RETROMOLAR FIBROSARCOMA - A DIAGNOSTIC DILEMMA
CASE REPORT

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Abstract

Fibrosarcoma is a malignant spindle cell tumor of the soft tissues uniformly composed of collagen-producing cells capable of exhibiting varying degrees of fibroblastic differenciation. This diagnosis was more liberally applied to many types of spindle and pleomorphic cell sarcomas that exhibited fibrosarcoma-like patterns, e.g., malignant schwannoma, synovial sarcoma, malignant fibrous histiocytoma, and some benign fibroproliferative lesions, particularly fibromatosis and reactive tumor-like lesions.

The major challenge in the diagnosis lies in over and under diagnose of fibrosarcoma and underdiagnosis of reactive fibrosis. But this histologic differenciation is necessary owing to different treatment strategies.

Keywords: fibrosarcoma, fibromatosis, spindle cells tumors

INTRODUCTION

Fibrous tumors and tumor-like lesions form a heterogeneous group of distinct entities differing in biologic behaviour but being histologically very similar and thus presenting considerable difficulty in pathologic diagnosis. Examination of various classifications reveal many diverse lesions with confusing and overlapping nomenclature (1).

Traditionally, fibrosarcoma (FS) has been defined as a malignant mesenchymal tumor, the cells of wich recapitulate the appearance of the normal fibroblasts. This admittedly broad definition has resulted in a great deal of subjectivity as to which spindle cell, collagen-forming tumors were appropriately termed FS (2).

As a result of the foregoing trends, a number of general statements can be made concerning the diagnosis of FS.

1. FS has become, in large part, a diagnosis of exclusion. It pressuposes that diagnoses such as monophasic fibrous synovial sarcoma and malignant peripheral nerve sheat tumor have been excluded by the appropriate immunohistochemical studies
2. FS, like other fibroblastic tumors (e.g., fibromatosis), may have a variable component of neoplastic cells with features of myofibroblasts. Therefore, the finding of various actin isoforms within these tumors does not mitigate against the diagnosis of FS.
3. Collagen-forming spindle cell tumors of high nuclear grade by convention are classified as malignant fibrous histiocytoma. Consequently, lesions diagnosed as FS, for the most part, occupy the low-grade end (grades 1 and 2) of a spectrum that includes malignant fibrous histiocytoma at the high-grade end (3).

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The term fibromatosis refers to a group of fibrous tumors or tumor-like lesions of soft tissues tht share similar microscopic characteristics and possess an intermediate biologic potential between benign and malignant lesions (4).

Here, we report a case of FS of the retromolar area. The histopathological pictures in all the areas was analyzed in great detail and an attempt was made to separate the neoplasm from other lesions of same origin on the basis of definite histopathological parameters.

CASE REPORT

A 25 year old female referred to the Clinic of Stomatology and maxillofacial surgery JMF CU and UHM, with the chief complain of 3 months tumorous proliferation of the left side of mandibular retromolar soft tissue. There was no pain. Patient had a history of traumatic superficial mucosal exulceration of tumorous lesion.

Intraoral examination revealed tumorous swelling 2 x 2 cm in the left distal mandibular region with ill defined borders of redish-violet color and firm consistency. Regional lymph nodes were not palpable.

On radiological examination, an superficial osteolytic lesion with irregular margins was seen in the lingual part of the retromolar bone compacta. The provisional diagnosis was of mandibular tumor .

An excisional biopsy was performed and gross examination showed two red-purple tissue bits (both measuring 1x 1,5 cm).

Bioptic examination revealed a cellular connective tissue proliferation of predominantly fibroblastic cells in a background of minimal amount of collagen tissue. The overall pattern was generally ranging from sheets, storiform pattern and a certain extent, in a fascicular pattern. A classic herringbone pattern was only minimal (Fig. 1). Abundant reticulin fibers parallel to the long axis of the tumor cells are accentuated by the reticulin silver impregnation technique (Gomori s silver stain). The cells were large, spindle shaped and fibroblastic in nature but pleomorphism was minimal. Occasionally atypic and plump nucleus within fibroblast-like cells is present. Mitotic activity varies among visual fields with value mitotic index 3/10 high power fields (HPF), sporadically atypical mitotic structure was identified

