma is a rare malignant neoplasm of soft tissue origin defined by the proliferation of spindle-shaped mesenchymal cells with myofibroblastic differentiation. The present report describes the case of a 55-year-old male with a four-month history of progressive swelling in the left posterior mandibular region. Clinical assessment demonstrated a mass originating from the left buccal mucosa, while histopathological examination revealed a densely cellular spindle-cell neoplasm arranged in elongated fascicular patterns within a collagenized and hyalinized stromal background. Immunohistochemical evaluation substantiated myofibroblastic differentiation and when integrated with the histopathological findings, supportedthe diagnosis of Myofibroblastic Sarcoma. The patient ultimately succumbed to the disease within 4 months, underscoring the potentially fulminant biological behaviour of this rare oral mesenchymal malignancy.

Key words:
Myofibroblastic sarcoma, Immunohistochemistry, Spindle cells, Mesenchymal cells, Malignant Neoplasm

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Introduction:

Myofibroblastic Sarcoma (MS) is a rare malignant soft-tissue neoplasm characterized by the proliferation of mesenchymal spindle cells with myofibroblastic differentiation. In 1998, Mentzel et al. described this tumour entity following the clinicopathological evaluation of 18 cases of myofibroblastictumours. [1] The current body of knowledge regarding Myofibroblastic Sarcoma remains largely confined to isolated case reports. [2-6]

In 2002, the World Health Organization (WHO) recognized Low-Grade Myofibroblastic Sarcoma as a distinct entity in its classification of soft tissue tumors, and it remains a recognized diagnostic entity in the current WHO classification. However, Intermediate and High-Grade forms remain insufficiently formally characterizedin subsequent WHO classifications. This unresolved taxonomic ambiguity is principally attributable to the scarcity of well-documented cases and the marked heterogeneity of their clinicopathological manifestations, factors that continue to impede unequivocal histopathological interpretation. [3,5,6]

Case presentation:

A 55-year-old male presented to the Government Dental College and Hospital, Hyderabad, with a chief complaint of swelling in the lower left posterior tooth region since 4 months. The lesion began as a small, inconspicuous mass and progressively expanded to its current dimensions. The swelling was accompanied by mild pain.

Extraoral evaluation revealed a subtle yet diffuse fullness involving the left middle and lower third of face, producing mild facial asymmetry and noticeable restricted mouth opening. The overlying skin exhibited a normal hue without surface alterations. On palpation, the swelling was firm and non-fluctuant, suggesting a solid underlying pathology.

On intraoral examination, a well-defined, nodular exophytic growth measuring approximately 3.0 × 4.0 cm^2 was identified on the left buccal mucosa, extending from the retrocomissure to the retromolar region. The lesion was firm and mildly tender on palpation, with no evidence of surface ulceration or bleeding. (Figure 1)

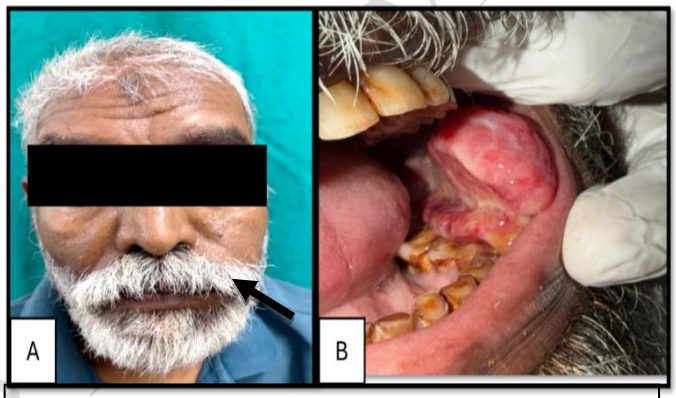

FIGURE 1: A) Clinical image showing a mild diffuse swelling noticed on left middle and lower third of the face. **B)** Well-defined, nodular exophytic growth of 3.0 x 4.0 cm^2 on left buccal mucosa.

