

A huge ossifying Fibromyxoid tumor of maxilla causing mandibular bowing - A rare case report with review of literature

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Abstract

Ossifying Fibromyxoid Tumor (OFMT) is a rare soft-tissue neoplasm of uncertain origin that occurs usually in the subcutaneous tissue of the extremities. Head and neck involvement is relatively rare and its occurrence in oral cavity is extremely rare. We, herein, present a case of 40 yrs female patient with a huge (approx 10 x 8cm in size), Solitary, Globular, painless swelling over right side of face since six years. FNAC showed spindle cells to ovoid cells in a myxoid background. Computed Tomography scan was suggestive of A Large globular mixed density mass over the alveolar margin of right upper alveolus with extensive calcification with bowing of the mandible. A punch biopsy was done which on microscopic examination revealed Subepithelium tissue showing spindle cells with moderate pleomorphism in a fibromyxoid background creating a possibility of fibromyxoid tumor. Complete excision of the tumour with right partial maxillectomy was done. The histopathological examination of the excised specimen showed extensive ossification rimmed by osteoblast in the periphery of tumor suggesting ossifying fibromyxoid tumour. On Immunohistochemistry the tumour tissue was found to be strongly positive for vimentin whereas Ki67 was positive in <1 % providing a low proliferative index thus confirming the diagnosis of Typical OFMT. The patient demonstrated no evidence of local recurrence till 2 years of follow-up.

Keyword: Ossifying Fibromyxoid Tumor (OFMT), FNAC, Computed Tomography, Immunohistochemistry.

Introduction

Ossifying Fibromyxoid Tumor (OFMT) of the soft tissue was first described in a series of 59 cases from the Armed Forces Institute of Pathology, by Enzinger, in 1989.⁽¹⁾ OFMT is an uncommon soft tissue neoplasm of uncertain origin composed of relatively uniform round to ovoid cells often arranged in a corded or trabecular pattern embedded in a fibromyxoid matrix along with a band of dense collagen with spicules of metaplastic bone at the tumor periphery.⁽¹⁻³⁾ OFMT mostly arises in subcutaneous tissue or skeletal muscle of the extremities, while it has been reported at other sites, such as the trunk, head and neck, mediastinum and retroperitoneum at low frequency.^(1,2,4-6) Head & neck involvement is seen in 13% of cases.⁽¹⁾ However, this tumor located in the oral cavity is extremely rare.^(2-4,7-9) with very few cases reported in literature involving lip,⁽²⁻⁷⁾ buccal mucosa,⁽³⁾ soft palate,⁽⁴⁾ hard palate, tongue,⁽¹⁰⁾ vestibule,⁽⁴⁾ mandible⁽³⁾ & only one case involving posterior maxilla.⁽¹¹⁾ We herein present a rare case of a huge OFMT of maxilla causing mandibular bowing along with a systematic review of literature.

Case Report

A 40 years old female came with c/o huge swelling right side of cheek for last 6 years which was insidious in onset, gradually progressive, associated with h/o difficulty in feeding, speech, chewing food and loosening of teeth.

On local examination a huge approx. 10 x 8cm in size, solitary, globular, bosselated, well defined,

swelling present right side of cheek. hard in consistency, mobile in vertical direction. Extending Superiorly-1cm short of infraorbital margin, Inferiorly-reaching the level of angle of mandible, Medially-involving nasolabial groove and right commissure & Laterally-stretching of skin upto preauricular region.



Fig. 1 (a, b): Clinical photograph of the patient (a) Front view (b) Lateral view showing a huge approx. 10 x 8cm in size, solitary, globular, bosselated, well defined, swelling present right side of cheek extending-Superiorly-1cm short of infraorbital margin, Inferiorly-reaching the level of angle of mandible, Medially-involving nasolabial groove and right commissure & Laterally-stretching of skin upto preauricular region

On Intraoral examination, the swelling was seen extending-superiorly up to right upper alveolus, medially extending to hard palate crossing midline with mucosal irregularity over hard palate, inferiorly about 1 cm short of lower Gingivobuccal sulcus causing distortion of teeth's and bowing of mandible and

Laterally, buccal mucosa was not involved as tongue depressor can be passed around swelling and b/w swelling and buccal mucosa.



