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Epithelioid Angiosarcoma of the Maxillary Sinus: About A Case and Review of the Literature

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Abstract **Case Report**

Summary: The objective of this publication is to report the case of a patient presenting an epithelioid angiosarcoma of the maxillary sinus with review of the literature in order to study the diagnostic, therapeutic and evolutionary aspects of this pathology. He is 60 years old. Active chronic smoker, who presented a painful swelling of the upper maxillary bone lateralized to the left. The radiological assessment described a lytic tumoral process at the expense of the floor of the maxillary sinus infiltrating the deep spaces of the face. A biopsy retained the diagnosis of a maxillary localization of an epithelioid angiosarcoma. Then, an extension assessment was able to eliminate the multifocal character and did not show any secondary localization. The patient subsequently underwent oncological surgery, with healthy excision limits. The evolution was favorable over a follow-up of one month. Angiosarcoma is a rare, high-grade malignant vascular tumour. For a third of the cases, these are multifocal tumours. There is a male predominance and a preferential location in the long bones and short bones of the extremities. They are observed at any age, with a median age of 51 years. In imaging, the radiological presentation is not specific but it is mainly to characterize the lesions and indicate their uni- or multifocality. Under microscopy, the most common angiosarcomas are epithelioid. One-piece surgical excision is the treatment of choice. They have an aggressive evolution with a 5-years survival rate between 10 and 30%. Adjuvant radiotherapy allows local control of 80% with good functional and cosmetic results. However, 50% of angiosarcomas develop metastases and irradiation does not improve survival.

Keywords: Epitheloid angiosarcoma - bone - treatment - metastases.

INTRODUCTION

Angiosarcoma is a high-grade malignant vascular tumour. It is rare and only accounts for less than 1% of malignant bone tumors [1]. There is a male predominance and a preferential location in the long bones and the short bones of the extremities, followed by the pelvis and the spine. Under microscopy, the most common angiosarcomas are epithelioid with large eosinophilic cells, often with nucleolated nuclei. One-piece surgical excision is the treatment of choice. While radiotherapy may be offered in some cases.

The objective of our publication is to report the case of a patient presenting an epithelioid angiosarcoma of the maxillary sinus with review of the literature in order to study the diagnostic, therapeutic and evolutionary aspects of this pathology.

OBSERVING AND PATIENT

This is a 60 years old patient. Active chronic smoker, without particular pathological antecedents. And who had been presenting a left cheek swelling for five months. The clinical examination objectified a left cheek swelling of 3*3cm, clean, without any inflammatory signs, painful on palpation. Examination of the oral cavity found poor oral condition, swelling of the upper maxillary bone lateralized to the left, with dental encroachment, without contact bleeding or inflammatory signs. The general condition of the patient during the consultation was WHO score 1.

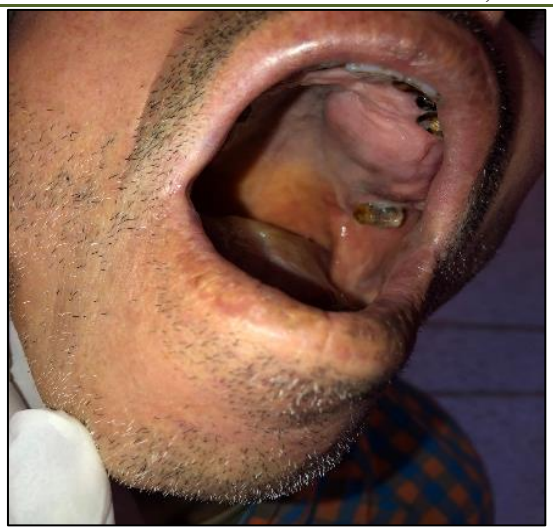

Fig 1: Swelling of the upper maxillary bone lateralized on the left with dental encroachment on a bad oral state

A naso-sinus CT showed a lesional process centered on the floor of the left maxillary sinus of 40*37*43mm. Downstairs; lysis of the ipsilateral palatine and alveolar process with total lysis of the 24th, 25th, 26th and 27th teeth, it bulges intra buccally and comes into contact with the free edge of the left hemi-tongue with no detectable sign of infiltration. It bulges above at the level of the left maxilla with bone lysis of the internal walls with discreet endo-nasal extension. It bulges forward at the level of the left soft parts of the cheeks and mouth with lysis of the anterior wall of the left maxillary sinus.

