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AMELOBLASTOMA – A CASE REPORT WITH REVIEW OF LITERATURE.

Dentistry

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ABSTRACT

Ameloblastoma, a benign but locally aggressive odontogenic tumour, predominantly affects the mandible. This case report presents a unique clinical case of ameloblastoma in the mandible of a 16 year old female patient presented with painless swelling in the right mandibular region, and subsequent radiological and histopathological investigations confirmed the diagnosis of ameloblastoma. The literature review section provides an extensive analysis of existing knowledge on ameloblastoma of the mandible, focusing on epidemiology, clinical presentation, radiographic features, histopathological variants, and treatment modalities, including conservative surgical approaches, enucleation, and radical resection, are critically evaluated based on their outcomes and recurrence rates. Additionally, the review explores recent advancements in treatment modalities, molecular markers, and targeted therapies. T

KEYWORDS

Ameloblastoma, Plexiform Ameloblastoma, Mandible, Conservative Management, Surgical Enucleation with Peripheral Ostectomy, Bismuth Iodide Paraffin Paste.

INTRODUCTION

Ameloblastoma is a benign but locally aggressive odontogenic tumour that primarily affects the mandible, making up approximately 1% of all jaw tumours. The term "ameloblastoma" originates from its presumed origin in the odontogenic epithelium, specifically from the enamel organ or its remnants.[8] While it typically presents in the third and fourth decades of life, cases across a broad age spectrum have been documented. 70% of ameloblastomas develop in the molar-ramus region of the mandible and are occasionally associated with an unerupted third molar tooth. It is characterized by its infiltrative growth pattern and high rate of recurrence if not adequately managed.[10]

The exact etiology remains uncertain, but genetic, environmental, and molecular factors may play roles in its development.[11] Moreover, there is considerable diversity in the clinical presentation of ameloblastoma, with a wide array of radiographic and histopathological subtypes, further complicating its management.[12]

Based on WHO 2017, ameloblastoma is divided into i) ameloblastoma, ii. unicystic type, iii. extraosseous/peripheral type, and iv. metastasizing ameloblastoma. Radiographically, ameloblastoma may present as a unilocular radiolucency with a well-defined margin or multilocular, often in the shape of soap bubbles or a honeycomb.[13] Histologically, ameloblastoma can present with a follicular, plexiform, acanthomatous, basaloid, granular cell or desmoplastic pattern, with no evidence of deviant biological behaviour among them. Follicular ameloblastoma is the most common histological variant (64.9%), followed by the plexiform (13.0%), desmoplastic (5.2%), and acanthomatous (3.9%) varieties.[13]

In the plexiform ameloblastoma, the ameloblast-like tumour cells are arranged in irregular masses or more frequently as a network of interconnecting strands of cells. Each of these masses or strands is bound by a layer of columnar cells and between these layers may be found stellate reticulum–like cells.[14]

Many investigators believe in radical treatment of ameloblastoma, with resection of at least 1 cm of bone beyond the tumour margins. This is because tumour cells may often remain in cancellous bone after conservative treatment, leading to recurrence of the tumour which in turn will result in removal of more bone and teeth. Radical procedures, such as segmental resection, will often lead to deformity and dysfunction of the jaws, which in turn will hamper not only the physical growth but also his/her mental well-being. Although conservative methods of treatment may lead to a higher recurrence rate, radical procedures might not be acceptable in young adults as the growth of jaws is not yet completed. At the very least, conservative treatment will gain time until the growth of the jaws is complete. In such cases, regular follow-up is a must.[15]

This paper describes a case of plexiform ameloblastoma of mandible in a 16 years old female patient managed conservatively with follow-up of four years with no evidence of recurrence and literature review regarding the conservative management of plexiform ameloblastoma.

Case Report

A 16-year-old female patient came with the complaint of swelling on the right side of the face for a duration of 5 months. The swelling was initially small which gradually increased without any associated pain or discharge. Patient has no relevant past medical, personal or family history.

On clinical examination, Extra-orally, a diffuse swelling seen in right side of the face. Skin over the swelling was normal with no ulceration, redness or discharge. (Shown in fig 1).

Fig 1. Profile Photographs Showing The Extension Of The Swelling Extraoral.

Intra-orally, swelling was seen in the buccal vestibule extending from 46 towards the ramus of the mandible. There was missing 47 and obliteration of the vestibule seen in the same region. Mucosa over the swelling was normal (shown in fig 2). On palpation swelling is hard, tender with expansion of buccal and lingual cortical plates.

The Panoramic Radiograph shows a Unilocular radiolucency extending from distal to lower first molar with displaced mandibular second molar near the lower border of the mandible till the sigmoid notch involving the ramus of the mandible on the right side.

