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# Multi-recurrent invasive ameloblastoma: A surgical challenge

Fatemah Faras*, Fawaz Abo-Alhassan, Yona Israël, Barbara Hersant, Jean-Paul Meningaud

*Department of Plastic and Maxillo-Facial Surgery, Henri Mondor Hospital, Créteil 94010, France*

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ABSTRACT

*INTRODUCTION:* Ameloblastomas are rare head and neck tumors, and yet the most common odontogenic neoplasms. They account for 1% and 11% of all head and neck and odontogenic tumors respectively. Embryologically, they originate from remnants of odontogenic epithelium. Their aggressive, destructive nature, as well as their anticipated high rate of recurrence, even after en bloc resection, poses a surgical predicament.

*PRESENTATION:* We present a case of a 56 year-old Asian female with a multi-recurrent invasive ameloblastoma. Initially, the lesion was mandibular in location for which she underwent a mandiblectomy. Later on, she presented with a maxillary ameloblastoma with invasion of both the anterior wall of the maxillary sinus and the floor of the orbit. The patient was operated twice and histopathology confirmed a cystic type recurrent ameloblastoma. A year later, she came with recurrent maxillary ameloblastoma and a maxillectomy was done. However, histopathology revealed a follicular ameloblastoma. Three years later, she presented with a retro-orbital ameloblastoma with infiltration to the temporal muscles. The patient was operated and the histopathologic examination revealed a partially cystic lesion with no malignant transformation.

*CONCLUSION:* This case discusses available treatment options and emphasizes on the importance of long-term patient follow-up due to the biological behavior of ameloblastoma.



## 1. Introduction

Ameloblastomas are common odontogenic tumors that arise from the dental epithelium. Proposed etiologies by Smith J.F. is that they arise from the dental lamina or basal cells of the oral epithelium, or from cells that differentiated to mimic the ameloblast [1]. Owing to modern radiology, the early detection and monitoring of such invasive tumors are now readily possible, acknowledging their tendencies for recurrence and malignant transformation.

In the current report we present a multi-recurrent case of ameloblastoma discussing the potential causes of the recurrence and available treatment options, recognizing the rarity of reported cases in the literature and lack of unanimous treatment guidelines.

## 2. Presentation of case

A fifty-six year-old Asian female, known case of multi-recurrent ameloblastoma, with a long history of multiple surgeries reported to the department of plastic and reconstructive surgery of Henri Mondor Hospital, Paris.

Back in 1986, she has been referred by her dentist upon finding a suspicious lesion on her panoramic radiograph and with a chief complaint of a non-tender swelling in that region to the Pitié-Salpêtrière Hospital where she underwent a hemimandibulectomy, as the first surgical intervention.

Her second presentation was in 2005 for the same reason, for which she underwent her second surgical procedure in a different hospital. However sufficient data concerning this presentation was lacking.

In 2009, the patient was referred to our department for the first time with a diagnosis of recurrent left maxillary ameloblastoma with orbital invasion, associated with lytic bony lesions of the zygomatic arch, the anterior wall of the maxillary sinus and the floor of the orbit. She underwent resection of the tumor that was attached to the orbital fat and anterior wall of the maxillary sinus. The orbital floor was reconstructed using Resorbix. Histopathological examination revealed a unicystic ameloblastoma with positive surgical margins, and the left infra-orbital nerve was of normal hitology. A follow-up MRI done 3 weeks post-operatively demonstrating an almost complete resection of the left maxillary lesion and persistence of small incidental tissues in the posteromedial wall of the left infra-temporal fossa. A repeated MRI confirmed the progression of the disease, and accordingly she was scheduled for another surgical intervention. Histopathologic examinations corresponded with a follicular type ameloblastoma. The lesion was formed by islands

* Corresponding author. Present address: 7 Rue Ginette Watelle, 21000 Dijon, France.
*E-mail address:* f.alfaras@gmail.com (F. Faras).

