Malignant Fibrous Histiocytoma of Mandible: A Review of Literatures and Report a Case

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Abstract: Malignant fibrous histiocytoma (MFH) is the most common soft-tissue sarcoma, however relatively uncommon in head and neck area. This tumor it is difficult histologically to distinguish from other sarcomas and carcinomas. The most reliable treatment for MFH is surgery. Prognosis is fairly poor and recurrence and local metastasis are common. In comparison with MFH of the extremities and trunk, the 5-year survival rate for cases of this tumor in the head and neck is low. It is important to consider to MFH in differential diagnosis of head and neck tumors because of its poor prognosis. Here we report a case of mandibular MFH, in addition to English literatures review of this entity, published in pubmed.

Key words: Malignant, fibrous histiocytoma, mandible, soft tissue

INTRODUCTION

Soft tissue sarcomas (STS), encompass a broad array of malignant tumors that are derived from cells of mesenchymal origin at any anatomical site. (Yamaguchi, Nagasawa et al. 2004) The originating tissue is diverse, that includes bone, cartilage, muscular, fibrous, vascular, fatty, and neural tissue. (Ohsawa, 1995)  
Soft tissue sarcomas mainly arise in the extremities and trunk and only 5–20% of the cases occur in the head and neck region. (Pandey, 2000)  
Among all malignancies occurring head & neck less than 1% originate in the oral cavity. (Pandey, T, 2000) Oral sarcomas, except malignant lymphoma, are extremely rare.  
The most common STS of the head and neck area is rhabdomyosarcoma (RMS), following with malignant fibrous histiocytoma (MFH), fibrosarcoma and neuro- fibrosarcoma (Vargas, E, 1987; Pandey, T, 2000)  
Malignant fibrous histiocytoma (MFH) is a rare mesenchymal tumor but the incidence of this tumor seems to be the highest among various types of adult malignant soft sarcomas. (Anavi, H, 1989)  
It considered to be a primitive mesenchymal tumor showing both fibroblastic and histiocytic differentiation. (Bras, B., 1987)  
This tumor originally described as a soft tissue sarcoma, but, it also well recognized as a primary tumor of bone which may occur in the jaws. (Besly, W., 1993)  
MFH has a predilection for the extremities and the incidence of head and neck MFH is relatively low (Sato, K., 2001)  
We report a case of malignant fibrous histiocytoma of mandible occurring in a young man and review the English literature published in pubmed from 1976 to 2010.

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Case Report:
Patient was a 27-year-old man referred to the Oral Medicine Department of the Mashhad dental school, complaining of a swelling on the mandibular alveolar ridge which had been appeared two months ago. For the first time he had noticed the swelling following the first molar extraction and then it grewed gradually. Only when it became ulcerated he felt little pain. His medical history was unremarkable and he was taking no medicine. He didn't use alcohol, tabatto or other drugs.

Clinical Examination:
By precise clinical examination of the oral cavity, an approximately 2×2 cm2 mass, was observed on the alveolar ridge of mandible extended between, right second premolar and second molar teeth. There were two ulcers on the mass seems to be caused from occlusal trauma.
The mass had implicated the alveolar ridge buccolingually and extended to the adjacent mandibular vestibule. (Figure 1). Right second premolar and second molar teeth were mobile. The mass had a firm consistency in most areas. It was mostly of firm consistency, without any reported tenderness or paraesthesia. Examination of the lymph node of the head and neck region didn't reveal any uncommon changes.

Radiographic Examination:
The panoramic radiograph showed the decreased bone density as a radiolucency with ill-defined borders on the right mandible. Also there was seen a mild displacement of right second premolar and second molar teeth.
Considering the fast growth of the lesion, and destruction of the mandibular bone, a malignant lesion was suspected.
For the accurate histopathological examination the incisional biopsy of the lesion was performed.

Histopathologic Findings:
Hematoxylin and eosin staining of the specimens demonstrated a proliferation of histocytic spindle-shaped cells and fibroblast-like cells with clear and vesiculated spindle-shaped nuclides.
Stroma contains dense and vascular collagen.
Lesion is in fascicular pattern and there is a fascicular and storiform pattern.
Imunohistochemical stain revealed that the tumor cells were positive for CD68 (Figure 5) and XIIIa.

Fig. 1: Intra-oral examination revealed mass measuring approximately 2×2 cm, was observed on the alveolar ridge of mandible extended from right second premolar to second molar tooth. Two ulcerations were observed on mass.

Fig. 2: The mass had implicated the alveolar ridge on buccal and lingual sides and the neighboring mandibular vestibule.
Fig. 3: Hematoxilin and eosin staining of malignant fibrous histiocytoma. Magnification: 100×. Highly pleomorphic, mitotically active, spindle-shaped cells in a storiform pattern.

