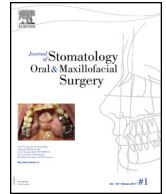




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## Case Report

# Maxillofacial Mazabraud's syndrome: A case report & review



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## ABSTRACT

Mazabraud's syndrome is characterized by myxomas of intramuscular type present in association with fibrous dysplasia. Up to this day, approximately 80 cases of Mazabraud's syndrome have been reported, although in the head and neck territory intramuscular myxoma reports in association with fibrous dysplasia of the bone are very scarce. An unusual case of Mazabraud's syndrome in a 63 years old female displaying fibrous dysplasia of the mandible and soft tissue myxoma in the edentulous alveolar ridge in the molar area is reported. After four years of follow-up, the clinical, imagenological and microscopical findings that led to the diagnosis and treatment are discussed. This report exemplifies the diagnostic and treatment challenge of this rare disease and enhances our clinical knowledge due to its long follow-up, highlighting the need of understanding better its behavior in order to establish proper guidelines for its treatment.

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## 1. Introduction

Mazabraud's syndrome (MS) is characterized by myxomas of intramuscular type present in association with fibrous dysplasia [1]. Intramuscular myxoma (IM) is a benign mesenchymal tumor and fibrous dysplasia (FD) is a benign intramedullary fibro-osseous lesion [2].

MS was first depicted by Henschen [2] in 1926 and in 1967 a pattern of association between FD and soft tissue myxomas was described by Mazabraud et al. [3]. Up to this day, approximately 80 cases of Mazabraud's syndrome have been reported [4].

Clinical features usually involve multiple IMs frequently located in lower limbs; typically, myxomas are located adjacent to the bone lesions [5]. Commonly associated with the polyostotic form of FD, but monostotic involvement has been reported as well. FD's onset precedes IMs, usually asymptotically and frequently involving women [1,5].

Solitary myxoma and monostotic FD is rarely reported, moreover, MS is extremely infrequent in the head and neck area.

Here, a case of mandibular Mazabraud's syndrome with a 4-year follow-up and a review of this rare disease are reported.

## 2. Case report

### 2.1. History and background

A 63-year-old female patient was referred to the oral and maxillofacial surgery service for assessment of a tumor located in the left mandibular body.

The patient reported the tumor had been present since adolescence. Given the lack of symptoms, no medical opinion was sought. When the patient was 47 years old, surgical removal of the tumor was indicated to craft a denture. The tumor relapsed soon after excision difficulting proper chewing years later.

Regarding her medical history, type 2 diabetes mellitus, hypertension, allergy to lysine clonixinate and a habit of 10 years cigarette smoking was reported.

### 2.2. Clinical findings

Upon examination, a large sessile tumor of rubbery consistence and 8 centimeters of major diameter was found in the edentulous alveolar ridge in the molar area. Notably asymptomatic, painless on palpation, with lobulated surface and traumatic ulcers related

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**Fig. 1.** Tumoral mass at the inner aspect of the left cheek, before excision.

to the occlusal plane of neighboring teeth. No other relevant findings were found (Fig. 1).

Blood samples were requested revealing alkaline phosphatase and glycosylated hemoglobin levels were higher than normal, evidencing poor metabolic control of type 2 diabetes and raising suspicion of endocrine disruption.

### 2.3. Imagenological findings

Computed tomography (CT) showed an expansive process in the body and ramus of the left mandible with ill-defined borders and thinned cortical bone expanding lingually and buccally. Two different patterns were observed: the body of the mandible showed ground glass appearance (Fig. 2A), while the ramus

showed an expansive process with cortical defects at the medial cortical outline (Fig. 2B). Cranial and distal displacement of the third left molar was noted (Fig. 2C). The process was associated with mucosal thickening of undetermined appearance.

It was agreed that a biopsy of the mandibular tumor and subjacent bone were necessary.

### 2.4. Surgical procedure

An incisional biopsy was performed at the proximal aspect of the intra-oral swelling. The sample was diagnosed as oral submucous fibrosis by a general pathologist.

Given the apparent benign character of the lesion, a second procedure was scheduled, with the aim of fully removing the soft tissue lesion and to perform an incisional biopsy of the subjacent bone. The full excision of the mass was successfully achieved (Fig. 3A). An incisional biopsy of approximately 2 centimeters was taken immediately distal to the second lower bicuspid comprising cortical bone and marrow (Fig. 3B). The resulting defect on the alveolar ridge was covered with a pedicled left buccal mucosa flap.