Fig. 2 (a, b): Clinical photograph of the patient (Intraoral examination view) showing a huge swelling over the right upper alveolus, medially extending to hard palate crossing midline with mucosal irregularity over hard palate (* arrow) , inferiorly about 1 cm short of lower Gingivobuccal sulcus causing distortion of teeth's and bowing of mandible (*arrow)

In the hunt of diagnosis, Fine-needle aspiration cytology (FNAC) of the mass was done intraorally which on microscopic examination showed spindle cells to ovoid cells in a myxoid background with occasional groups of squamous cell and few benign serous acinar cells creating a possibility of fibromyxoid tumor.

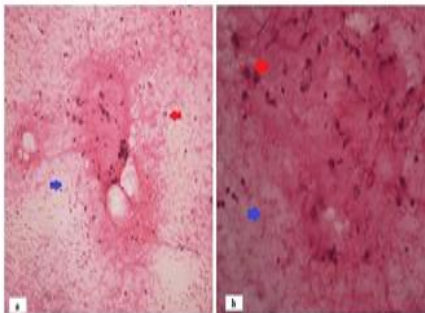


Fig. 3 (a, b): Fine-needle aspiration cytology (FNAC) of the mass on microscopic examination showing- spindle cells (* red arrow) to ovoid cells in a fibromyxoid background (* blue arrow) with occasional groups of squamous cell and few benign serous acinar cells creating a possibility of fibromyxoid tumor

To know the extent of the tumour and involvement of maxillary antrum a Computed tomography (CT) scan was done which was suggestive of A Large globular mass attached to the alveolar margin of right upper alveolus with focal calcification within the tumour alongwith incomplete rim of calcification at the tumour periphery with intact antrum.

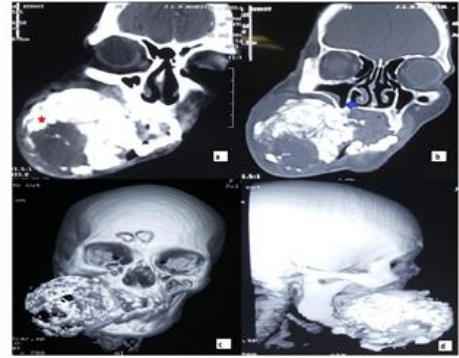


Fig. 4 (a, b, c, d): CT scan PNS Coronal view (a, b), Reconstructed view (c, d) A Large globular mass attached to the alveolar margin of right upper alveolus with focal calcification within the tumour alongwith incomplete rim of calcification at the tumour periphery (* red asterisk) with intact antrum (*blue arrow)

For confirmation of diagnosis a punch Biopsy was taken from irregular mucosal lesion which was extending on hard palate. On Microscopic examination sections showed stratified squamous epithelium with Subepithelium tissue showing spindle cells in fibromyxoid background. Cells showed moderate amount of pleomorphism, hence making a diagnosis of fibromyxoid tumor more crystal pointing more towards benign nature of the tumour.

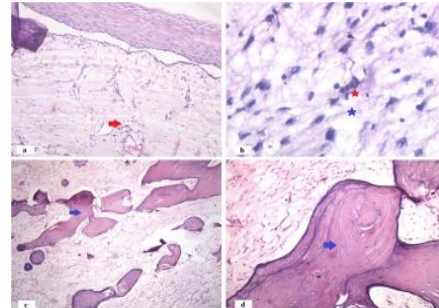


Fig. 5 (a, b, c, d): Histopathological examination: Biopsy specimen (a, b); Photomicrograph (a) showing spindle cells in fibromyxoid background (* red arrow) and Photomicrograph (b) showing ossification areas (*blue arrow) in the tumour periphery. Post operative specimen (c, d); Photomicrograph (c) showing mild pleomorphism in spindle cells (* red asterisk) in fibromyxoid background(* blue asterisk). Photomicrograph (d) showing extensive ossification rimmed by osteoblast (*blue arrow)

However Surgical Management was planned keeping in mind a chance of malignant variant which comprised of wide local excision of mass with right partial maxillectomy and repair of defect by local buccal mucosal advancement flap. The overall excised specimen in toto was sent for Histopathological examination.