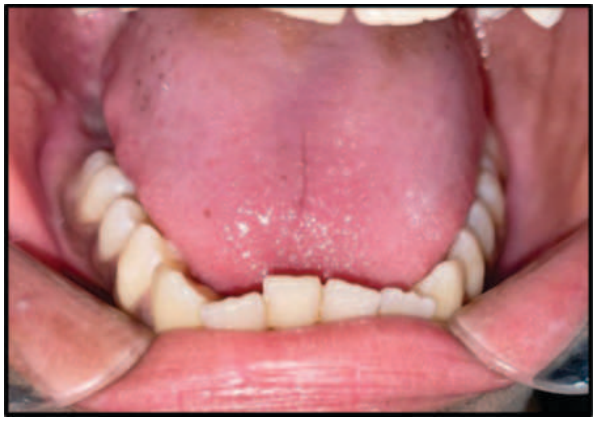

Fig 2. Intra-oral Photograph Showing Intraoral Extension Of The Swelling

In CBCT a large multilocular expansile lesion noted in the right mandible extending from distal to mandibular first molar to sigmoid notch of the mandible with well-defined, well corticated and scalloped margins. Thinning and perforation of buccal and lingual cortical plates at multiple sites with buccolingual expansion of the cortical plates were noted with vertically impacted second molar which is displaced to the lower border of the mandible and resorption of mesial and distal roots of first molar.

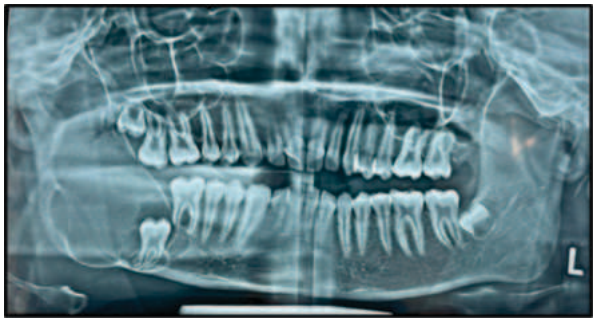

Fig.3 OPG Showing Radiolucuency Involving the Ramus of the Mandible

Incisional biopsy was done and sent for histopathological examination The histopathological report was of 'Ameloblastoma' with interconnecting strands & cords forming Plexiform Pattern interspersed in the connective tissue stroma.

Patient was explained about the treatment plan of resection of the tumour followed by reconstruction for which patient was not willing and requested for conservative management. After pre-operative investigations were carried out and with proper written informed consent, patient was planned for surgery under local anaesthesia. With all intra-operative measures surgical enucleation of the lesion followed by peripheral ostectomy with chemical cauterisation using Bismuth Iodide Paraffin Paste dressing which was changed once in two weeks for 6 months (fig.4 and 5). 4 years follow-up was done and patient showed no signs of recurrence of the lesion. (fig.6 and 7).

