

## Radiological Monitoring of the Evolution of Initially Misdiagnosed Advanced Maxillary Osteosarcoma: A Case Report

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### Abstract

Osteosarcoma is a malignant neoplasm of the bone, commonly affecting the long bones. The involvement of the jaws is rarely noticed. This neoplasm often shows a typical clinical behavior as well as varied radiological appearances. To confirm the final diagnosis of an osteosarcoma, it is often required to carry out a histopathological examination of the multiple biopsy specimens. Moreover, a vigorous discussion amongst experts is as well required. In light of their aggressive behavior, an early diagnosis is crucial to determine the adequate treatment. Dental professionals may be the first to detect jaw osteosarcomas in their initial stages. This article presents a case of maxillary osteosarcoma in a 45-year-old male patient with important evolution due to delayed diagnosis. It also highlights the importance of CT scan and MRI in the control of tumor progression and in the choice of the adequate treatment.

**Keywords:** Osteosarcoma, malignant neoplasm, histopathological examination, delayed diagnosis.

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### INTRODUCTION

Imaging plays a critical part in the staging and subsequent clinical management of patients with head and neck neoplasms such as osteosarcoma. Osteosarcoma of the jaws (OSJ) is a rare, aggressive, malignant mesenchymal tumor [1]. It seems that predisposing factors such linear bone growth, and genetic and environmental factors have some role in his formation [2, 3]. The World Health Organization (WHO) has recognized several variants of OSJ that differ in location, clinical behavior, and the degree of cytological atypia [3, 4].

Regardless of its favorable biological behavior, the patients of OSJ usually exhibit advanced tumor, as it often goes unnoticed by the dental professional. Misdiagnosis of OSJ, as tumors or cysts of odontogenic or non-odontogenic origin, leads to alternative treatments such as enucleation, marsupialization, curettage or extraction. This only helps in spread of tumor and metastasis [5]. Thus stressing on the need for an early diagnosis of the lesion. The aim of this case report was to draw attention to the importance of evolution and invasion of the lesion if misdiagnosed and highlights the importance of CT and MRI in the

control of tumor progression and the challenging therapeutic.

### CASE REPORT

A 45-year-old man with painful swelling in the left maxillary bone was referred to the Department of oral medicine and oral Surgery at the Faculty of Dental Medicine of Monastir. The patient had noticed a slowly-growing mass for two months. The pain was severe, pricking, and continuous in nature and it did not subside with medication. He underwent drainage of the swelling and many sessions of bone curettage through the ulcerative lesion as the tumor was diagnosed as a dental abscess in connection with a residual root.

On extra-oral examination, a swelling on the left cheek causing asymmetry of the face was observed with restricted mouth opening (Fig-1).

The overlying skin appeared normal on inspection as well as on palpation. There was absence of palpable submandibular lymph nodes.

The intra-oral examination revealed a firm bony mass of the posterior left maxillary alveolar ridge with an ulcerative lesion extending to the alveolobuccal

sulcus (Fig-2). The size of the lesion was 4x3cm. It had inflamed margins and it was covered with slough. The overlying mucosa was red on the buccal and lingual sides. The mass was tender and without any signs of active bleeding.



**Fig-1: Extraoral view: asymmetry of the face caused by a swelling on the left cheek**



**Fig-2: Intraoral view: A barely visible ulcerative lesion due to limited mouth opening**

The panoramic radiograph revealed an extensive ill-defined mixed radiolucent radiopaque lesion involving the left maxillary bone extending to the maxillary sinus. Loss of lamina dura and widening of the periodontal ligament space (WPLS) involving the adjacent molar and premolars were noticed (Figure-3). The incidence of Blondeau showed a destruction of the antral floor and an invasion of the left sinus (Fig-4).