Fig. 6 (a, b): (a) Intra-operative photograph showing a huge tumour arising from right upper alveolus after elevating a right cheek flap (*blue arrow). Using a Weber Ferguson incision. (b) Intra-operative photograph after removal of tumour showing mandibular bowing (*blue arrow) with distortion of teeth

On gross examination, the excised specimen was a well-circumscribed mass, measuring 10 x 8cm in size alongwith distorted maxillary teeth attached to it. During cutting it was found to be hard in consistency with a gritty sensation near the subcapsular area as well as in between the tumour tissue. The cut surface was gray-white, solid, heterogenous comprising of soft myxoid areas and hard ossified areas.



Fig. 7 (a, b): (a) Gross specimen showing a well-circumscribed mass, measuring 10 x 8cm in size alongwith distorted maxillary teeth (* red arrow) attached to it. (b) Cut specimen showing gray-white, solid, heterogenous surface with soft myxoid areas(*blue asterisk). and hard ossified areas (* red arrow)

Histopathological examination microscopically showed extensive Ossification rimmed by osteoblast in the periphery of tumor, Center of lesion showed focal ossification and calcified area. Epithelium shows reactive hyperplasia with moderately dense lymphoplasmocytic infiltrate in submucosa with neither mitotic figures nor cellular atypia. Neither granuloma formation nor malignant features could be appreciated and the surgical margin was free of the tumor. Immunohistochemistry was done for further confirmation of diagnosis and knowing the proliferative index for ruling out atypical variant. The tumour tissue staining for Vimentin was strongly positive but it was found negative for S-100 and Pancytokeratin whereas Ki-67- was positive for < 1% indicating a low proliferative index thus confirming the diagnosis of Typical OFMT.

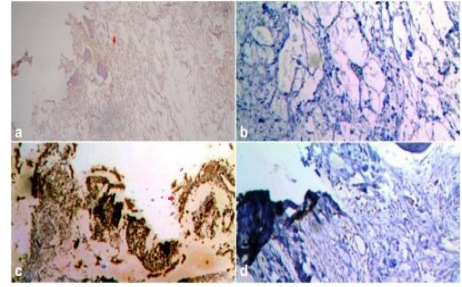


Fig. 8 (a, b, c, d): Immunohistochemical staining (a) Vimentin (20X); diffuse positive in stromal cells(* red arrow) (b)KI 67; negative with only <1% positivity indicating a low proliferative index (c) Pancytokeratin; negative in tumour (*blue arrow) while positive in overlying epithelium(* red arrow) and (d)S-100; negative in tumour

The patient was kept for regular follow up and showed no evidence of recurrence of disease till 2 years of follow up.



Fig. 9 (a, b): Post-Operative follow up clinical photographs (a) Front view showing near normal facial symmetry. (b) Intraoral view showing well healed buccal mucosa with normal mouth opening (*blue arrow)

Discussion

Ossifying fibromyxoid tumor is a rare mesenchymal neoplasm of uncertain lineage presenting histologically as cords and trabeculae of ovoid cells in a fibromyxoid matrix surrounded by partial shell of lamellar bone.⁽¹²⁾ The age of presentation is 14-79 years with a median age of 50 years.⁽¹²⁾ It is most common in the fifth to seventh decades of life,^(1,2) with only rare examples documented in children⁽¹³⁾ & newborn.⁽¹¹⁾ Males are affected more frequently than females with a ratio of approximately 1.5:1.⁽¹⁴⁾ OFMT in the head and neck region accounted for about 13-23% of cases. OFMT Involving Scalp,⁽¹⁵⁾ Ethmoid sinus,⁽¹¹⁾ Oral cavity,⁽¹⁰⁾ Masseter muscle,⁽¹⁶⁾ Parotid /zygomatic arch region⁽¹⁷⁾ & Parapharyngeal space⁽⁴⁾ has been reported in the literature. In the oral cavity involvement of mandible is frequent whereas maxillary involvement is extremely rare. The present case of a 40 yrs female patient with a huge tumour arising from maxillary gingiva of right side causing such mandibular bowing with distortion of teeth is never reported in literature.