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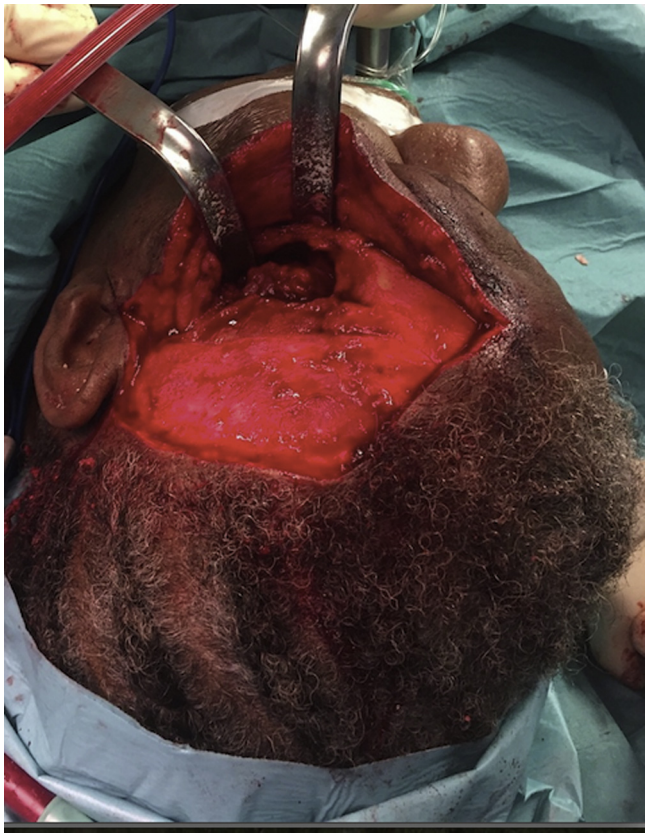

**Fig. 1.** Resection of recurrent ameloblastoma of the left anterior wall of the maxillary sinus, the zygomatic arch, and of the floor of the orbit.

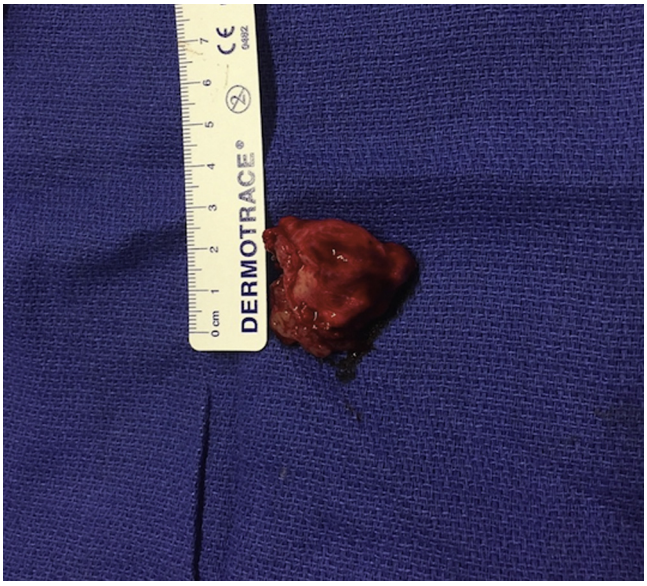


**Fig. 2.** Ameloblastoma with 1 mm of margins.

of odontogenic epithelium, limited by a palisading border with reverse polarization. Although surgical margins were negative, they were only located 1 mm from the lesion. All the subsequent follow-up imaging modalities substantiated a complete surgical resection of the tumor, with no evidence of recurrence.

In 2015, the patient's MRI demonstrated a heterogeneous mass posterior to the left eye, pushing the left medial rectus muscle, suggestive of either a recurrent or a progressive disease. Furthermore, 2 suspicious enlarged nodularities were seen on lower levels. No meningeal invasion could be identified. A CT facial bone revealed a homogeneous nodular tissue formation on the external wall of the left eye measuring 32 mm in the largest diameter, pushing against the greater wing of the sphenoid bone with no adjacent bone remodeling. Accordingly, the patient underwent an excision of the left retro-orbital ameloblastoma (Figs. 1 and 2). Using Hematoxylin-Eosin-Saffaron stains, the histopathology corroborated the diagnosis of a recurrent cystic ameloblastoma with positive surgical margins. The tumor was formed by massive basophilic cells infiltrating the center. The post-operative period was uneventful and her succeeding follow-ups confirmed no evidence of recurrence or malignant transformation.