Fig. 4: Hematoxilin and eosin staining showing highly pleomorphic, mitotically active, spindle-shaped cells in a storiform pattern. Magnification: 400×.

Fig. 5: Immunohistochemical stain for CD68 showing positive reaction in tumor cells. Magnification: 100×.

Diagnosis:
Given the results of histopathologic, immunohistopathologic, radiographic and clinical examination of the patient, the lesion was diagnosed as Malignant fibrous histiocytoma. The patient was referred to a hematologist and an oncologist for further evaluation and spiral CT scans of the chest, abdomen and pelvic cavity with contrast media were ordered. CT scans of the cardiovascular system, liver, gall bladder, spleen, pancreas, adrenal glands, urinary bladder and retroperitoneal areas were of no pathologic changes. Metastasis and lymphoadenopathy were not observed.

Treatment:
The patient was referred to the Department of Oncology and Oral and Maxillofacial Surgery. The patient underwent radical surgery and histopathologic findings confirmed the diagnosis. All of margins resection were free of tumor. The tumor recurred after 8 months. He was treated by the means of radiotherapy in addition to radical surgery and hemimandiblectomy.

Discussion:
There are some previous reports on sarcomas of the head and neck, but only few reports focus on sarcoma of the oral and maxillofacial region (Pandey, T., 2000; Yamaguchi, N., 2004)

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Oral sarcomas, include fibrosarcoma, malignant fibrous histiocytoma, liposarcoma, leiomyosarcoma, rhabdomyosarcoma, angiosarcoma, alveolar soft-part sarcoma, solitary plasmacytoma, and osteosarcoma, and performed ultrastructural studies of these tumors. (Yamaguchi, N., 2004)

Malignant fibrous histiocytoma is one of the most common malignant tumors among the elderly. (Sato, K., 2001; Kanazawa, W., 2003)

Head and neck MFH has been reported to account for 3-10% of MFH formed in various parts of the body. In a series of 1215 soft tissue sarcomas, 128 tumors (10.5%) were classified as malignant fibrous histiocytoma, of which 9 tumors (7%) were found in the head and the neck. (Solomon and Sutton 1973; Anavi, H., 1989)

MFH is a sarcoma composed of a bimodal cell population, fibroblasts and histiocyt-like cells, arranged in a cartwheel or storiform pattern. (Colmenero, G, 1990)

MFH was first described as a new malignant tumor by O’Brien and Stout1 in the early 1960s, and the details of the histopathologic features of MFH were first described by Kempson and Kyriakos(Sato, K., 2001)

Feldman and Norman in the 1970s first described primary malignant tumor of bone that satisfied the histologic criteria of MFH. (Jamal, T., 2001; Weiss and Enzinger 1978)

MFH is classified into primary and secondary types. 70% of MFH are primary tumors that involve younger patients than the secondary tumors are seen in sixth and seventh decades of life. The secondary tumors are more aggressive than the primary ones. They are associated with an underlying condition such as paget disease, fibrous dysplasia, or prior radiotherapy. (Colmenero,G. 1990)

The tumor usually arises in the soft tissues of the extremities, but it can occur in any part of the body. (Sidhu, B., 1978)

A primary MFH in bone commonly occurs in the metaphysis of long bones of extremities, such as the femur and tibia, and its occurrence in membranous bones is quite unusual. (Kanazawa, W., 2003)

In the head and neck, the nasal cavity and the paranasal sinuses are the most commonly affected sites and subsequently the maxillary alveolar bone is often affected(Sato, K., 2001).

Mandibular MFH accounts for only 3% of all MFH bone lesions (Kanazawa, W., 2003).

Regarding the site of the mandibular lesion, there was a strong tendency for localization in the posterior part of the mandible. According to review done by kanazawa, all mandibular MFH cases were between the posterior mandibular body and ascending ramus. No anterior region of the mandible was reported in these series. (Kanazawa, Watanabe et al. 2003)(8)

According to review done by kanazawa, among the MFH cases, 65% men and 35% women, showing a distinct gender predilection. Any age may be affected. The age distribution at diagnosis varied from 1.5 to 69 years, occurring at all ages, but was more common in the latter half of life, with a mean age of 41.

These data are consistent with MFH in the other bones. (Kanazawa, W., 2003) Other studies reported a peak incidence in the fifth through the seventh decades of life with age range of 6-89 years (Kearney, S., 1980; Pandey, T., 2000; Sato, K., 2001)

Another study revealed that it usually occurs in the fourth and fifth decades. (Sato, Kawabata et al. 2001) (Sidhu, B., 1978)

The most common presenting symptom of MFH was a painless gradually progressing mass without any mucosal ulceration. (Pandey, T., 2000)

According to review article published in 2003 those mandibular lesions were usually first noticed by swelling, pain, paresthesia, and loosening of teeth, almost the same as other malignant mandibular tumors. Clinical symptoms were usually present from 2 weeks to 6 months before diagnosis, (Kanazawa, W., 2003)

Our studied patient, who was a 27 years old man suffered from swelling from 8 weeks ago and ulcers on the swelling appears to be caused due to the trauma from maxillary teeth. He was younger than the mean age of almost of the studies.

