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Malignant fibrous histiocytoma of the mandible – A case report and review of published case reports

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ABSTRACT

The natural history of malignant fibrous histiocytoma (MFH) is still heavily debated. It's anonymous natural history is precisely denoted by its new adapted terminology 'undifferentiated pleomorphic sarcoma (UPS)'. Thus to diagnose a lesion as UPS, it is vital to correlate its histopathological features along with its immunohistochemical (IHC) expressions to confirm the tumor cell lineage. MFH is extremely rare in mandible with the literature search in PubMed database revealing only 13 case reports of MFH involving the mandible. Among these, only 7 case reports provide IHC details of the case. Without IHC data it is not possible to determine the accuracy of the diagnosis in the remaining 6 cases. Here we report an additional 8th case of MFH involving the ramus and angle of the mandible. Histopathology revealed proliferating malignant spindle cells interspersed with histiocyte-like cells. The tumor cells were strongly positive for vimentin and CD68 and were negative for S-100, epithelial membrane antigen (EMA) and cytokeratin (CK). The diagnosis was made by correlating the histopathological findings with the IHC profile. The report also provides the data (clinical, radiographic, histopathological, immunohistochemical features and treatment details) extracted from the 7 confirmed MFH case reports involving the mandible.

1. Introduction

It is estimated that about 3–10% of malignant fibrous histiocytoma (MFH) occur in the head and neck region. MFH is more common in the extremities and its occurrence in gnathic bone is relatively scarce with an estimated 3% incidence rate in the mandible.[1] Although about 70% of MFH cases present as primary tumor, a significant number of cases (30%) are secondary to pre-existing conditions, especially in individuals with a history of radiation therapy.[1] MFH is more prevalent among the elderly with a peak incidence rate in the 5th to 7th decades of life.[2] Histopathologically MFH is a malignant tumor with a mixed cell matrix largely composed of cells differentiating as histiocytes and fibroblast. The immunohistochemistry (IHC) characteristics of MFH include a strong positivity for vimentin, histiocyte marker – CD68 and no reaction to the epithelial membrane antigen and cytokeratin.[3] Among the head and neck regions, MFH involvement of mandible is associated with relatively poor prognosis.[4] Here, we present a case of MFH involving the ramus and angle of the mandible with a review of the literature.

2. Case report

A 32-year old male presented with a painless, progressive swelling on the left side of his face since 2 year. He had no noteworthy family history or past medical history. Extra-oral examination revealed normal appearing overlying skin. The swelling extended from para-symphyseal region to the posterior border of the ramus of the mandible and superior-inferiorly from the preauricular region to the inferior border of the body of the mandible (Fig. 1A). Intra-oral examination presented an asymptomatic swelling on buccal mucosa near third molar region and retromolar area (Fig. 1B). The labial cortical plate was expanded with no apparent mucosal changes. On palpation, the swelling was hard in

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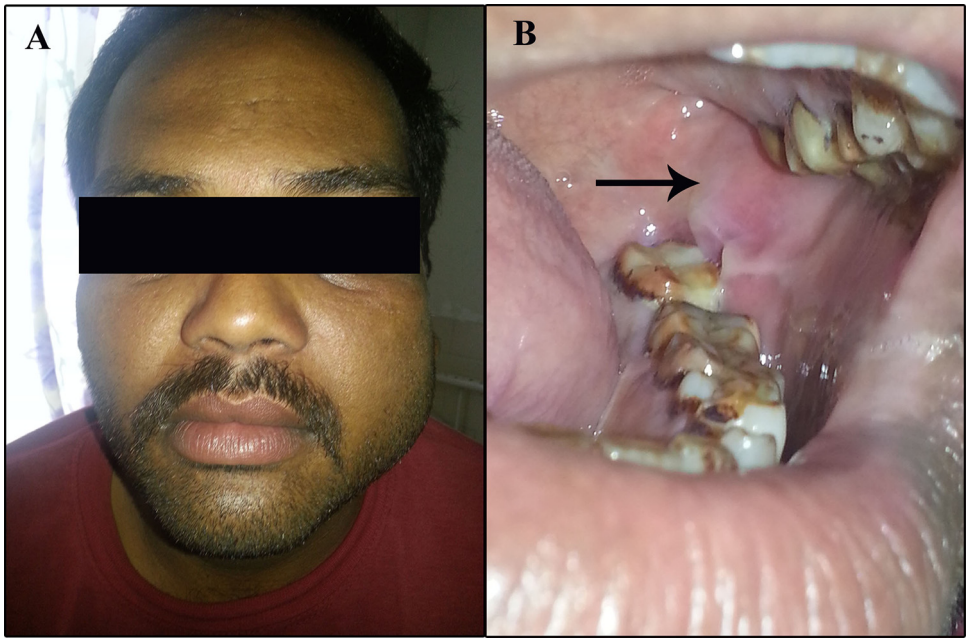

