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Case Report

UNICYSTIC Ameloblastoma of the Mandible About a Case and Review of the Literature

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Abstract

Unicystic ameloblastoma is a rare benign entity which represents 5-15% of all intraosseous ameloblastomas, less aggressive and less invasive, which is observed mainly in younger patients. We report a case of unicystic ameloblastoma in a 25-year-old woman with a rapid evolution in a few months in the symphyseal and parasymphyseal region and illustrate the complexity of the differential diagnosis and the means of management with a brief review of recent literature.

Keywords: Ameloblastoma; Unicystic Ameloblastoma; Genetic Mutation

Introduction

Unicystic ameloblastoma was described by L. Robinson and MG. Martinez. in 1977 with three histopathological variants: luminal, intraluminal and mural [1]. It is a benign odontogenic tumor of local aggressiveness, developed from the epithelial debris of Malassez after regression of the enamel organ, epithelial residues of the periodontium or the epithelial wall of odontogenic cysts [2]. Since the anterior mandibular location is not the site of choice for ameloblastomas, it is therefore legitimate to recall the importance of the differential diagnosis of the unicystic form, which is essentially made with other cysts or tumors derived from the odontogenic apparatus. Treatment for ameloblastoma varies based on clinical, histopathological, and radiographic features [3]. Unicystic forms are thought to be less recurrent; however, a more conservative approach, although recommended, is rarely adopted in practice [4,5].

Case Report

A 25-year-old woman presented to our oral pathology and surgery department at the CHU Issad Hassani de Béni-Méssous in Algiers, Algeria, with a painless swelling in the chin, associated with tingling of the right hemi-lip, Appeared approximately 3 months previously and which rapidly increased in volume, without affecting the general condition. Exo-oral examination revealed a hard, painless swelling covered with healthy-looking integuments of a non-inflammatory nature, with free submental and submaxillary lymph node areas and a positive Vincent's sign on the right side (Figure 1).

Figure 1: Exo-oral view.

The endobuccal examination revealed a normal mouth opening, with at the level of the region concerned, namely the antero-mandibular region, a vestibular filling which extended from canine to canine, of hard consistency, painless, covered with a mucous membrane. normal color. On the lingual side, there was continuity of the lingual table. The incisor-canine group next to the swelling presented an overlap, without mobility, and the vitality tests were positive (Figure 2).

Figure 2: Endo-oral view.

The panoramic X-ray revealed a vast osteolytic image, localized at the level of the symphyseal and parasymphyseal region, which goes from the region of 33 to that of 44 over the entire height of the mandible, with blurred limits, without border of peripheral osteocondensation and with what appears to be a sign of root resorption (Figure 3).

Figure 3: image (OPT).

Faced with the signs of aggressiveness of the lesion, a dent scan-type extension assessment was requested, which revealed signs of local aggressiveness with damage to the basilar and repression of the lingual roots rather than resorption as left appear panning. In addition, he also showed a spiculated reaction at the level of the basilar (Figure 4).

Figure 4: Image (Dentascan).

The differential diagnosis was discussed between unicystic ameloblastoma and a keratocyst, given the signs of local aggressiveness encountered in this patient, namely: rapid development of the lesion within 3 month, positive Vincent d'Alger sign and basilar involvement with speculated periosteal reaction. The patient was referred to the maxillofacial department where she underwent enucleation of the lesion associated with supported curettage by endobuccal route under AG. The surgical specimen was sent for pathological examination (Figure 5).

Figure 5: Surgical enucleation and surgical specimen.

Histological examination of the specimen showed ameloblastic epithelial proliferation architecture lined by an ameloblastic type epithelium, made up of cells with indistinct cytoplasmic limits endowed with basophilic nuclei without atypia. We note in the thickness of the wall spans and nuclei bordered by the same epithelium described above. This wall surmounts a fibrovascular chorion. The diagnosis of unicystic ameloblastoma was made. (Figure 6).

Figure 6: Histological result.

Discussion

Ameloblastoma is a locally invasive benign odontogenic tumor with a high recurrence rate. In terms of frequency, it is the second most common odontogenic tumor (11%) after odontomas. The term ameloblastoma was coined by Churchill in 1923. The first case of a tumor resembling an ameloblastoma was reported by Guzack in 1826. However, the first detailed description of the tumor was made by Falkson in 1879 [6].

About 80% of ameloblastomas appear in the mandible, mainly in the posterior region, and the remaining 20% in the maxilla [7,8].

Ameloblastomas have been classified by the World Health Organization (WHO) into solid/multicystic, desmoplastic, unicystic, and peripheral types [9]. However, in the new 2017 WHO classification, ameloblastomas have been reduced to conventional, unicystic, extraosseous/peripheral and metastasizing ameloblastoma due to the introduction of perspectives based on updated studies genetics. The term solid/multi cystic has been dropped [10]. The unicystic type of ameloblastoma is one of the least encountered variants, accounting for 5-15% of all ameloblastomas [11]. The preferred seat is the mandible in the posterior region, the ratio between maxillary and mandibular unicystic ameloblastoma is 13:1 [12].

The unicystic type most often appears in a younger population (2nd-3rd decade) than its conventional counterpart (4th decade) [13,14]. Our case therefore falls within the age range that has been reported in the literature. Some authors report an even older age. Meshram., *et al.* described a mean age of 13 years and a male to female sex ratio of 1.5:1 in a case series of 15 patients [12]. Bhutia., *et al.* reported the case of a 5-year-old child with a unicystic ameloblastoma in the right parasymphyseal region [15].