### 2.5. Microscopical findings

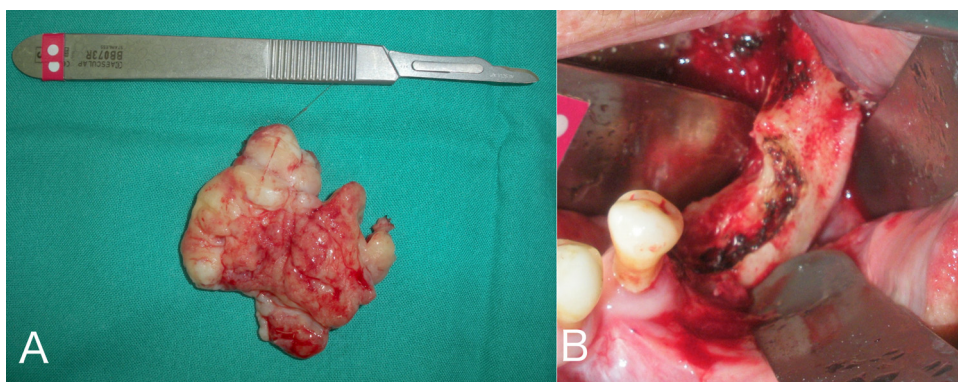
The mandibular soft tumor microscopically showed spindle to stellated cells disposed over a moderately loose matrix (Fig. 4A) and vimentin staining was positive (Fig. 4B). It was diagnosed as mesenchymatous proliferation.

The subjacent bone sample was composed of mature compact vital bone that changed into a pagetoid appearance with basophilic cementum lines resembling a mosaic, which was diagnosed as pagetoid bone (Fig. 4C).

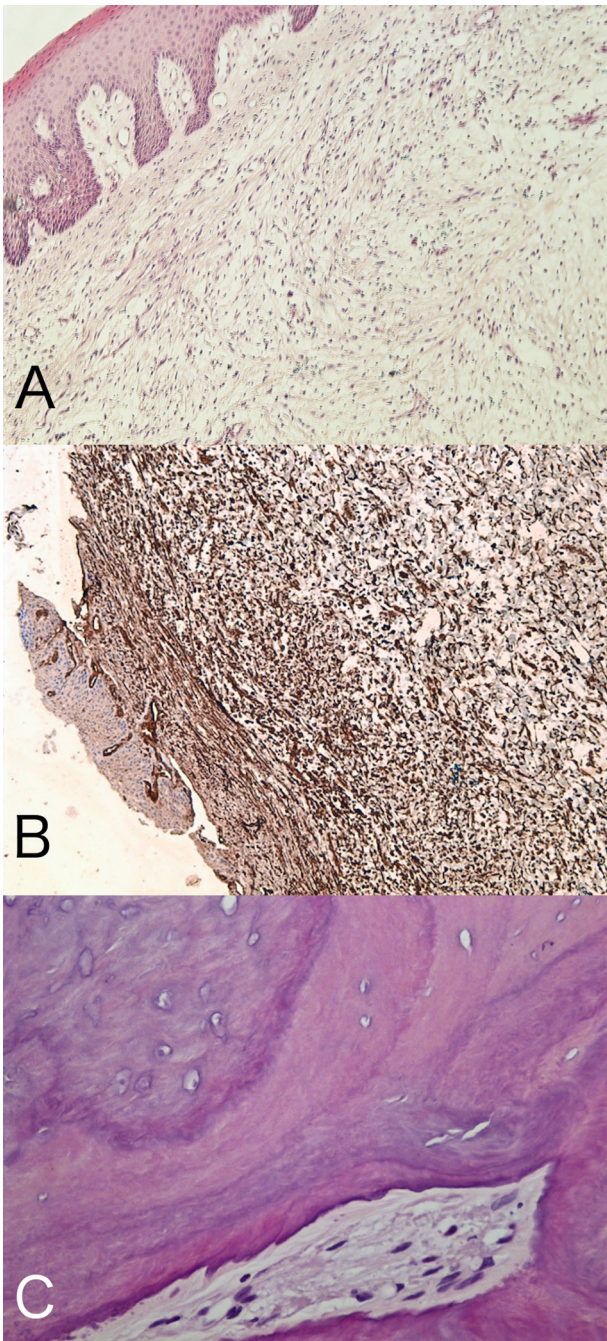
It was suggested to further study the patient regarding the high level of alkaline phosphatase and the presence of pagetoid bone, as well as screening for additional lesions with the aid of a bone scintigraphy.