Fig. 1. Clinical photograph showing extra-oral diffuse swelling over the ramus of mandible (A) and intra-oral diffuse swelling in the retro-molar region (B).

consistency with no fluctuation elicited. No evidence of cervical lymphadenopathy.

An orthopantomogram showed large radiolucent lesion in the ramus of the left mandible extending superior-inferiorly from sigmoid notch to the lower border of mandible and from anterior to the posterior border of ramus of the mandible (Fig. 2A). A break was observed in the anterior border of mandible. Condyle and coronoid processes were unaffected. Computed tomography (CT) scan confirmed an osteolytic lesion on the left side of the ramus with perforations of cortical plates (Fig. 2B and C). Routine hematological and urine investigations ascertained values within normal limits.

Fine needle aspiration ruled out the vascular lesion, which was followed by an incisional biopsy of the mass. Biopsy from the lesional tissue revealed a highly cellular matrix consisting of spindle shaped cells arranged in the form of a storiform pattern (Fig. 3A). The tumor cells were predominantly of pleomorphic type and interspersed with histiocytes like cells and multinucleated giant cells (Fig. 3B). On IHC examination, tumor cells showed strong cytoplasmic positivity for vimentin (Fig. 4A) and CD68 (Fig. 4B). However, S-100, epithelial membrane antigen, and cytokeratin were negative. Based on the histopathological and IHC features, a final diagnosis of MFH (pleomorphic type) was rendered.

Standard hemi-mandibulectomy with disarticulation of the condyle was done. A titanium 2.0 mm reconstruction plate with condylar head, which was preadapted on the cadaveric mandible, was prepared to give the best patient profile. Arch bars were fixed to the maxilla and right mandible and maxillo-mandibular fixation (MMF) was done. The reconstruction plate was fixed with three screws in the anterior mandible. The MMF was released and condylar movement was observed. Suture removal was done after 8 days and MMF was done with elastics for three weeks for maintaining occlusion. Post-operative facial appearance and oral function were satisfactory. All of the margins resection was free of tumor. The histopathological findings of the excised specimen were similar to the incisional biopsy findings. 5 years post-surgery, the patient had recovered well with no apparent recurrence or metastasis.

3. Discussion

The clinical, radiographic, histopathological, IHC features, treatment details of published case reports and series of MFH involving the mandible were identified from the PubMed database using the MeSH terms Histiocytoma, Malignant Fibrous; Sarcoma; Mandible. PubMed database had 13 case reports of MFH involving the mandible, but due to the lack of IHC details in 6 cases, it is not possible to confirm the diagnosis of MFH. Data extracted from the remaining 7 confirmed MFH cases (with IHC details) involving the mandible are tabulated in Table 1.

The term malignant fibrous histiocytoma (MFH) was reserved for lesions exhibiting malignant cells resembling histiocytes and fibroblasts. The cell of lineage for MFH is not conclusively determined, thus the term MFH was replaced by the term undifferentiated pleomorphic sarcoma (UPS). The term UPS aptly denotes the anonymity of the entity but confirms its mesenchyme origin and its malignant nature. The incidence of MFH in the mandible is significantly high in the age group of 50–70 years.[11] Yougest patient involving mandible was reported at the age of 15 years.[7] reported MFH has a significant gender predilection with over 65% cases occurring in males.[3] In most cases, MFH presents clinically as a progressively enlarging mass associated with pain.[1] In the present case, the patient was a 32 year old male. The presenting complaint was a rapidly enlarging swelling in relation to the left side of the face for the past 2 years. Although our case did not report any history of trauma, about 20% of MFH cases are associated with a traumatic history. This has led to a theory of MFH being a proliferative response to trauma, although there is a lack of any substantial evidence for the same.[12] Most MFH cases manifest as primary tumors. Secondary UPS are relatively less frequent but have been closely associated with a history of irradiation.[13]