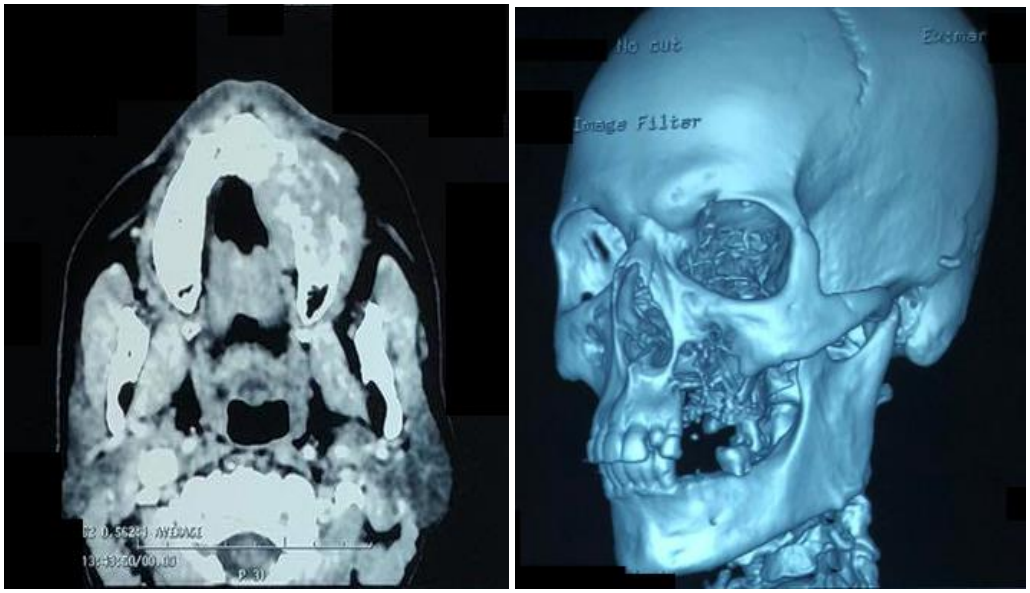

Fig 2: Naso-sinus CT showing a lytic tumoral process centered on the floor of the left maxillary sinus

Complementary facial MRI showed an osteolytic lesion process of the left upper maxillary bone of 41*43*42mm well limited with lobular contours. It is responsible for an infiltration of the alveolar bone and the 23rd, 24th, 25th, 26th teeth, with rupture of the cortical bone opposite. In the top: it infiltrates the floor of the homo lateral maxilla with bone lysis of the internal walls with discreet endonasal extension. Below: it infiltrates the alveolar bone as well as the ipsilateral cheek region and pushes back the left lateral edge of the body of the tongue which remains of normal signal. On the inside: it infiltrates the bony palate with rupture of the cortex. Outwards and forwards: it comes into intimate contact with the ipsilateral infratemporal fossa without detectable signal abnormalities.

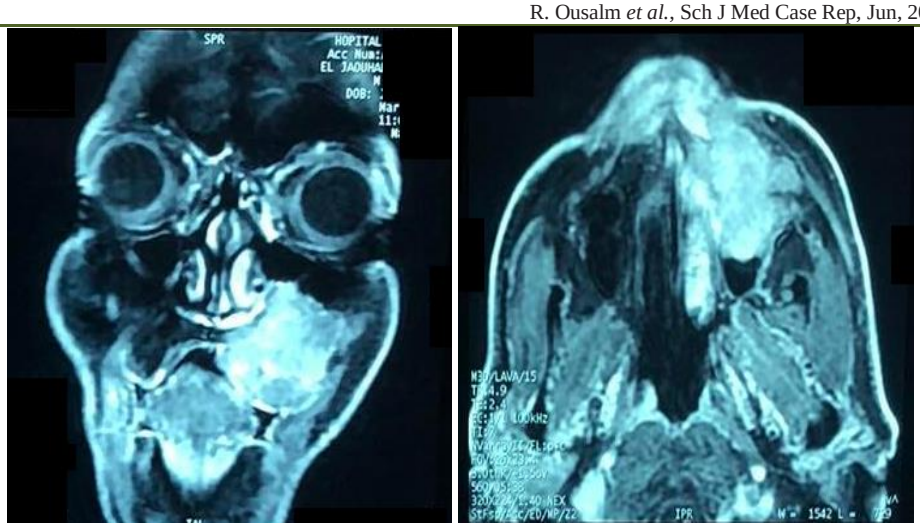

Fig 3: Facial MRI in axial and coronal section showing a lesional process centered on the floor of the left maxillary sinus

Anatomopathological study of a maxillary biopsy revealed fibrous tissue, largely infiltrated by a sarcomatous-like proliferation. Tumor cells are spindle-shaped, their cytoplasm is moderately abundant and eosinophilic. With presence of vascular cleft. The immunohistochemical study has objectified an intense and diffuse cytoplasmic expression of tumor cells of anti-CD-31 and anti-ERG antibodies. Suggesting an epithelioid angiosarcoma.