Most of the reported lesions presented as an extensive, ill-defined, osteolytic lesion without marginal sclerosis and periosteal reaction. Only 2 case had a fairly well-defined multiloculated feature, suggesting a benign process(Kanazawa, W., 2003)

A classic presentation of MFH is a posterior mandibular osteolytic lesion in an adult man with swelling and hypoesthesia. (Jamal, T., 2010)

Similar to almost of the patients were reported, in our patient, in panoramic radiograph, radiolucency with ill-defined borders was observed.

Salivary gland tumors and other mesenchymal tumors are taken in differential diagnosis of sarcomas. With respect to the differential diagnosis of MFH from other malignant tumors in the head and neck, squamous
cell carcinomas, malignant lymphomas, malignant giant cell tumors, fibrosarcomas, and osteolytic osteosarcomas must be considered. (Sato, 2001)

Squamous cell carcinomas can be differentiated from MFH by the relatively smooth surface. Other tumors show radiographic findings that are similar to those of MFH, and in those cases, clinical features for example, the age, sex, and site of tumor—are required to determine MFH (Sato, K, 2001).

It may be difficult to make a diagnosis of MFH only on the basis of light microscopy. Because of the high rate initially misdiagnosis of this tumor, immunohistochemical investigation should be used for suspicious soft tissue lesions. (Jamal, T,2010; Kanazawa, W., 2003)

MFH has been divided into the following five subclasses: storiform-pleomorphic type, myxoid type, giant cell type, angiomatoid type and inflammatory type (Jamal, T,2010; Rapidis, A.,t al. 2005)

Our findings show that the MFH of the present patient belongs to the storiform-pleomorphic type, which is the most frequent one.

The choice treatment for the MFH is extended surgical resection provided that adequate margins of normal surrounding tissues can be obtained (Jamal, T,2010)

Yamaguchi et al revealed that surgical resection is the best treatment for sarcomas of the oral and maxillofacial region. Wide resection with clear margins is very important for improving survival (Yamaguchi, N., 2004)

But it is often difficult to conduct extended resection of a head and neck lesion with a wide margin of safety. Therefore the treatment for head and neck MFH results in a significantly adverse outcome when compared with the treatment for MFH arising in other regions.

Because of regional lymph nodes are involved in 10-18% of cases ,consideration should be given to elective neck dissection for patients with advanced – stage(Jamal,T.,2010; Rapidis, l., 2005)

The decision about radiotherapy depends on the size ,site, histopathologic grade , and attainment of safe surgical margins. (Yamaguchi, N, 2004)

However, Kearney et al. conducted radiotherapy on 45 patients with a measurable tumor and reported that six of them showed a partial response (13%). Many researchers have reported that radiotherapy for MFH was less effective.  (Kearney, S,1980)

But Yamaguchi et al revealed however local recurrence was less common in patients with adjuvant therapy (radiation therapy and/or chemotherapy) comparing with patients treated by surgery alone, (Yamaguchi,N., 2004)

Nevertheless another study revealed that the overall survival rate in patients with adjuvant therapy was lower than patients treated by surgery alone(Yamaguchi, N, 2004)

Chemotherapy has been used in patients with predictably high risk of pulmonary metastasis(Yamaguchi, N., 2004)

MFH was originally reported to be a soft tissue tumor, but there are some intraosseous ones which have been reported to have a tendency to be indicated as a poor prognosis.(Sato, K,2001)

The 5-year survival rate of MFH of bone is reported to be 36.5-53%. (Jamal,T,2010)

The prognosis of MFH lesions is influenced by the depth of tumor infiltration into the surrounding tissues, the mass of the tumor, the anatomic location of the tumor . oral and Jaw bone tumors are more aggressive than the tumors of the other sites of head and neck. (Barnes and Kanbour 1988)

MFH metastasizes to the lung by hematogenous routes. Regional lymph nodes are involved in 10-18% of cases. (Huvos 1976; Weiss and Enzinger 1978)

According to the Rapidis study, MFH frequently developed a local recurrence (16-52%)
(Rapidis, A,2005) According to Yamaguchi study about oral and maxillofacial region sarcomas, despite of the patients with osteosarcoma developing with distant metastases, MFH only involved regional lymph nodes.(Yamaguchi,N., 2004)

Another study showed that distant metastases are very common in MFH, for example, in the lung and the bone. In various studies reported that MFH has a tendency to cause metastases to develop in the distant sites from 10-44%. This behavior makes the prognosis very serious.(Webber and Wienke 1977; Weiss and Enzinger 1978)

In Sato study, the cases showed distant metastases in the lung, bone, skin, and regional lymph nodes (Sato, 2001)

Ohsawa et al concluded that the tumor angiogenesis was apparently not a key factor in the formation of metastases.They found that there were no prominent differences in the number of microvessels in cases with and in cases without metastasis.(Ohsawa, 1995)
Briefly, sarcomas are often difficult to distinguish from many of the common tumors in the oral cavity. It is important for the clinicians and pathologists to remain alert about the diagnosis of these lesions. Proper clinical, histopathologic and immunohistopathologic examination can help them for the proper diagnosis and suitable treatment of these malignancies.