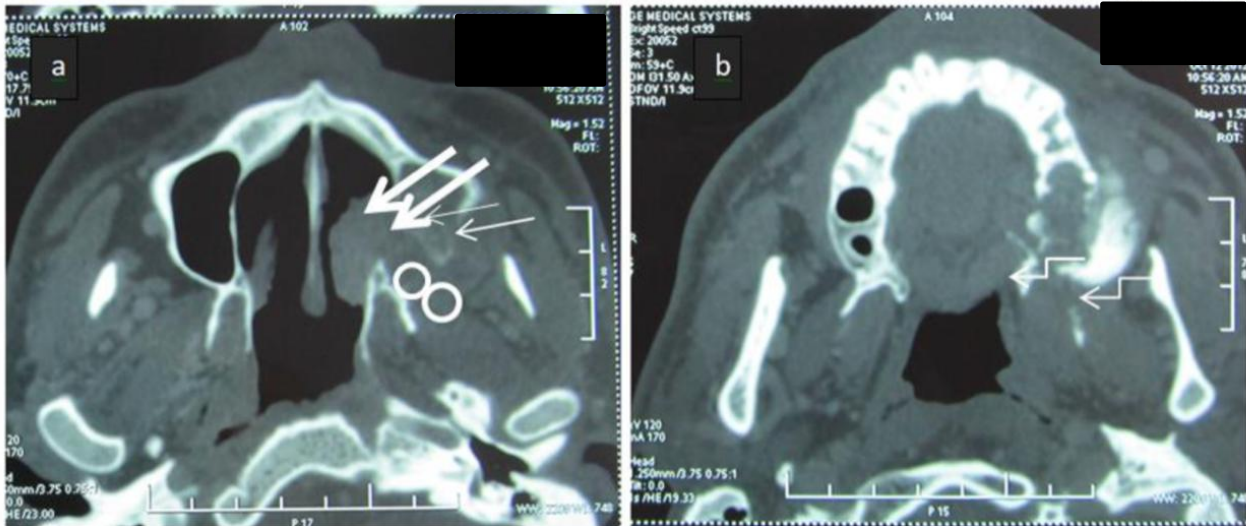
**Fig-3: Panoramic radiography: an ill-defined mixed lesion extended to the left maxillary sinus causing WPLS**



**Fig-4: incidence of Blondeau: destruction of the antral floor and invasion of the left sinus**

Based upon the clinical findings and the panoramic radiograph, a provisional diagnosis of OSJ was made. Differential diagnosis included osteitis, ossifying fibroma, fibrous dysplasia and other mesenchymal malignancies of the jaw like fibrosarcoma.

The Computerized tomography (CT) image showed a bone-destructive lesion in the left maxilla (3x4cm) with the presence of radial spicules spreading outside the jawbone, known as a “sunburst appearance”. The lesion destroyed the lateral nasal wall with infiltration of the left nasal cavity, the posterior maxillary sinus wall and the lateral plate of the pterygoid process with infiltration of the infratemporal fossa (Figure-5).