Radiographic examination of left posterior mandibular region revealed no underlying bony destruction. (Figure 2)

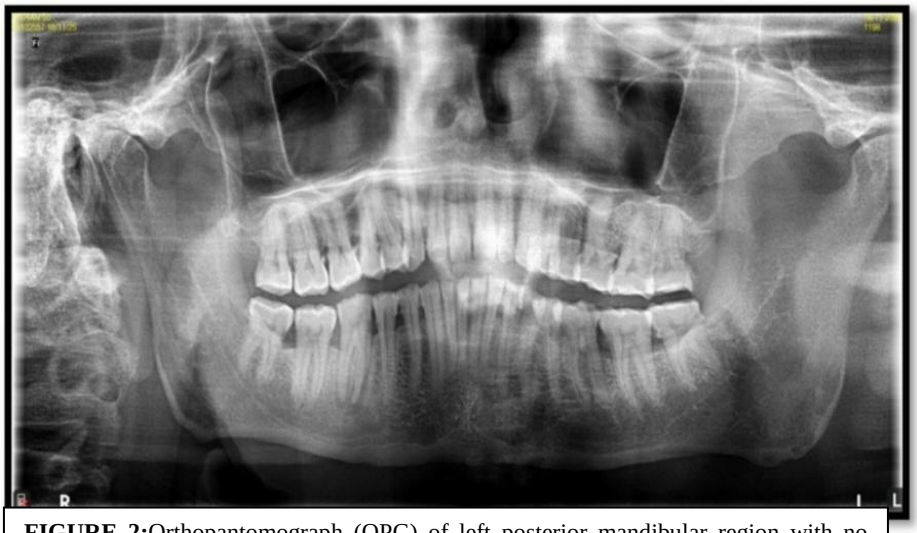

FIGURE 2: Orthopantomograph (OPG) of left posterior mandibular region with no obvious destruction of the bone

An incisional biopsy of the lesion was subsequently performed, and the tissue specimen was submitted to the Department of Oral and Maxillofacial Pathology, Government Dental College and Hospital, Hyderabad, for histopathological evaluation.

On gross examination, two cream-brown soft-tissue bits measuring about 1.1 × 0.8 cm^2 were received, which were firm in consistency. (Figure 3)

FIGURE 3: Two cream-brown soft-tissue bits measuring about 1.1 × 0.8 cm^2 were received, which were firm in consistency.

Microscopically, the lesion showed highly cellular stroma composed of spindle shaped cells arranged in long fascicles within a collagenous and hyalinized background. These fascicles are admixed with pleomorphic cells showing vesicular nuclei and pale cytoplasm. The lesional cells showed marked atypia in the form of cellular and nuclear pleomorphism, nuclear hyperchromatism with prominent nucleoli and

increased and abnormal mitosis. Less than 50% tumour necrosis and up to 6 mitotic figures per high-power field (HPF) was observed.Mild chronic inflammatory infiltrate and vasculature were also evident. (Figure 4)