Follow Up

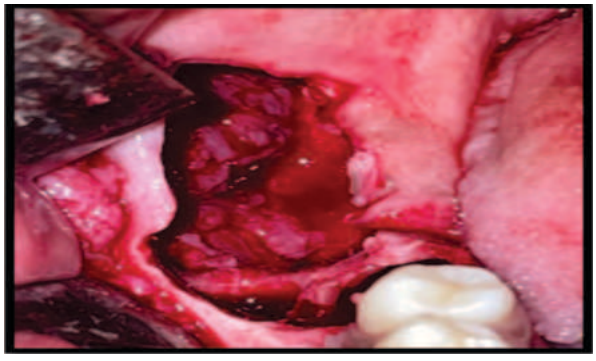

Fig.4 Exposure Of The Lesion

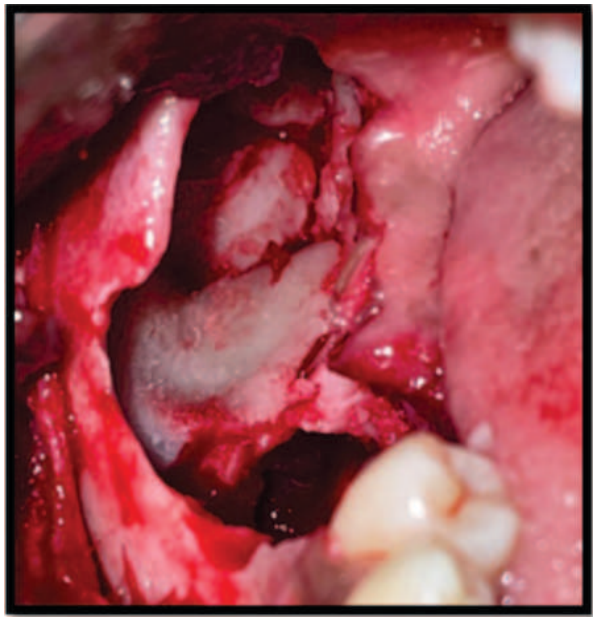

Fig.5 After Peripheral Ostectomy

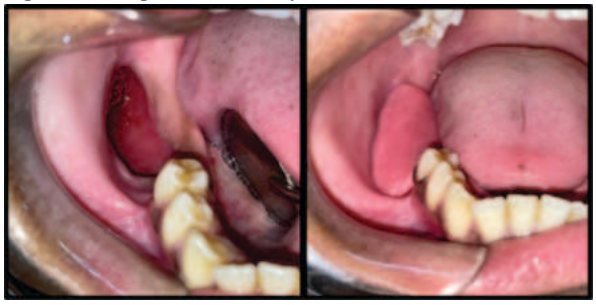

Fig.6 Healing Of The Wound After 2 Months Post-op And Splint Placement To Cover The Surgical Site

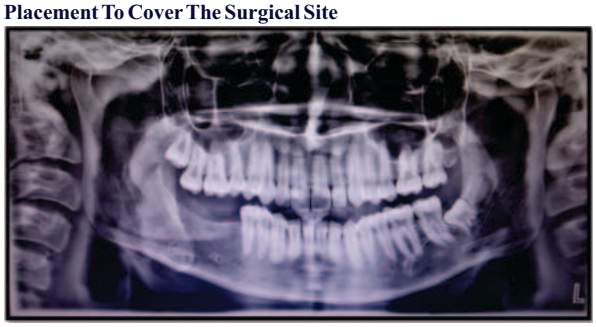

Fig.7 Follow-up Opg After 2 Years

DISCUSSION

Ameloblastoma is a common tumour of odontogenic origin which is locally invasive or aggressive.[1] Odontogenic tumours are rare entities that constitute a heterogenous group of neoplasms with a variety of histological types and clinical behaviours. Their classification has seen many changes, from attempts to classify these lesions based on their histogenesis or mechanisms of differentiation to reach the latest classification scheme set by the World Health Organization in 2017.

Among all odontogenic tumours, ameloblastoma are the most common to encounter. [1]This latest classification is simplified from the previous versions and describes ameloblastoma of the following four types: ameloblastoma; unicystic ameloblastoma; extraosseous/ peripheral ameloblastoma; and metastasizing ameloblastoma.[4] The adjective 'solid/multicystic' for conventional ameloblastoma was removed because it has no prognostic significance and can lead to confusion with unicystic ameloblastoma.[4] Desmoplastic ameloblastoma, which had been sub-categorized under ameloblastoma in the previous 2005 WHO classification, was also removed, as it was considered merely a histological variant of conventional ameloblastoma. Similarly, odontoameloblastoma, from the 2005 classification, has also been removed and is now more

accurately described as ameloblastoma arising in an odontoma.[4] Metastasizing ameloblastoma was reclassified as a benign tumour rather than a malignant odontogenic tumour, as this tumour shows benign histopathology, in spite of its metastatic potential, thus rendering it difficult to differentiate histopathologically from conventional ameloblastoma. [4] Recently, there has been an effort for the inclusion of adenoid ameloblastoma as a sub-type of ameloblastoma in the next revision of the WHO odontogenic tumour classification.[4] Adenoid ameloblastoma is a hybrid odontogenic tumour showing histopathological features of both ameloblastoma and adenomatoid odontogenic tumour.[4] These tumours arise from the remnants of odontogenic epithelium such as cell rests of dental lamina, developing enamel organ, lining of an odontogenic cyst or basal cells of oral mucosa.[2]

Conventional ameloblastoma presents as a painless swelling of the posterior mandible frequently being associated with unerupted tooth and hence easily detected.[3] Maxillary ameloblastoma in contrast to mandibular ones have a more aggressive clinical course which can be explained partially by lack of early symptoms, leading to diagnosis of an advanced disease when the tumour had already extended beyond maxilla.[3] When symptoms develop, they include facial deformity, usually unilateral, intra-oral ulceration, toothache, headache, nasal obstruction, nasal epistaxis, and visual disturbances.[3]

Unicystic ameloblastoma is the second most common ameloblastoma and accounts for 5 to 15% of all cases.[3] Ackerman et al reported that mean age of unicystic ameloblastoma is 23.8 years and male/female ratio found to be 1.3:1 as per study of Ademola.[1] Majority of unicystic ameloblastoma resembles dentigerous cyst because of their association with an unerupted tooth. It is reported that 15 to 30% dentigerous cyst transforms into ameloblastoma.[1] Most common in paediatric age group and third molar region is the most common location.[4]

Depending on how early patient presents for evaluation, clinically ameloblastoma can appear from innocuous intra-oral swelling to a gross orofacial swelling. Different imaging techniques should be combined for evaluation, diagnosis and treatment planning. These includes OPG, CT, CBCT, MRI or functional imaging that combine PET scan with CT. plain radiograph displays the extent of the ameloblastoma while CT is gold standard for primary and metastatic ameloblastoma.[4]