Radiographic features of the present case were predominant radiolucent but it may vary from a predominant radiolucency to mixed radiolucent/radio-opaque appearance depending on the degree of bone destruction and the presence of calcification or ossification. A diagnosis of MFH mandates the use of IHC. The IHC profile of MFH consists of a strong positivity for vimentin and CD68 and is negative for CK, SMA, CD31, CD43, S-100, HMB-45, desmin, LCA and EMA.[3] Our case showed a strong positivity to vimentin, CD 68 and was negative for CK, EMA, and S-100.

MFH cases involving the mandible are associated with poor prognosis, thus requires an early aggressive intervention. Radical surgery with clear margins is often the primary treatment modality.[8] Elective neck dissection is indicated in the presence of cervical metastasis. Due

Table 1
Detailed description of the included case reports of MFH occurring in the mandible.

Sr.no	Author	Age/ Sex	Location	Radiology	Histopathology	Immunohistochemistry		Type	Treatment	Follow up
						Positive	Negative			
1	Jamal et al. [5]	38/M	Angle	Radiolucent	Stellate and fusiform-shaped cells with marked pleomorphism in a myxomatous stroma.	Vimentin, Ki-67, α_1-antitrypsin	Pan CK, S-100 protein, MyoD1, PTAH, CD34, α-SMA	Myxoid type	Surgical excision with reconstruction	NA
2	Maeda et al. [6]	68/M	Retro-molar	Radiolucent	Storiform pattern with pleomorphic cells	Vimentin, α-SMA, α-ACT, S-100, lysozyme, CD68	Myoglobin, pan-keratin, EMA	Storiform-pleomorphic pattern	Surgical excision	Death (8 months)
3	Fleury et al. [7]	15/M	Posterior	Diffuse bone rarefaction	Pleomorphic spindle-shaped/stellate cells, multinucleated giant cells within a myxoid stroma.	Vimentin, CD68, colloidal iron	Amyloid	MFH	Surgical excision	Local recurrence (1 year)
4	Senel et al. [8]	32/F	Body	Radiolucency with Cortical destruction	Atypical spindle cells in a storiform pattern with pleomorphic, multinucleated cells.	Vimentin	Cytokeratin, SMA, desmin	MFH	Surgical excision	Local recurrence (2 months)
5	Koyama et al. [9]	34/F	Angle	Radiolucent	pleomorphic spindle-shaped cells in storiform fashions along with large, multinucleated giant cells.	Vimentin, α-SMA, CD68, Ki-67	Desmin, keratin, EMA, CD45, S-100, HMB45	Radiation-induced UPS	Surgical excision with reconstruction.	No recurrence (58 months)
6	Tanaka et al. [10]	80/M	Posterior	NA	Spindle cells with storiform pattern. Multinucleated giant cells with pleomorphic and atypical nuclei	Vimentin, α-1-antitrypsin, α-1-ACT, CD68, p53, Ki-67	α-SMA, S-100, EMA.	MFH	Previous diagnosis: BFH; Autopsy: MFH	Death (6 months)
7	Kim et al. [3]	44/M	Posterior	Ill-defined mixed lesion	slit-like vascular spaces, Generalized myxoid pattern, fibroblast-like spindle-shaped cells, sand osteoclast-like giant cells	Vimentin	S-100, desmin, CK	UPS	Surgical excision followed by adjuvant chemotherapy. metastasectomy and palliative chemotherapy after 2 years	Local recurrence and metastasis to lungs (2 years)

SMA - Smooth muscle actin, CK - Cytokeratin, ACT- Anti-chymotrypsin, EMA - Epithelial membrane antigen, MFH - Malignant fibrous histiocytoma, BHF - Benign fibrous histiocytoma.