## 3. Discussion

Ameloblastomas are histologically benign, locally invasive odontogenic tumors. Accounting for 1% of all head and neck tumors, and 11% of odontogenic tumors, they are considered the second most common odontogenic tumors after odontomas. They were first recognized by Cusack in 1827, and named in 1930 by Ivy and Churchill [2]. They are histopathologically divided into 6 subtypes: follicular, plexiform, acanthomatous, basal, unicystic and desmoplastic ameloblastomas. Mixed pathological patterns are not uncommon, and the lesion is usually classified according to the predominant type.

Amelobastomas are more common in adults than in children, with the average age being 20–40 years [2]. They have no sex or race proclivity, although some reports allege an increased rate in the Asian and black population [2].

Ameloblastomas arise more frequently in the mandible 80%, especially in the area of the molar and the ascending ramus, and in the maxilla 20% [3].

Due to their aggressive behavior, several interventions have been proposed in the literature to prevent their local recurrence, invasion to adjacent structures and transformation to malignancy.

Ameloblastomas are managed conservatively by enucleation with bone curettage, or radically by surgery with segmental or marginal resection. Many surgeons advocate margins of 1.5 cm of clinically normal bone. Additionally, the use of radiotherapy is controversial. Most clinicians find no place for radiotherapy in treating ameloblastomas, considering them radioresistant. This belief was supported by literature published in premegavoltage days of radiation therapy [4]. Advancement in radiotherapy resulted in cases of ameloblastoma responding to them, and respectively, several articles reported their success [4–7].

The pathogenesis of ameloblastoma had not been clear until recently when research groups published their results postulating the genes involved [8–10]. The BRAF protein in the mitogen-activated protein kinase pathway (MAPK) has been commonly found to be mutated, rendering the pathway constitutively active [9]. This is also the most common activating mutation found in cancers such as colorectal, thyroid and melanoma [11]. Another gene discovered to play a role in ameloblastoma is the hedgehog pathway gene, however it is less commonly found than MAPK [8,10]. Several target therapies to mutated genes are currently in clinical trial, and some have shown to inhibit some pathways in vitro or vivo [8,12]. Therefore, since MAPK is the commonest pathway involved, it should be carefully studied as a target therapy for ameloblastoma.

Concerning the presented case, due to the proximity of the lesion to vital structure and the level of local invasion, sufficient margins were not conceivably achieved. With reported recurrence rates ranging as high as 92% with conservative treatment [13], and 14–25% with radial approach [14], we opted for monitoring the patient clinically with regular follow-ups and CT scans. However, deliberating the risk of malignant transformation, the addition of

an adjuvant radio-therapeutic treatment is possible in case local control could not be obtained.

A recent WHO classification, distinguished between ameloblastoma and malignant ameloblastoma [15]. Malignant ameloblastoma was further categorized into two types: metastasizing ameloblastoma and ameloblastic carcinoma (AC). Metastasizing ameloblastoma was defined as benign ameloblastoma histologically with metastatic spread to distant sites, while the latter demonstrated malignant histology and furthermore subdivided into: primary and secondary types. Primary AC arises de novo, while secondary AC result from malignant transformation of a primary lesion after repeated postsurgical recurrences [16].

## 4. Conclusion

This case presents our experience with a multi-recurrent unicystic ameloblastoma that until present revealed no signs of malignant transformation, yet poses a surgical predicament. In this report we aim to support the critical significance of regular follow-ups of patients with ameloblastoma, in an attempt to minimize the risks of local recurrence and malignant transformation.

## Conflict of interest

I affirm that we have no financial affiliation (e.g., employment, direct payment, stock holdings, retainers, consultantships, patent licensing arrangements or honoraria), or involvement with any commercial organization with direct financial interest in the subject or materials discussed in this manuscript, nor have any such arrangements existed in the past three years. Any other potential conflict of interest is disclosed.

## Author contribution

All authors have contributed and approved the final article.

## Funding

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## Ethical approval

Not applicable, as it is a report of one case.

## Consent

Patient in the study design has been informed and aware about the study and that her intreoperative images will be included. A signed release from the patient showing informed consent and permission to publish was obtained. Her identity, nevertheless, cannot be recognized from the case history and images.

## Guarantor

None.

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