The CT scan most commonly shows a well-defined, uni- or multilocular radiolucent expansile lesion with scalloped margins. Multilocular ameloblastoma appears as a soap-bubble appearance on the radiographs.[4] Since none of the radiologic features are pathognomonic definite diagnosis is established only by biopsy.[4]

The unicystic ameloblastoma deserve special consideration on the basis of its clinical and radiological appearance, its histopathology and its response to treatment.[5] A review of English literature taken from case reports and reviews from 1977 to 2006 disclosed a total of 123 cases of unicystic ameloblastoma of which only 18 had recurred (14.6%).[5]

Histologically, solid/conventional ameloblastoma shows follicular or plexiform pattern. In addition to these there are cystic, granular, acanthomatous, spindle cell, basal cell, clear cell, and other microbiological types.[6]

Peripheral ameloblastoma is the least common variant accounting for only 1% of all cases. Metastasizing ameloblastoma is a benign ameloblastoma that has metastasized to distant site usually the lungs.[4]

There are three histologic variants of unicystic ameloblastoma described in the literature. In the first type, Luminal, tumour is confined to the luminal surface of the cyst. In the second type, Intraluminal, tumour nodules project from the cystic lining into the lumen of the cyst. In the third type, Mural, fibrous wall of the cyst is infiltrated with tumour nodules. Third type is considered aggressive with recurrence rate as high as 35.7% hence incisional biopsy should be taken for planning the treatment.[5]

Treatment modalities for ameloblastoma are many and varied and can be divided into conservative and radical therapies. Prognosis of ameloblastoma is more dependent on the method of surgical treatment rather than the histological variant.[5] The conservative surgical treatment can be in the form of enucleation and cauterization, curettage, cryotherapy or marsupialization.[3] Conservative surgery preserves patient's normal tissues, minimizes facial disfiguration and adequate quality of life post-surgery but it is proven to have high recurrence up to 60-90% especially if the ameloblastoma is aggressive sub-type.[6] This is because the architectural pattern of ameloblastoma is such that the border of the tumour within cancellous bone lies beyond the apparent macroscopic surface and the radiographic boundaries of the lesion.[5]

Currently recommended surgery for classic ameloblastoma is complete en-bloc resection with adequate margin of safety, which is classified as segmental or marginal osteotomy of mandible and partial or total maxillectomy. Due to high recurrence wide margin of 1 to 1.5cm bony margin is recommended.[4]

Regardless, the unicystic ameloblastoma deserves special consideration on the basis of its clinical and radiological appearance, its histopathology and its response to treatment and this variant of ameloblastoma is found to have shown less aggressive behaviour than conventional ameloblastoma hence can be managed conservatively.[5]

So, in our patient considering the age, we managed conservatively with enucleation and peripheral ostectomy followed by cauterization.

Ameloblastoma presents clinically as a locally aggressive tumour, which can rapidly become a massive and expansile tumour. Recently, a somatic mutation of the “mitogen activated protein kinases” signalling pathway is detected. In particular BRAF V 600E mutation which is a single nucleotide mutation which leads to the activation of the downstream MEK/ERF pathway.[7] The constitutive activation of BRAF V 600E associated with development of ameloblastoma has also been attributed to its progression.[3] BRAF is an essential link in Epidermal Growth Factor Receptor (EGFR) signal transduction pathway. The activated enzyme-coupled EGF receptor can bind several enzymes at their SH regions. Thus, the activated EGFR transduction pathway forces proliferation and prevents apoptosis.[7]

In many tumours BRAF is in activated state and relays growth promoting signals independently of EGFR pathway activation.[7]Thus, blocking EGFR with anti-EGFR therapies in tumours with BRAF mutation fails to silence EGFR signalling. On the other hand, mutant BRAF represents a target for handful of new drugs. These includes, Dabrafenib or Vemurafenib, as selective, reversible inhibitors of RAF kinases.[7]

Considering the fact that depending on the studies, on an average 2/3rd of ameloblastoma shows BRAF-V-600E mutation and standard therapy currently does not include a standardized drug therapy. Even the use in children showed an acceptable side effect profile, so that the therapy with BRAF-inhibitors seems to be a conceivable therapy alternative to surgery.

Rather, their use to reduce tumour size with consecutive surgical treatment seems reasonable. Therefore, BRAF inhibitor therapy should be at least considered in the treatment of ameloblastoma if mutation is detected especially in view of the fact that there is no specific treatment for metastasizing ameloblastoma.[7]

CONCLUSION

These clinical presentation, and various treatment modalities for ameloblastoma emphasizes the need for individualized treatment plans based on factors such as tumour size, location, and histological subtype. Surgical intervention remains the primary mode of treatment, with conservative and radical approaches tailored to the specific characteristics of each case.

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