The tumor's histogenesis is uncertain, but when first described it was suspected to be of cartilaginous or neural origin.⁽¹⁾ Since then studies have also suggested that it may be of Schwann cell, smooth cell, myoepithelial, skin adnexal, osseous, and chondroid origin, with Schwann cell origin being the most highly suspected type.⁽¹⁸⁾ Cytogenetic analyses have yielded insights into the clonal nature of OFMTs. Clonal abnormalities of chromosome band 6p21 are prominent. Notably, a balanced or unbalanced t(6;12)(p21;q24) translocation appears to be characteristic for OFMT. A recent Fluorescence in situ hybridization (FISH) study by Graham et al,⁽¹⁹⁾ revealed INI-1 deletion in 71% of cases. Most recently, Gebre-Medhin et al⁽²⁰⁾ demonstrated that PHF1 (at6p21) is frequently rearranged in OFMT, including atypical and malignant variants. Moreover, PHF1 was fused to EP400(at 12q24) in one atypical case with the t(6;12) translocation. A FISH assay for PHF1 rearrangements would therefore be useful for the differential diagnosis of OFMT and its histopathological mimics⁽²¹⁾ Characterization of an OFMT in a 40-year-old male demonstrated an abnormal clonal karyotype described as 45,XY, der(6; 14) (p10;q10), add(12) (q24.3), which was felt to correlate better with a mesenchymal origin rather than a neural origin.⁽²²⁾

The biological behavior of this tumor varies. Most cases of the tumor are benign. However, there has been controversy over the classification of this tumor as benign versus malignant. To address this issue, In 2003 Folpe and Weiss⁽²³⁾ proposed that OFMT may be classified as typical, atypical or malignant on the basis of its cellularity, nuclear grade and mitotic activity. Recently, Graham et al⁽¹⁹⁾ demonstrated that histopathologically malignant OFMTs exist. Folpe and Weiss considered OFMTs to be malignant with a high metastatic potential if they were characterized by or high nuclear grade or high cellularity and >2 mitotic figures (MF) per 50 high-power fields (HPF).^(23,24)

A few imaging findings of OFMT have been described in detail in the literature.^(25,26-29) Plain radiographs typically reveal a non-specific soft tissue mass with an incomplete rim of ossification. Erosion or periosteal reaction of the underlying bone is rarely observed. CT scans clearly demonstrate the presence of surrounding or intralésional ossification.⁽²⁶⁾ In the present case CT Scan showed a large globular mass attached to the alveolar margin of right upper alveolus with focal calcification within the tumour along with incomplete rim of calcification at the tumour periphery with intact antrum. The MRI appearances of OFMT are variable. The lesion is isointense to muscle on T1-weighted images and shows intermediate-to-high signal intensity on T2-weighted images. There are high signal intensity areas on T1- and T2-weighted images, suggesting hemorrhage and implying a high degree of vascularity.^(27,28) In addition, areas of ossification demonstrate low signal intensity on T1- and T2-

weighted images. The ossific element of OFMT has osteoblastic activity that is detected on bone scintigraphy.^(25,28,30)

Differential diagnosis may include non-neoplastic proliferative processes that affect the gingiva in the maxillary and mandibular region such as peripheral giant cell granuloma, peripheral ossifying fibroma, plasma cell granuloma and pyogenic granuloma⁽³¹⁾ as well as other lesions with more aggressive behavior such as ossifying fibromyxoid tumor, epithelioid hemangioendothelioma and angiosarcoma.^(19,32-33) OFMT may be mistaken for a number of other benign and malignant conditions, including myositis ossificans, ossifying hematoma, tumoral calcinosis, extraskeletal chondroma, low-grade Fibromyxoid sarcoma, synovial sarcoma and extraskeletal or parosteal osteosarcoma.⁽²⁵⁾