As part of the extension assessment, a PET scan was performed which described an intensely pathological hyper metabolic character of the known tumor process located at the floor of the left maxillary sinus (max SUV = 16.5) of 35*25*46mm without locoregional extension or remotely detectable.

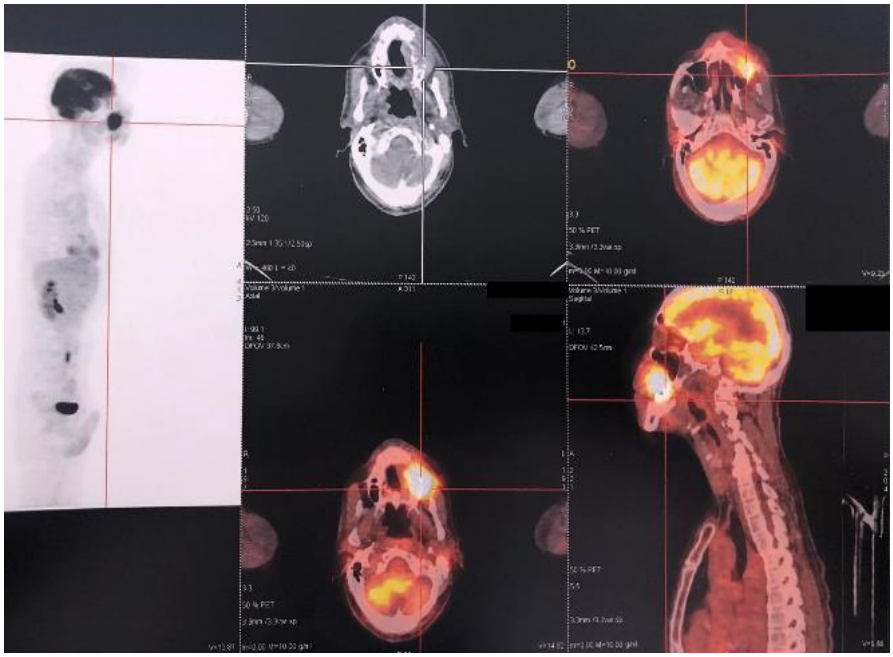

Fig 4: Pathological hyper metabolic character of the tumoral process located at the floor of the left maxillary sinus

The patient underwent cancer surgery. Macroscopy objectified a whitish tumor focus of 4.5*3.5*3.5cm the excision limits are healthy, the closest is 0.5cm microscopic examination found tumor proliferation organized in a sheet and in diffuse patches, with no formation of glands or papillae or horny cysts. It is made up of cells with rounded or oval nuclei presenting mild to moderate atypia with rare mitoses. The cytoplasm is scanty and poorly circumscribed. The stroma is partially fibrous with dilated and congested thin-walled vessels without calcification or neoplastic vascular emboli. The bone resections received are free from tumor proliferation. The immunohistochemical study confirmed the diagnosis already made. The evolution was favorable over a follow-up of one month.