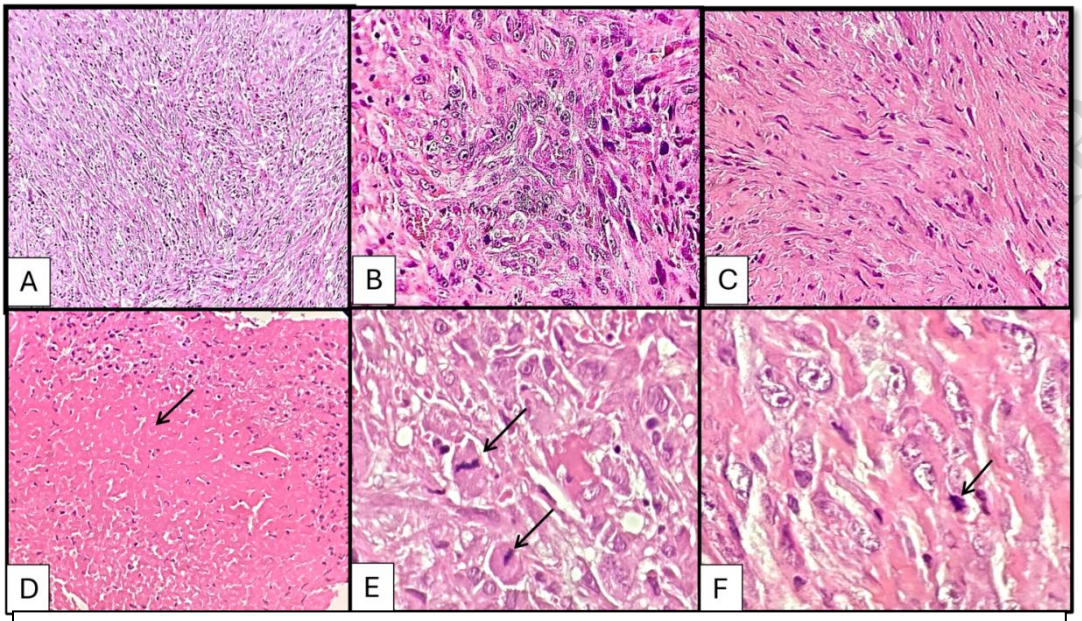

FIGURE 4: **A)** Spindle shaped cells arranged in long fascicles within a collagenous and hyalinized background admixed with pleomorphic cells. **(H&E20 X**). **B)** Pleomorphic cells showing vesicular nuclei and pale eosinophilic cytoplasm with marked atypia and mitotic figures. **(H&E 40X). C)** Streaming fascicles of spindle shaped cells with marked cellular and nuclear pleomorphism. **(H&E 40X). D)**High-magnification photomicrograph showing extensive acellular eosinophilic, glassy areas consistent with tumour necrosis. **E) & F)** High magnification photomicrograph showing mitotic figures.

Immunohistochemical analysis was performed to determine the lineage of spindle cells. The tumour cells demonstrated strong positivity for vimentin, alpha-smooth muscle actin, and p53. Conversely, the tumour cells were negative for desmin, CD68 and S-100. (Figure 5)