Surgery is the treatment of choice.⁽¹⁾ In the present case surgical management comprising of wide local excision of mass with right partial maxillectomy and repair of defect by local buccal mucosal advancement flap was done. However, chemotherapy and radiation treatment should be evaluated as alternative options, especially given that not every patient may be a candidate for surgery. In their study, Suehiro et al found inconclusive evidence for the use of radiotherapy or chemotherapy, again emphasizing the need to further investigate the role of this treatment.⁽³⁴⁾

Taking into consideration the pathology of the resected specimen, grossly the tumors vary in size from 3 to 5 cm with a median size of 4 cm. However, cases as large as 17 cm have also been reported. In our case the excised specimen was a well-circumscribed mass, measuring 10 x 8 cm in size along with distorted maxillary teeth attached to it. The tumors are circumscribed with a fibrous pseudocapsule having an incomplete shell of bone at the periphery. Microscopically, there are lobules of uniform, round to fusiform shaped cells arranged in nests and cords set in a fibromyxoid stroma. The neoplastic cells have scanty eosinophilic cytoplasm with round to oval nuclei having inconspicuous nucleoli. Incomplete shell of hypocellular metaplastic bone is seen at the peripheral edges of the tumor. Calcifications and/or nodules of metaplastic cartilage are also occasionally identified.^(4,35) A histological diagnosis of OFT is more favourable which are more common at this site clinically, when a cellular tumor with fibromyxoid background, metaplastic bone and a shell of lamellar bone at the periphery is seen. Frequently, there is random deposition of osteoid by the neoplastic cells within the centre of the lesions. Atypical and malignant ossifying fibromyxoid tumors are hypercellular with increased mitotic figures. In the absence of metastasis, the lesion is regarded as atypical variant while in the presence of metastasis, it is classified as malignant.⁽²³⁾

Based on immunohistochemistry and ultrastructural findings, there is preponderance of evidence to suggest a Schwann cell or cartilaginous

origin.^(1,23,12) Upon immunohistochemical stain, the tumors most frequently stain positive for S-100 (66%) and vimentin and are usually PAS negative.^(1,18) They may also stain variably for desmin, smooth muscle actin, Leu-7, neuron-specific enolase (NSE), glial fibrillary acid protein (GFAP), and collagen type IV.[18]in the present case the tumour tissue staining for Vimentin was strongly positive but negative for S-100 and Pancytokeratin whereas Ki-67- was positive for < 1% indicating a low proliferative index. Uniquely, the tumor often demonstrates well-formed re-duplicated basal lamina on electron microscopy which correlates immunohistochemically with positivity for collagen type IV.⁽¹⁸⁾ Ultrastructural analysis revealed prominent intermediate filaments without myofilamentous organization, and a discontinuous, focally reduplicated basal lamina surrounding cells, confirmed in a recent study.⁽³⁶⁾

Ossifying fibromyxoid tumors are likely to recur with reports of up to 27% recurrence.⁽¹⁾ A more recent study found local recurrence in 9 of 51 (18%) patients and metastasis in 8 of 51 (16%) patients.⁽²³⁾ However, recurrence usually occurs ten or more years after resection of the primary lesion. Malignant lesions (those with > 2 MF/50 HPF) and infiltrative growth patterns are associated with a higher potential for recurrence but surprisingly necrosis, tumor size, presence of satellite nodules, and positive margins were not associated with recurrence risk.⁽²⁾ Fortunately, metastases are much more rare but have been reported in lungs, mediastinum, thigh, and kidney.^(2,34)

Conclusion

OFMT is a rare mesenchymal tumor of intermediate malignancy and uncertain line of differentiation

Head and neck is an unusual site of occurrence and maxillary gingival involvement is extremely rare. Surgical management is the gold standard

Recurrence, metastasis and histologically increased mitotic count are indicative of atypical or malignant ossifying fibromyxoid tumors.

Histopathology report is important, leading surgeon to decide how often and how long to follow-up patient with OFMT.

Immunohistochemistry is helpful in confirmation of diagnosis

Long-term follow-up is mandatory.

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