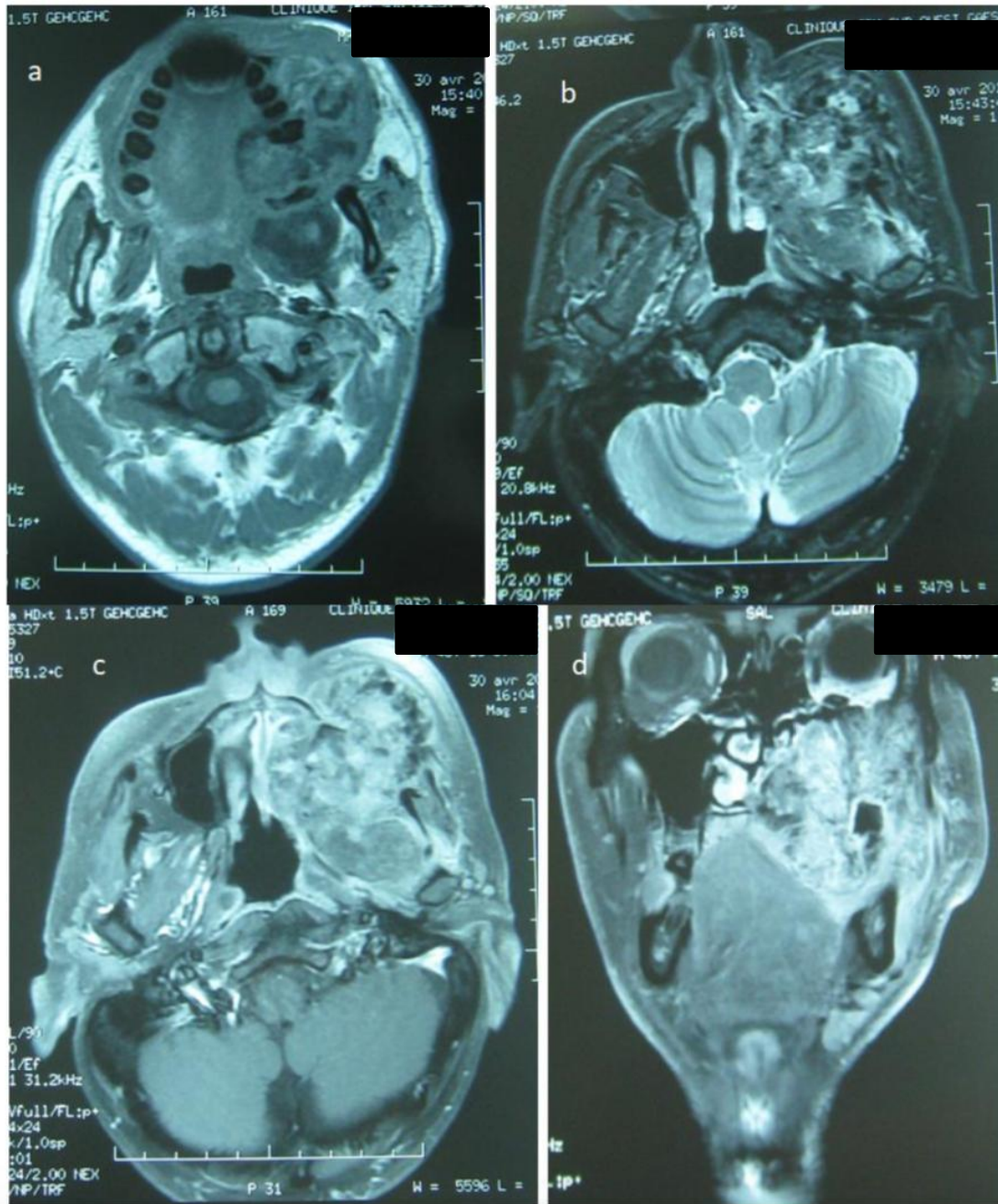
**Fig 5(a, b): CT scan axial cut, showing a bone-destructive lesion with radial spicules: destruction of the lateral nasal wall (➔), the posterior maxillary sinus wall (➞), the lateral plate of the pterygoid process (↗) with infiltration of the infratemporal fossa (○)**

The patient was referred to the department of maxillofacial surgery at Sahloul Hospital, Sousse, Tunisia, with a diagnosis of OSJ. Other investigations, such as chest radiographs and scintigraphy, were carried out and they were negative.

A biopsy was taken from the buccal lesion and sent for histopathological examination. It showed a mesenchymal lesion mainly composed of atypical neoplastic osteoblasts with considerable variation in shape and size, showing large deeply stained nuclei arranged in disorderly fashion without the presence of chondroid areas, which gave a conclusive diagnosis of osteoblastic variant of OSJ.