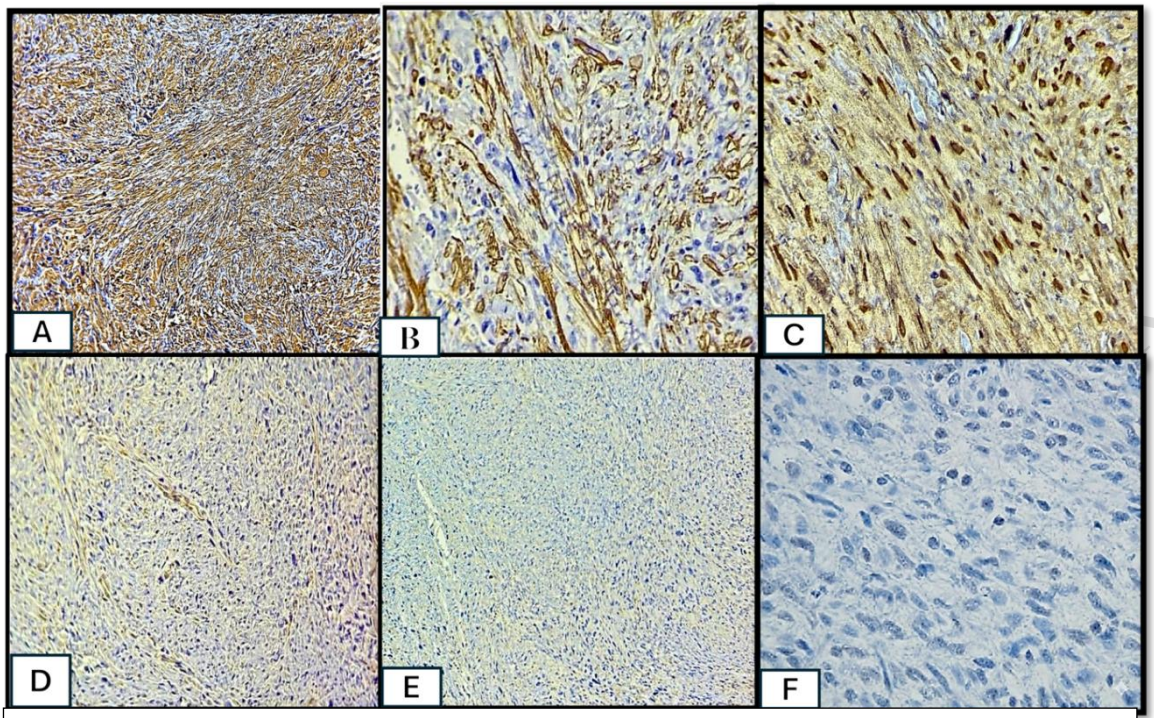

FIGURE 5:A) Immunohistochemistry shows strong positivity for Vimentin (20X) **B)** Immunohistochemistry shows positivity for α-SMA (40X) **C)** Immunohistochemistry shows positivity for P53 (40X) **D**) Immunohistochemistry shows negativity for Desmin (20X) **E)** Immunohistochemistry shows negativity for CD68 (10X). **F)** Immunohistochemistry shows negativity for S100 (10X).

Based on cumulative histopathological and immunohistochemical findings, a final diagnosis of High grade Myofibroblastic Sarcoma was established. The tumour was graded as Grade 2 according to the French Federation of Cancer Centres (FNCLCC) sarcoma Group grading system.

Complete surgical resection with negative margins is the first-line treatment for Myofibroblastic Sarcoma. Owing to financial constraints, the patient was referred to a Government Medical Hospital, Hyderabad for further management; however, he succumbed to the disease within 4 months of diagnosis while undergoing treatment.

Discussion:

Myofibroblastic Sarcoma represents an exceptionally infrequent malignant mesenchymal neoplasm arising from aberrant proliferation of myofibroblastic cells. [1] In 1998, retrospective analysis of more than 11,000 cervicofacial lesions was done where Gorsky et al. identified 139 Sarcomas, of which only 16 involved the oral soft tissues. Myofibroblastic Sarcoma represents an exceedingly rare malignant entity, accounting for only 0.14% of head and neck malignancies. [7]

In 2001, Mentzel introduced a histopathology-based classification system for Myofibroblastic Sarcomas. This framework stratifies these lesions into four principal variants: Congenital Myofibrosarcoma, Inflammatory Myofibrosarcoma, Low-Grade Myofibroblastic Sarcoma and High-Grade Myofibroblastic Sarcoma. [1]

In 2002, the World Health Organization (WHO) recognized Low-Grade Myofibroblastic as a distinct entity in its classification of bone and soft tissue tumours, thereby establishing its status as a separate clinicopathological entity. Despite subsequent updates to the WHO classification, formal diagnostic criteria for Intermediate- and High-Grade Myofibroblastic Sarcomas have not been established. This ongoing uncertainty is primarily attributable to the limited number of reported cases and their heterogeneous clinicopathological features, which continue to pose significant challenges in histopathological diagnosis and grading. [3,5,6]

WHO grading parameters does not include Intermediate and High-Grade Variants, hence is generally undertaken with reference to the National Cancer Institute (NCI) and French Federation of Cancer Centres Sarcoma Group (FNCLCC) system. [3]

Owing to its exceedingly limited incidence, the etiopathogenesis of Myofibroblastic Sarcoma remains insufficiently elucidated, with only a small number of reports addressing its possible causative factors.[3]