Unicystic ameloblastoma may present with common clinical and radiological manifestations with other odontogenic lesions making the diagnosis difficult. Dentigerous cyst, odontogenic keratocyst, residual cyst, adenomatoid odontogenic tumor, and giant cell lesion may be the differential diagnosis of unicystic ameloblastoma [12]. In the case reported here, the signs of local aggressiveness led us to discuss the differential diagnosis essentially between two benign but locally aggressive entities, in this case a unicystic ameloblastoma and a keratocyst. However, the keratocyst generally spreads along the axis of the mandible and rarely in the vestibulolingual direction [12].

Bajpai M, Agarwal D, Bhalla A, Kumar M., *et al*. reported a rare case of unicystic ameloblastoma (UA) of mandible which showed multilocular radiolucency on the left side of mandible on radiographic examination which is very unusual, and the majority of the cases of UAs till date has been reported of unilocular radiolucency.

The authors conclude that at present, histologic examination is the most sensitive tool for differentiating between odonto-genic cysts and UAs. However, both clinical and radiologic findings share equal contribution to the final diagnosis [16].

Our patient benefited from intraoral enucleation with intensive curettage. The choice of a conservative approach was motivated by the unilocular appearance of the lesion, the concern to preserve functionality and aesthetics and the possibility of practicing combined conservative treatment.

Various treatment modalities for unicystic ameloblastoma have been proposed. The treatment of choice for ameloblastoma is surgery, but the use of conservative or radical techniques depending on the clinical type has always been controversial, especially in the treatment of conventional and unicystic types. When talking about radical surgery, the term refers to segmental or marginal resection. In the case of conservative surgery, we speak of enucleation, curettage or marsupialization, associated or not with supporting techniques such as curettage, the application of tissue fixatives such as Carnoy's solution or cryotherapy with l liquid nitrogen [17,18].

Radical surgery involves margins of 1-1.5 cm, as ameloblastic cells are found up to 8 mm from the radiological and clinical margins of the tumor [19,20]. Restoring functionality and aesthetics after radical surgery remains a challenge. However, the low recurrence rate makes this technique a very good option to avoid recurrences.

The recurrence rate after treatment of unicystic ameloblastoma remains lower than that of its conventional counterpart and ranges from 10 to 25% [1].

In a recent literature review, D. Neagu., *et al.* recommend treating unicystic ameloblastoma with an enucleation technique associated with a support technique using Carnoy's solution or cryotherapy. Enucleation alone is associated with a high recurrence rate and should not be used. In case the tumor is large, more aggressive or there is no possibility of combined treatment, radical surgery with margins of 0.5 to 1 cm is recommended. In the same review, D. Neagu., *et al*, recommend radical surgery for conventional ameloblastoma with margins of 1-1.5 cm [18].

Importantly, patients should be followed for life due to unpredictable biological behavior [21].

Histologically, the follicular and plexiform variants are the most frequent. They belong to the conventional type. Unicystic ameloblastoma, on the other hand, presents as a cyst lined by an amelo-

blastic type epithelium of variable thickness ranging from a few layers to several layers of cells showing the typical cytomorphological characteristics of ameloblastoma given by Vickers and Gorlin, including peripheral cells in palisades of cylindrical or cubic form, with reversed polarity and a hyperchromatic nucleus [22]. This coincides with what was observed in the patient reported here.

The development of non-invasive therapies has been impeded by a lack of understanding of the molecular pathology of ameloblastomas. However, new sequencing technologies have paved the way. Recently, oncogenic mutations have been discovered that constitutively activate transduction pathways relating to developmental stages of odontogenesis, including the mitogen-activated protein kinase (MAPK) pathways and the hedgehog pathway [21].

These studies demonstrated a high frequency of mutations in the BRAF V600E gene, up to 80% in some samples, causing constitutive activation of the MAPK pathway in mandibular ameloblastomas from younger patients, whereas SMO mutations implicated the hedgehog signaling pathway predominantly in maxillary ameloblastomas of elderly patients [23,24,25]. Most BRAF V600E mutations concerned conventional ameloblastomas, but this mutation was also found to a lesser extent in unicystic ameloblastomas [26].

The BRAF gene also known as B-Raf proto-oncogene is located on chromosome 7 codes for a protein called B-Raf, more formally known as serine/threonine-protein kinase B-Raf. It is a protein composed of 766 amino acids involved in the transduction of signals that of the MAP kinase/ERK pathway, which affects cell division and differentiation [27,28].

Mutations in the BRAF gene were demonstrated for the first time in 2002 in certain human cancers, particularly in melanoma, the most frequent mutation of which is BRAF V600E, i.e., at position number 600 on the B-Raf protein, valine is replaced by glutamic acid [29].

The BRAF mutations highlighted in ameloblastomas are also largely BRAF V600E mutations. This paved the way for further research on targeted therapy of the MAPK/ERK pathway, which resulted in the development of vemurafenib, an inhibitor of the MAPK pathway which obtained marketing authorization from the FDA in the USA in 2011. for the treatment of melanoma [30].

These new advances therefore suggest that, hypothetically, the use of MAPK/ERK pathway inhibitors may find their indication in the treatment of ameloblastomas.

Fernandes., *et al*. [31] treated a 29-year-old patient with recurrent mandibular ameloblastoma with vemurafenib. She experienced complete resolution of symptomatology and imaging showed continued resolution of the lesion.

Dabrafenib, another MAPK/ERK pathway inhibitor has also been used by Tan., *et al*, as well as Faden., *et al.* with very favorable results [32,33].

However, the evidence on the effectiveness of these non-invasive treatments remains insufficient, and randomized studies are needed to have more conclusive evidence.

Conclusion

Ameloblastoma is a benign tumor, but its invasive nature justifies early diagnosis and, above all, appropriate treatment.

Radiological imaging is not specific and allows for several possible diagnoses.

Unicystic ameloblastoma does not recur less frequently than its conventional counterpart, however patient follow-up is essential.

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