The patient was referred to an oncologist to start chemotherapy to stop the tumor evolution. The protocol OSS4 was performed. After the treatment, a radiographic check-up using magnetic resonance

imaging (MRI) showed poor response and local progression. A protocol of Cisplatin in combination with Adriamycin was therefore adapted. During treatment, a new radiographic check-up with MRI showed stabilization of the lesion progression. It was conducted in several sequences and it described the tumor as a heterogeneous T1 hypointense and T2 hyperintense sinus mass with intense enhancement after gadolinium injection. It specified the exact size (8×7×6 cm) and the degree of invasion of the neighboring regions. The tumor invaded the anterior part of the zygomatic arch and protruded subcutaneously. It also invaded the left hard palate and projected in the oral and nasal cavity, the pterygoid process, the pterygoid muscles and it extended to the prestylian space. It invaded the orbital floor and projected in the orbit and it extended downward to the tonsillar fossa (Figure-6). The MRI also showed the presence of bilateral spinal and left jugular- carotid lymph nodes.



**Fig-6: MRI: a.axial T1-weighted cut without injection of contrast material, b. axial T2-weighted cut , c. axial T1-weighted spin-echo cut(T1SE) with gadolinium injection: A lobulated heterogeneous on T1 and T2 aggressive mass with destruction of the left jawbone and an invasion of the homolateral maxillary sinus, nasal cavity, and infratemporal fossa, d. invasion of the orbital floor**

Then, the patient underwent hemimaxillectomy of the affected side while retaining the 21, taking a portion of the orbit floor, the left nasal mucosa and the zygomatic bone. The anatomical limitations in the face made it difficult to reach the uninvolved margins. For this reason, the patient returned with important local recurrence highlighted by the appearance of an endonasal mass. The biopsy

showed a lesion having the same nature as the first and the CT scan visualized an extension to the contralateral maxillary sinus after destruction of its medial wall, a complete lysis of the left pterygoid process, a filling of the left fossa of Rosenmuller (Fig-7a) and a filling of the left ethmoid cells (Fig-7b). A surgical revision associated with chemotherapy was indicated.

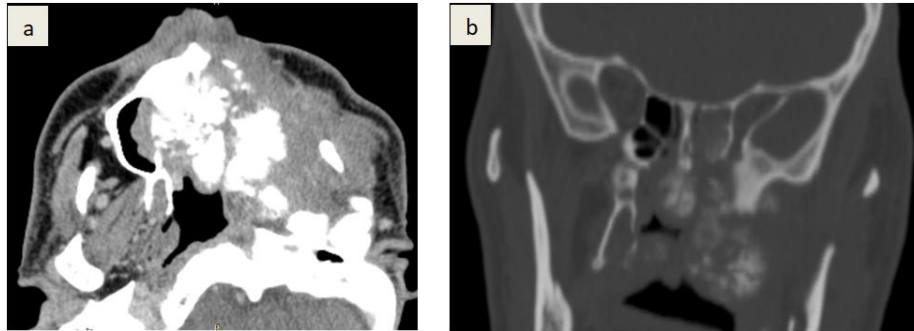


Fig-7: a. CT scan axial cut, b. CT scan coronal cut

## DISCUSSION

Osteosarcoma is a highly malignant tumor with extensively destructive potential. It is also the most common primary malignant lesion of bone. Craniofacial osteosarcoma, most often located in the mandible or maxilla, accounts for only 5–13% of all osteosarcomas and 1% of all head and neck malignancies [6, 7].

The maxilla and the mandible are equally involved. The mandibular tumours arise more frequently in the posterior body and in the horizontal ramus, whereas the maxillary tumours are discovered more commonly in the alveolar ridge, the sinus floor, and the palate as in this case [1, 8-10].

Jaw osteosarcomas usually present in the third and fourth decades of life, almost a decade after their presentation in the long bone tumors.

The median age of maxillary osteosarcoma is reported to be higher than the mandibular one [8].

This patient was in fourth decade, a finding similar to earlier statistics.