The lesion most commonly presents within the soft tissues of the head and neck region. [3,5,8,9] Nevertheless, occurrences have also been documented at less frequently involved anatomical sites, including the extremities, chest wall, axillary and inguinal regions, abdominal cavity, and bony tissue. [5]

Myofibroblastic Sarcoma has been reported in children and adults, with age of onset ranging from 6 to 75 years, and an average age of 40 years and a slight male predominance. [5,8]

The clinical presentation of Myofibroblastic Sarcoma is typically characterized by the presence of a firm, asymptomatic soft-tissue swelling, with pain being an infrequent finding. [3,12]ss

Microscopic examination of Myofibroblastic Sarcoma is characterized by proliferation of spindled to stellate shaped cells arranged into intersecting fascicles, sheets, or storiform whorlsin a myxomatous stroma with scanty inflammation. The myofibroblastictumour cells have poorly defined, pale, eosinophilic cytoplasm and fusiform nuclei with stippled chromatin. [10]

In the present case, application of the French Federation of Cancer Centers Sarcoma Group (FNCLCC) grading system assigned a tumour differentiation score of 2, as the lesion demonstrated a clearly definable sarcomatous histological subtype. The mitotic activity corresponded to a score of 1, with 0–9 mitoses per

10 high-power fields, while tumour necrosis involving less than 50% of the lesion was assigned a score of 1. Accordingly, the aggregate FNCLCC score was 4, categorizing the tumour as Grade 2.

Although the FNCLCC score was 4 (Grade 2), the aggressive clinical course culminating in patient death within 4 months, warranted classification of the tumour as high grade.

Ultrastructurally, Myofibroblastic Sarcoma is characterized by clefted nuclei, abundant rough endoplasmic reticulum, microfilaments, subplasmalemmal plaques, discontinuous basal lamina, and occasional micropinocytic vesicles. [8]

Immunophenotypically, these tumours show variable positivity for α-SMA, muscle actin, calponin, collagen IV, laminin, CD99, CD57, BCL-2, CD68 and occasional desmin, while typically lacking S-100, epithelial markers, nuclear β-catenin, and h-caldesmon. [3,11] In the present case, positivity for vimentin, α-SMA, and p53, with negativity for desmin, CD68, and S-100, supported mesenchymal origin, Myofibroblastic differentiation, and exclusion of muscular, histiocytic, and neural lineages. Although electron microscopy remains confirmatory, diagnosis is now generally established through integrated clinicopathological, histological and immunohistochemical evaluation. [2,3,5,8,12]

Complete surgical resection with negative margins constitutes first-line management of Myofibroblastic Sarcoma. [13] Fisher et al. reported that positive margins were associated with a 32% rate of recurrence and 68% rate of metastasis. [14]

Cai et al. reported recurrence rates of 44–75% and metastasis in 44% of cases with positive margins. Although postoperative radiotherapy is often recommended, the benefit of adjuvant radiotherapy or chemotherapy remains inconclusive. [3,5]

In the present case, the patient succumbed to the disease within 4 months of diagnosis while undergoing treatment, underscoring the aggressive clinical course of Myofibroblastic Sarcoma and the critical importance of early diagnosis, timely intervention and close follow-up. Further studies with larger case series are warranted to elucidate better its biological behaviour, prognostic determinants and optimal therapeutic strategies.

Conclusion

Myofibroblastic Sarcoma represents a rare mesenchymal malignancy with substantial histopathological resemblance to other fibroblastic and myofibroblastic neoplasms, thereby rendering its diagnostic confirmation particularly challenging. This difficulty is accentuated when assessment is based on limited incisional biopsy specimens obtained from a heterogeneous tumour mass. The classification of lesions

exhibiting high-grade morphology remains contentious because of the absence of universally accepted diagnostic criteria. Hence, extensive tumour sampling, careful clinicopathological correlation, and a systematic diagnostic strategy are essential for arriving at an accurate and definitive diagnosis.

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