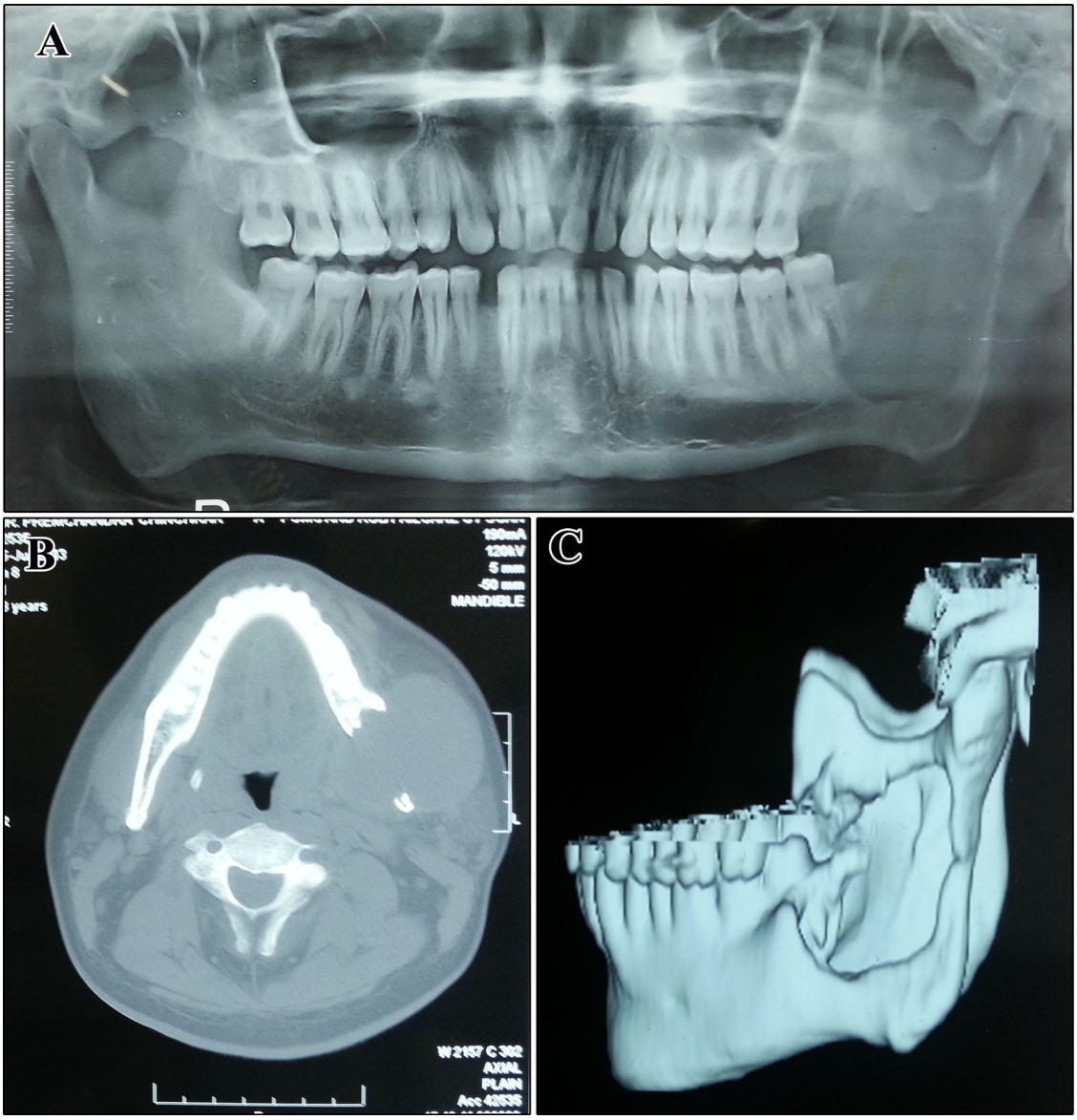

Fig. 2. Orthopantogram showing large unilocular lesion involving ramus of the left side of mandible (A). The computed tomography revealed large osteolytic lesion with destruction of cortical plates (B and C).