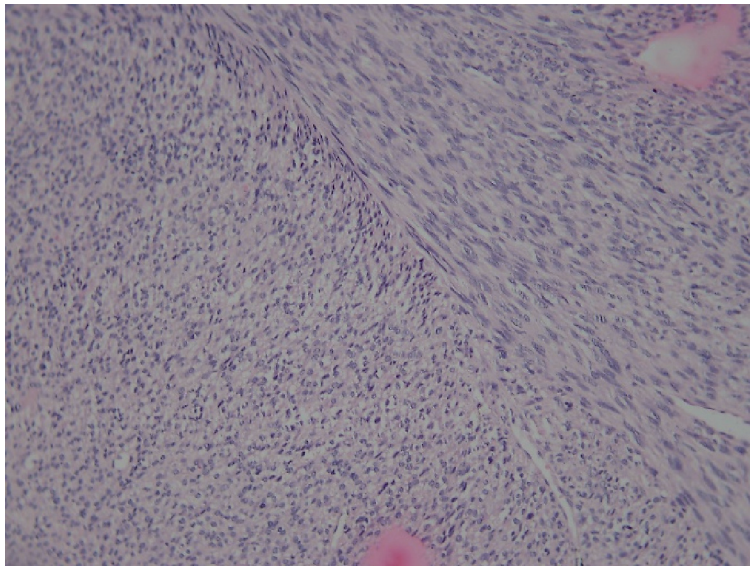

Fig.1 Fibrosarcoma consisting of uniform spindle cells showing little variation in size and shape and a distinct fascicular pattern with district of „herringbone“ pattern (HE 120x)

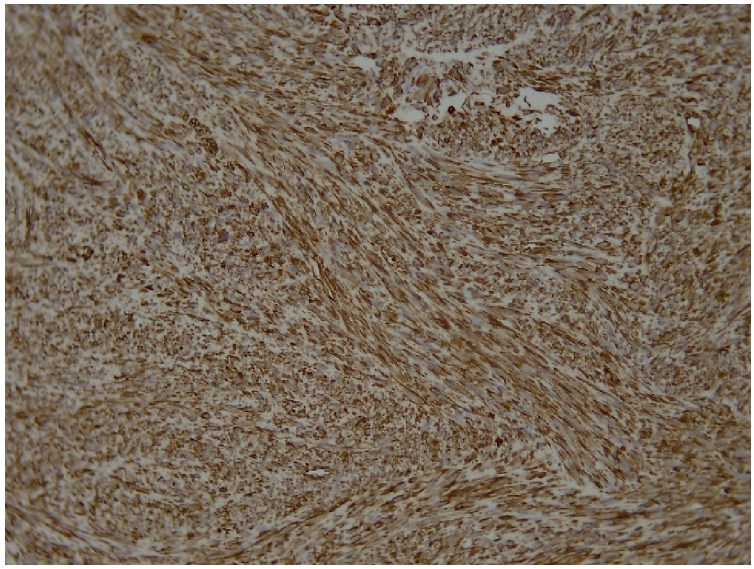

Fig. 2 As seen by immunohistochemistry, the cells are marked with antibodies for vimentin (Anti-vimentin Ag, 120x)

too. Small districts of necrosis was present within tumor. Focal infiltration by lymphocytes and plasma cells, and prominent focally dilated blood vessels lined by plump endothelial cells were found.

Immunohistochemically tumor cells demonstrated strong positivity for vimentin (<95 %) (Fig. 2) and was negative for EMA (epithelial membrane antigen), cytokeratins (CkAE1/AE3 and CkHMW), S-100 protein, desmin, caldesmon, CD117 (cluster of differentiation), and was lightly focally positive for smooth actin (>2 %) – (all used antibody from DACO). The lesion was nuclear positive for proliferative factor Ki-67 protein expression (<50 %) (Fig. 3).

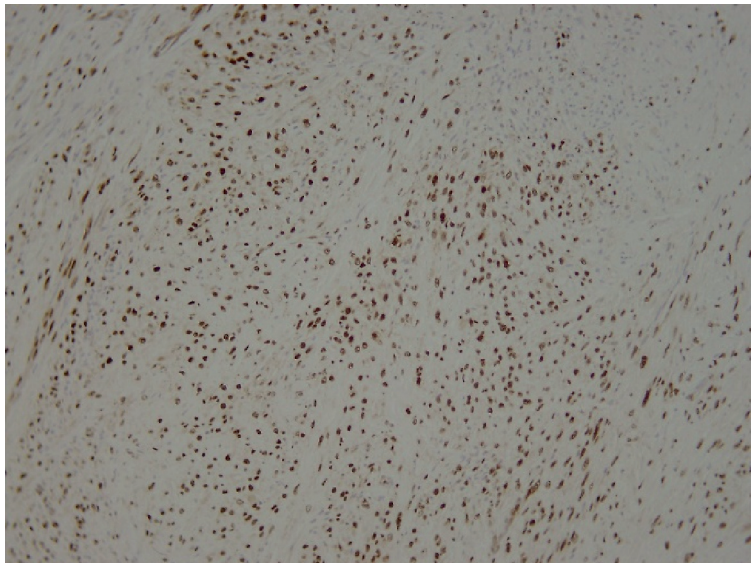

Fig. 3 The lesion was nuclear positive for proliferative factor Ki-67 protein expression (Ki-67 Ag, 120x)

The final diagnosis given was that of low grade fibrosarcoma. The patient was subjected to whole body scan and no distant metastasis was detected. The lesion was operated and chemotherapy was started.