**Fig. 2.** A. Axial plane CT Scan exhibits ground glass appearance at the body of the mandible. B. Axial plane CT scan exhibits a heterogeneous expansive process with cortical involvement at the mandible ramus. C. Sagittal plane CT scan exhibits cranial and distal displacement of the left lower third molar.



**Fig. 3.** A. Tumoral mass of the left cheek after complete excision. B. Alveolar ridge of the mandible after incisional biopsy sample was taken.



**Fig. 4.** A. Mesenchymatous proliferation as seen with hematoxylin-eosine staining. B. Positive staining of spindle cells by vimentin staining. C. Pagetoid bone as seen stained with hematoxylin-eosin protocol.

### 2.6. Diagnosis

As it was suggested by the pathologist to rule out Paget's disease, the patient was further studied for the high alkaline phosphatase level and a diagnosis of hyperparathyroidism was made, for which a thyroidectomy was performed.

Bone scintigraphy with Tc-99m MDP demonstrated foci of increased radiotracer uptake in the body and ramus of the left mandible with deformed appearance (Fig. 5A). No additional lesions were found (Fig. 5B).

Upon discussing the microscopical, imagenological and clinical features of the case, a diagnosis of Mazabraud's syndrome was reached, once it was clinically ruled out that other co-morbidities

pertinent to other syndromes were absent, i.e. Paget's disease, McCune-Albright and osteosarcoma.

### 3. Discussion

The etiology of MS is unknown, it has been proposed that the affliction is caused by a basic metabolic error of both soft and bone tissues during the initial growth period; however, this remains inconclusive [6].

MS is defined by the clinical association of IM and FD as observed in the current case. Histological and imagenological findings contribute to the diagnosis of IM and FD, however none of the aforementioned findings is conclusive for the syndrome by itself, therefore clinical correlation is crucial.

The present case exhibited the presence of a fairly loose matrix in which stellate to spindle cells could be seen (Fig. 4A), the richer content of fibers could be explained by the protruded mass into the occlusal plane. However, the full sample was strongly resembling of a mesenchymal tissue, hence the diagnosis of "mesenchymatous proliferation", which is in agreement with the description found in the literature. The appearance may vary but differential diagnosis should include juxta-articular myxoma, myxofibrosarcoma, low-grade fibromyxoid sarcoma and myxoid liposarcoma [7].

IMs are completely benign, as there have been no recurrences in any of the modern series, therefore multiple intramuscular myxomas should not be confused with recurrences, as they probably have been in the past [7].

To the authors' knowledge in the head and neck territory IM reports in association with fibrous dysplasia of the bone are very scarce.

Only in 1967, a pattern of association between FD and soft tissue myxomas was described by Mazabraud et al. [3]. When multiple IMs occur, they are associated with monostotic or polyostotic FD (MS) and occasionally, with McCune-Albright's syndrome (polyostotic fibrous dysplasia, *cafe-au-lait* spots and endocrine hyperfunction, most commonly precocious puberty) [7].

FD is a benign, non-inheritable disease [2]. Microscopically, the trabeculae are described as resembling Chinese script letters. Typically, they are composed of immature woven bone, rich in osteoid and not rimmed with osteoblasts which results in a dysplastic skeletal anomaly in which normal bone is distorted and replaced by poorly organized and inadequately mineralized immature bone and fibrous tissue [8].

Presumably, all fibrous dysplasias would arise during childhood or puberty, yet they use to be detected later in life. They can affect the craniofacial bones, particularly the maxilla and mandible, however, 25% of monostotic FDs occurs in the maxillofacial skeleton and in this area, lesions frequently cross suture lines by continuity, therefore the term craniofacial FD is preferred for accuracy [9].

The present case is different to most of the reports to date, given that the FD is located monostotically in the mandible, and the IM is solitary as well. However, since the patient was treated surgically for the IM many years ago, it cannot be ruled out that a new IM developed in the same area, instead of it representing a relapse of the first lesion.

The changes in the bone adjacent to the lesions radiographically include cortical thickening, areas of cystic translucencies and exostoses [10] as well as ground glass appearance [1]. In CT scans, the extent of bone compromise is clear, while soft tissue is not well visualized. In addition, radiographs do not always show the classical ground glass appearance, but CT scans consistently reproduce this finding [1,10].