The exact cause of OSJ is unknown. It may arise de novo or subsequent to a number of risk factors as follows [8, 10, 11]:

- Environmental factors such as radiation. Radiation-induced osteosarcoma is a form of secondary osteosarcoma.
- Genetic predisposition: Bone dysplasias, including Paget's disease, fibrous dysplasia, enchondromatosis, and hereditary multiple exostoses giant cell tumor, chronic osteomyelitis, osteoblastoma, chondroid neoplasms, osteochondroma, and retinoblastoma (germ-line form). Isolated cases of trauma have been stated as contributory factors.

Among the related lesions, fibrous dysplasia (FD) and Paget's disease are considered as important predisposing factors for developing osteosarcoma.

The association of OSJ and Florid cemento-osseous dysplasia FCOD is extremely rare and could

simply represent a collision between a benign and malignant lesion or may represent OSJ arising in FCOD. However, as the doubt persist it is important that patients with FCOD be followed and monitored in a regular basis [11, 12].

This case appears to have developed de novo; as no history of any predisposing factors could be elicited from the patient.

The main clinical manifestations of OSJ are swelling of the bone and the adjacent soft tissues, pain of variable intensity, tooth bulging and dislocation, lack of healing and swelling at the site of the tooth extraction, trismus and hypoesthesia or paresthesia in the case of the mandibular tumors, and nasal obstruction in the maxillary tumors [7, 1]. The average time between presenting of symptoms and diagnosis range from 3 to 5 months [3, 2].

The chief complaint of the present patient was pain and restricted mouth opening, which signified an advanced stage of the tumor.

The radiographic appearance varies, depending on the amount of bone formed by the neoplasm.

Panoramic radiography is commonly available imaging modality and has a low radiation exposure. Though significant distortion and superimposition is seen, but a provisional differentiation of benign or malignant process can be made. It may clearly express bone remodeling, cortical destruction, tumor margins supero-inferiorly and antero-posteriorly that often provides a clue to the initial diagnosis, aggressiveness of the tumor and hence prognosis and provides a summary differential diagnosis. The main limitations are underestimation of the tumor's extent within and outside of the bone and other bone lesions, such as Ewing sarcoma, chondrosarcoma, and fibrosarcoma, infections or Langerhans cell histiocytosis may resemble OSJ.

Once the diagnosis is suspected, multiplanar imaging (CT and especially MRI) have an important role in staging, assessment of local tumor extension and follow-up of tumor response to therapy. CT and MRI

may also be helpful to guide biopsy and to demonstrate the most viable area within the tumor. Bone scintigraphy is used for detection of distant bone metastases [4, 1]. Biopsy should be performed following MRI evaluation as hemorrhage occurring at the biopsy site alters the signal intensity characteristics of the tumor at subsequent MRI examinations [13].

MRI forms the imaging modality of choice to assess the extent of the tumor distribution within the bone and associated soft tissue component. As calcium returns no signal, MRI is insensitive to small foci of calcification.

MRI can evaluate treatment response to chemotherapy. Oka *et al.*, evaluated the role of Diffusion-weighted MRI in 22 patients with OS, before and after chemotherapy, using the average and minimum apparent diffusion coefficient (ADC). The authors found the minimum ADC a better tool than the average apparent diffusion coefficient ADC for evaluating the chemotherapeutic response of patients with osteosarcoma. Conventional and diffusion-weighted MRI can predict chemotherapeutic response of OS early in the disease course, and it correlates well with necrosis. In addition, newly derived parameter diffusion per unit volume appears to be a sensitive substitute for response evaluation in OS [14]. WHO classified the radiographic pattern of OSJ into lytic, sclerotic, and mixed, mentioned that no relationship was found between the radiographic pattern and the histological type of osteosarcoma [11]. Widening of the periodontal ligament space WPLS or attenuation of the lamina dura around the OSJ are the common radiographic findings [4, 15, 16]. Codman triangle and sunburst appearance SA can be noted [12] (SA appears in approximately 25% of cases) [17]. Concerning the WPLS, it is considered a sign of malignancy including osteosarcoma, chondrosarcoma, and Ewing's sarcoma of the jaw. Therefore, WPLS is a significant sign which helps to distinguish malignant bone diseases, including OSJ, from benign diseases, although WPLS may not always be found in all OSJs [15, 18]. Lindquist *et al.* reported that the WPLS and the inferior dental canal, together with sunburst effect are almost pathognomonic of osteosarcoma of jaw bone [19]. Widening of the mental foramen was reported to be the only radiological finding in a case reported by Doval *et al.*, [20].