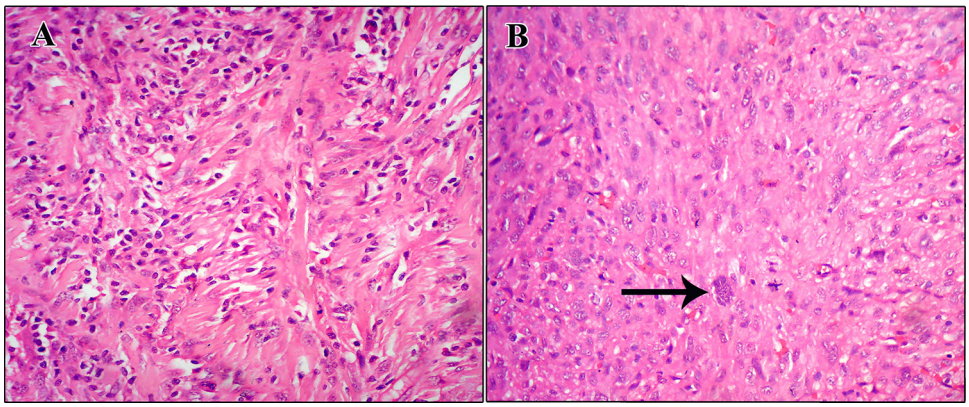

Fig. 3. Photomicrograph showing spindle shaped tumor cells arranged in the form of storiform pattern (A) and multinucleated giant cells (black arrow) (B). (Hematoxylin and Eosin stain; magnification X400).

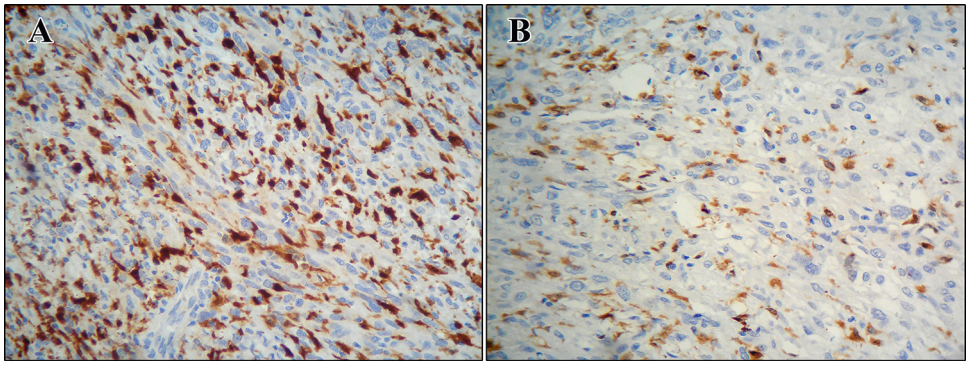

Fig. 4. Photomicrograph showing strong cytoplasmic expression of vimentin (A) and CD68 (B). (Immunohistochemistry; magnification X400).

to its high recurrence rate and metastatic potential, treated cases of MFH must be closely followed up. The overall efficacy of chemotherapy and radiotherapy in UPS remains questionable.[14] High-risk cases such as those with a history of local recurrence, higher histological grade have greater chances for subclinical metastasis. Post-surgical adjunct chemotherapy is often indicated in these cases.[7] 3.2–18 % of head and neck UPS have cervical lymph node metastasis.[15] 25–35 % head and neck MFH cases develop distant metastasis, with the lung being the most frequently metastasized site followed by bone and liver.[3] The present case did not reveal any local recurrence or distant metastasises during the 5 years post-surgical follow-up. The factors determining the prognosis of MFH case include the tumor size, tumor presentation (primary or secondary), histopathological grade and the status of the surgical margin.[16] Irrespective of the treatment modality employed, MFH involving the mandible has an overall 5-year survival rate of 45%.[3]

4. Conclusion

To conclude, a correlation of the histopathological features with the IHC profile is necessary for a diagnosis of MFH. Based on the follow-up data from the reported MFH cases involving the mandible, one can assess the associated high risk of local recurrence and distant metastasis. Thus it is vital to diagnose such MFH cases at an early stage and aggressively treat them with radical surgery with or without adjunct post-surgical chemo/radiotherapy. It is of utmost importance that the treated UPS cases are kept under close follow for a minimum period of 5 years, to detect any post-surgical recurrence/metastasis.

Conflict of interest

None declared.

Funding source

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