**Table 1:** Summary of studies and case reports about oral MFH in the English literature cited in pubmed from 1976 to 2011.

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Number of patients</th>
<th>Age</th>
<th>Site</th>
<th>Sex</th>
<th>Country</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Huvos</td>
<td>1976</td>
<td>1</td>
<td>11</td>
<td>Body oh mandible</td>
<td>F</td>
<td>?</td>
<td>S</td>
</tr>
<tr>
<td>Albright, et al</td>
<td>1976</td>
<td>1</td>
<td>newborn</td>
<td>Anterior body of mandible</td>
<td>F</td>
<td>USA</td>
<td>S</td>
</tr>
<tr>
<td>Webber et al</td>
<td>1977</td>
<td>1</td>
<td>66</td>
<td>Body and ramus</td>
<td>M</td>
<td>?</td>
<td>S+R+C</td>
</tr>
<tr>
<td>Blitzer et al</td>
<td>1977</td>
<td>1</td>
<td>58</td>
<td>Body and ramus</td>
<td>M</td>
<td>?</td>
<td>S</td>
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<tr>
<td>Yoshimura, et al</td>
<td>1978</td>
<td>1</td>
<td>21</td>
<td>TMJ</td>
<td>M</td>
<td>Japan</td>
<td>S</td>
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<tr>
<td>Limacher et al</td>
<td>1978</td>
<td>1</td>
<td>65</td>
<td>mandible</td>
<td>M</td>
<td>?</td>
<td>S+R+C</td>
</tr>
<tr>
<td>Daou et al</td>
<td>1983</td>
<td>1</td>
<td>50</td>
<td>Body of mandible</td>
<td>M</td>
<td>?</td>
<td>S+R+C</td>
</tr>
<tr>
<td>Nakashima et al</td>
<td>1985</td>
<td>1</td>
<td>61</td>
<td>?</td>
<td>M</td>
<td>?</td>
<td>S+R+C</td>
</tr>
<tr>
<td>Varges, et al</td>
<td>1987</td>
<td>1</td>
<td>53</td>
<td>Body and ramus</td>
<td>F</td>
<td>?</td>
<td>S</td>
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<tr>
<td>Happonen, et al</td>
<td>1988</td>
<td>1</td>
<td>52</td>
<td>Ramus and coronoid</td>
<td>M</td>
<td>Finland</td>
<td>S+R</td>
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<tr>
<td>Anavi, et al</td>
<td>1989</td>
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<td>17</td>
<td>Posterior of mandible</td>
<td>M</td>
<td>Israel</td>
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<tr>
<td>Kiest, et al</td>
<td>1989</td>
<td>1</td>
<td>1.5</td>
<td>Body and ramus</td>
<td>M</td>
<td>?</td>
<td>R</td>
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<td>Colmenero, et al</td>
<td>1990</td>
<td>2</td>
<td>33,42</td>
<td>2 mandible</td>
<td>M1,1F</td>
<td>Spain</td>
<td>S+R+C,S</td>
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<td>Narvaez</td>
<td>1996</td>
<td>1</td>
<td>16</td>
<td>Mandibular symphysis</td>
<td>F</td>
<td>Spain</td>
<td>S,S</td>
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<tr>
<td>Yamagushi, et al</td>
<td>2004</td>
<td>2</td>
<td>43, 48</td>
<td>2 mandible</td>
<td>2M</td>
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<tr>
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<td>38</td>
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<td>Jamal et al</td>
<td>2010</td>
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<td>38</td>
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<td>USA</td>
<td>S</td>
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<tr>
<td>Dalirani et al</td>
<td>2011</td>
<td>1</td>
<td>27</td>
<td>Posterior of mandible</td>
<td>M</td>
<td>Iran</td>
<td>S+R</td>
</tr>
</tbody>
</table>

S = surgery  R = radiotherapy  C = chemotherapy  
F = female  M = male

Although MFH is rare in the oral cavity, it should be included in the differential diagnosis of the lesions observed in the oral cavity because the treatment protocol is somewhat different. Clinical evaluation, histopathology and proper immunohistopathologic examination of the biopsy can be helpful for correct diagnosis and successful treatment.

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**REFERENCES**