Some OSJs showed aggressive signs on the diagnostic imaging findings, while others showed diagnostic imaging findings similar to those of benign cemento-osseous lesions, which thus made it difficult to make an accurate diagnosis based on the imaging examinations alone [15]. Therefore, in presence of swelling and/or pain at the site of a lesion with no evidence of any active odontogenic inflammatory diseases is at least a warning sign of the possibility of an underlying OSJ, even if a lesion shows diagnostic

imaging findings similar to those of benign cemento-osseous lesions [21].

Because of the complexity of the clinical features, the radiographic appearances and their rarity in the daily clinical practice, the preoperative diagnosis of osteosarcoma is often difficult and includes differential diagnosis as chondrosarcoma, Ewing's sarcoma, bone metastasis, fibrous dysplasia, osteomyelitis, and even lesions that do not usually affect the jaw bones, such as fibrosarcomas, leiomyosarcomas, or rhabdomyosarcomas [1, 22].

In the present case, the misdiagnosis of the lesion and its curettage accelerated the evolution of the tumor. It was observed that the bone destructive lesion was mixed (radiolucent radiopaque) in appearance, in accordance with Clark *et al.*, classification, with WPLS and SA. A diagnosis of malignancy was given based upon the panoramic radiograph and confirmed based on the CT findings.

In addition to its precise definition of the extraosseous extent of the tumor and its relationship with neighboring tissues, the MRI in this case with the CT, were beneficial in the evaluation of tumor progression, the choice of the appropriate treatment and assessment of response to chemotherapy.

The reported patient had osteoblastic osteosarcoma. The histological type influences the prognosis. In fact, Clark *et al.* reported that the patients with chondroblastic osteosarcomas of head and neck had a better overall survival rate than the patients with osteoblastic or fibroblastic tumors [11]. In another study, three distant metastases and five deaths were recorded; and all were of osteoblastic type [23].

Bielack *et al.*, in their analysis of prognostic factors in high grade osteosarcoma, concluded that incomplete surgery was the most important negative prognostic indicator, followed by poor response and primary metastases as well as tumor size in those patients where it could be evaluated [24, 25].

Diagnosis of tumor in its early stages and complete resection are the most important factors in increasing prognosis of OSJ, but anatomical limitations in face can sometimes cause difficulties in achievement of uninvolved margins and for this reason local recurrence of these lesions is high and still the leading cause of death. For the same reason, mandibular osteosarcomas have a better prognosis than maxillary osteosarcomas [1, 2, 8]. In OSJ, metastasis are rare and late, occurring in only 18% of the cases [1]. For this patient, the bad prognosis was the result of a multiplicity of factors including the delayed diagnosis, the anatomical location, the histopathological type, the incomplete surgery, and the absence of response to the first protocol of chemotherapy.

## CONCLUSION

Jaw osteosarcoma presents a wide spectrum of clinical, histological and radiological features. Therefore, all these features have to be correlated to reach a conclusive diagnosis. Early diagnosis and radical surgery are the keys to high survival rates.

The use of multiple imaging modalities facilitates the surgical planning and the appropriate use of neoadjuvant chemotherapy. The continuously improving knowledge of the molecular and cell-signaling pathways involved in OS will lead to more effective therapies and ultimately to improved patient survival.

## Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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