DISCUSSION

Angiosarcoma is a rapidly growing and aggressive tumor of vascular origin. These tumors are rare and account for less than 1% of malignant bone tumors. The majority of these tumors are primary. However, there are secondary forms described as developing after radiotherapy [2, 3] or after bone infarction [4], or on Paget's disease [5], or even on overload disease [6] or in contact with orthopedic implants, and metallic materials [7, 8]. A recent study carried out on 42 bone angiosarcomas reveals that angiosarcomas are observed at any age, with two frequency peaks at 60 and 80 years and a median age of 51 years [9]. There is a male predominance and preferential localization in the long bones and short bones of the extremities (74%), followed by the pelvis (15%), the spine (7%) [10] and finally the trunk (4%). For the majority of cases, these are single tumors (71%). A third of cases are multifocal [11, 12]. It is unclear whether this multifocality is synchronous in the form of multiple small foci or the result of metastases [13, 14]. Clinically, patients most often present with chronic pain and/or a mass at diagnosis. A revealing mass is mostly seen in patients with a single lesion. Under microscopy, bone angiosarcomas represent a heterogeneous group of lesions ranging from well-differentiated tumors with vascular formations, to solid tumors that may mimic metastatic carcinoma. In bone, the most common angiosarcomas are epithelioid with large eosinophilic cells, often with nucleolated nuclei. These angiosarcomas express cytokeratins in 69% of cases. Apart from cytonuclear atypia and mitoses, the morphological criteria for defining these tumors are controversial. In imaging [15], the radiological presentation of bone angiosarcomas is not specific, but standard radiographs are essential to characterize the lesions and indicate their uni- or multifocality. An isolated lesion is present in the form of an osteolytic lesion with irregular edges or a mixed lytic and condensing aspect and readily a blown aspect of the bone, cortical destruction and extension to the soft tissues. The vascular nature of this tumor is suggested in a third of cases by the multicentric and synchronous nature of the lesions affecting several bones of a given extremity or anatomical region. Bone angiosarcoma can present a so-called “soap bubble” appearance due to an extension above and below the main lesion in the affected bone. If the spine is affected, the locoregional extension readily affects several contiguous vertebral bodies. On CT, bone angiosarcoma has an invasive and possibly multicentric appearance, as on standard radiographs. On MRI, bone angiosarcoma has a decrease in nonspecific signal or a signal of variable intensity in T1 and an increase in signal in T2. The lesions take gadolinium. MRI is particularly useful for determining soft tissue extension and invasion of vascular and articular structures. In bone scintigraphy, intense fixation is usually noted although there may also be an extinction of fixation in the case of very destructive lesions. This examination is useful for the differential diagnosis with other vascular multifocal processes of the bone, in the case of myeloma or Langerhans cell histiocytosis. The realization of a local treatment imposes to check the absence of multifocality. Monoblock excision is the treatment of choice. Amputation can be discussed [16]. On the other hand, curettage is inevitably followed by recurrence [11, 17]. Adjuvant radiotherapy achieves local control rates of 80% with good functional and cosmetic results [18-20]. However, 50% of angiosarcomas develop metastases and irradiation does not improve survival. MRI is essential for defining irradiation volumes and fields. The irradiation technique, and in particular the place of intraoperative radiotherapy and brachytherapy, is not consensual. Some offer preoperative radiotherapy when the surgical indication is immediately mutilating, or to limit the risk of spin-off. However, the level of evidence is low and it is estimated that this delays the healing time by one week per 10 Gy delivered [18-20]. The rarity of this bone entity explains the limited data we have to assess treatments [21]. Most of the reported data therefore concern soft tissue angiosarcomas or mixed series of soft tissue and bone lesions, particularly with regard to chemotherapy data [21]. The high rate of metastases makes it necessary to carry out an extension assessment and justifies the place of chemotherapy. Neoadjuvant chemotherapy can be discussed collegially in a multidisciplinary consultation meeting in the event of multifocal lesions, to avoid mutilating surgery or to avoid positive margins. The compilation of several randomized studies using neoadjuvant doxorubicin-based chemotherapy in a meta-analysis suggests an improvement in local control and disease-free survival, but there is no advantage in overall survival. Chemotherapy identical to that performed as a neoadjuvant is repeated postoperatively for good responders. In case of poor response, an alternative regimen based on cyclophosphamide, etoposide and cisplatin can be discussed postoperatively [22]. To our knowledge, there is no specific study on the systemic treatment of metastatic bone angiosarcoma [23]. Several clinical trials have recently been carried out on metastatic angiosarcomas, regardless of the primary location (bone and soft tissue). In addition, multicenter studies have supplemented the findings of phase II trials. Schematically, the chemotherapies associated with an improvement in overall survival compared to supportive care are protocols based on doxorubicin and weekly paclitaxel [24]. Weekly paclitaxel seems to give the same clinical benefit in first and second lines [25]. Doxorubicin and paclitaxel give, a priori, the same level of first-line efficacy. The overall survival of patients with metastatic angiosarcoma is around 8 months. Poor prognostic factors are general condition and metastatic bone disease. Antiangiogenics used alone (bevacizumab or sorafenib) have proven to be rather disappointing [26]. An ongoing study compares weekly paclitaxel to the paclitaxel-bevacizumab combination. Vascular endothelial growth factor (VEGF) receptor 2 (KDR)

mutations appear to be associated with greater sensitivity to antiangiogenic tyrosine kinase inhibitors (sunitibib, sorafenib) [27, 28]. As a third line, gemcitabine seems to provide clinical benefit [29].

CONCLUSION

Vascular tumors are a heterogeneous group of diverse entities that have been better classified over the past decade. The majority of bone angiosarcomas are epithelioid and an expression of cytokeratins is observed in the majority of cases. These angiosarcomas are in a third of the cases multifocal and can lead to a misdiagnosis of metastatic carcinoma. CD31 is the most frequently expressed, although non-specific, vascular marker. Angiosarcomas have an aggressive evolution with a 5-year survival rate between 10 and 30% [30, 31]. Metastases are common [17].

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