In this case, the CT image showed expansive process in the body (Fig. 2A) and ramus of the left mandible, ill-defined borders and thinned cortical bone (Fig. 2B), moreover, expansion lingually

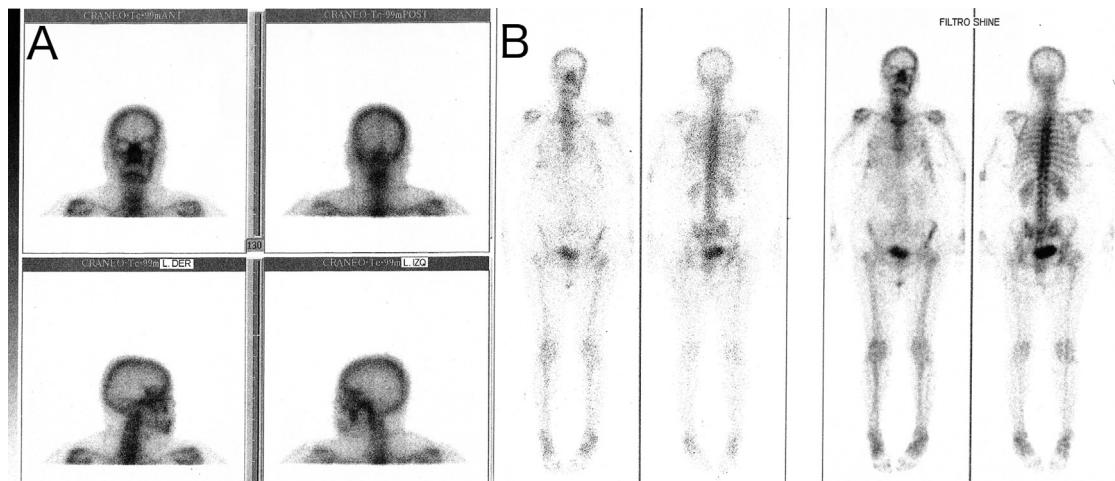


Fig. 5. A. Head & neck bone scintigraphy (2012). B. Full-body bone scintigraphy (2012).



Fig. 6. Left alveolar ridge and cheek 4 years after surgery.

and buccally was noted. The slight degree of deformity is corresponding, but not a classical presentation of FD, however, conventional and unconventional features were observed here: the body of the mandible showed ground glass appearance while the ramus showed a heterogeneous expansive process with cortical defects and displacement of the third left molar (Fig. 2C).

Pagetoid bone was observed microscopically (Fig. 4C). Its presence can be seen in mature FD lesions as here.

Treatment of FD involves different approaches, without current consensus, from periodic check-ups to excision followed by grafting with normal autologous bone or acrylic implants, which may reduce the rate of recurrence [9].

Malignant degeneration has been reported in a few cases of FD of which most are osteosarcomas and less frequently fibrosarcoma or chondrosarcoma. Of these, the vast majority had previous history of radiation therapy, which has been used in the past as primary treatment for FD. Given the risk of malignant transformation, radiation is strictly contraindicated in FD cases nowadays. Nonetheless, recent reports show spontaneous sarcomatous transformation unrelated to radiation exposure in very rare cases [11].

It is recommended to enrol patients affected by FD in long-term follow-up visits as any patient showing clinical or radiographic evidence of malignant changes must rule out sarcomatous transformation [12]. FD progression is slow and has a favorable prognosis if the involvement is local.

It must be said, that malignant transformation of fibrous dysplasia is not a feature in MS, although, there have been some reports highlighting the importance of clinical follow-up for these cases [12]. However, the significance of osteosarcomatous transformation in MS remains dubious [7]. Treatment goals remain to prevent skeletal deformity and fracture [1].

Once the risks were discussed with the patient, it was agreed that the FD was going to be closely followed, as the patient was not concerned about aesthetical defects and there were no evident asymmetries or functional impairment. At 4 years of follow-up, the FD remains without signs of change and in the follow-up CT the process showed no significant changes in shape, moreover, bone scintigraphy evidenced signs of decreased radiotracer uptake when compared with the first record and no signs of newer lesions.

Regarding the IM's treatment, full conservative excision was the strategy employed, given that the behavior of IM is absolutely benign, the prognosis is excellent. At 4 years of follow-up, the patient has not presented any sign of recurrence of the IM following full excision (Fig. 6).

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#### Disclosure of interest

The authors declare that they have no competing interest.

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