DISCUSSION

FS is a malignant tumor that arises from the fibroblasts (cells that produce connective tissue). This is a type of sarcoma that is predominantly found in the area around the bones or in soft tissue. In earlier studies of soft tissue neoplasm, this tumor has been greatly overdiagnosed, and this diagnosis has been frequently applied to virtually any richly cellular, collagen-forming spindle cell tumor, including malignant fibrous histiocytoma, malignant Schwannoma and a host of other sarcomatous and pseudosarcomatous lesions (2). Malignancies of the fibroblasts are decidedly rare in the oral and oropharyngeal region, but FS is, nevertheless, the most common mesenchymal cancer of the region, representing more than half of all sarcomas. Of all the FS occurring in humans, only 0.05% occurs in the head and neck region. Of this, 23% of head and neck FS occur within the oral cavity (5, 6).

It is often difficult to distinguish FS from other spindle cells tumors, and in many instances only careful examination of multiple sections and ancillary studies permit a correct diagnosis. In bioptic differential diagnosis crucial role plays immunohistochemical investigation. Positivity for pertinent immunoreactans in malignant spindle cells tumor was initiated in Tab. 1.

Table 1 Percentages of positivity for pertinent immunoreactants in malignant spindle cells tumor

Antigen/ Tumor	Ck	VIM	DES	SMA	CALD	S-100
FS	0	100	0	<5	0	2
LMS	<10	91	75	88	85	8
MPNST	<10	100	11	<1	<1	63
MFH	76	100	0	12	<1	30

Note: FS- fibrosarcoma, LMS- leiomyosarcoma, MPNST- malignant peripheral nerve sheath tumor, MFH- malignant fibrous histiocytoma
Ck- cytokeratins, VIM- vimentin, DES- desmin, SMA- "smooth muscle" (alpha isoform) actin, CALD- h-caldesmon, S-100- S-100 protein /monoclonal/
/Adapted according to: Cerilli LA, Wick MR, 2006 (7)/

Monophasic fibrous synovial sarcoma may also closely simulate FS, althouhg it is generally composed of more ovoid-appearing cells arranged in an irregular fascicular growth pattern. Moreover, many of thease sarcomas have areas in which the cells contain more eosinophilic cytoplasm with a suggestion of cellular cohesion, even if well-formed glands are not present. Immunohistochemically, almost all cases of synovial sarcoma expressed at least one epithelial marker, a feature not found in FS. The identification of t(X;18)by fluorescence in situ hybridisation (FISH) is a highly sensitive and specific method for identification a tumor as a synovial sarcoma (8).

Agressive fibromatosis may also show a distinct spindle cell pattern as in FS. The fibromatosis constitute part of a spectrum of poorly understood proliferative lesion whose histologic features overlap to such an extent that the pathologist may be more influenced by the anatomic location of the lesion, sex and clinical behavior than by the histologic appearance

in rendering his of her diagnosis (9). It has been defined as a non neoplastic spindle cell proliferation of childhood which may be locally aggressive but has no metastatic potential. The fibromatosis that occur in the head and heck including those that involve oral and paraoral structures is considered under the heading of extraabdominal fibromatosis, infantile fibromatosis is the childhood counterpart of extraabdominal fibromatosis (Enzinger). The histopathologic differenciation between agressive fibromatosis and FS is a challenge to the pathologists as it requires expertise to differentiate the finer details. The grade 1 FS is usually discernable from fibromatosis by the presence of occasional larger nuclei with ominous chromatin clumping, greater cellularity, greater mitotic acticity and thin rather than thick collagen bundles (1). Immunohistochemistry is of little help in differential diagnosis because positive immunostaining against vimentin can be observed in all fibrous connective tissue tumors (10).

Table 2. Comparison between histological features of low-grade fibrosarcoma and fibromatosis /adapted according Weis SW, and Goldblum JR., 2001 (8)/

Parameter	Low grade fibrosarcoma	Fibromatosis
Cellularity	Low to moderate	Low to moderate
Nuclear overlap	Present	Usually absent
Nuclear hyperchromasia	Present	Absent
Nucleoli	More prominent	Inconspicuous
Mitotic figures	1+ to 3+	1+
Necrosis	Rare	Absent
Vessel and infiltration	Rare	Absent

The final diagnosis of fibrosarcoma was based on a number of factors which included spindle shaped monotonous population of fibroblasts arranged in a fasciculated pattern, little presence od collagen, nuclear overlap, small districts of necrosis and presence of mitotic figures including atypic form (Tab. 2).

Immunohistochemical methods was helper in establishing the diagnosis too (Tab.1).

CONCLUSION

There is a very fine distinction between low grade fibrosarcoma and other types of spindle cell sarcomas, or fibromatosis. Careful microscopic examination with acurate sampling, and practical experience of pathologist is required to render the correct diagnosis. An acurate diagnosis is imperative since it changes the line of treatment.

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