International Journal of Medical Science in Clinical Research and Review
Online ISSN: 2581-8945
Available Online at http://www.ijmscrr.in Volume 6|Issue 05 (September-October)|2023 Page: 928-934

Case Report

A Case Report: Ameloblastoma of Mandible

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Article Received: 03-September-2023, Revised: 23-September-2023, Accepted: 13-October-2023

ABSTRACT:
Ameloblastoma, is derived from the English word "amel" which means enamel and the Greek word "blastos" which means the germ. The World Health Organization (WHO) (1991) defined ameloblastoma as a benign but locally aggressive tumor with a high tendency to recur, consisting of proliferating odontogenic epithelium lying in a fibrous stroma.[1] In this case report, we present the case of a 60 year old male patient who came to the Civil Hospital Ahmedabad with a massive swelling on the right side of the face. The swelling was painless and non-tender but causing massive facial deformity, obstruction of nasal passages and loss of vision in the right eye. Diagnosis was confirmed via clinical and radiological investigations.

Keywords: Odontogenic tumor, Mandible.

INTRODUCTION:

Ameloblastoma is a rare, benign, locally aggressive odontogenic tumour. Odontogenic tumors are considered destructive neoplasms of the jaw bones. Ameloblastoma makes up of about 1 % of oral ectoderm tumors and 9% of odontogenic tumors. It is considered enigmatic which is attributed to its characteristic of slow growth rate similar to benign tumors and being locally invasive, high recurrence rate and metastatic potential resembling a malignant tumour.[2] This aggressive tumor originates from the epithelial crests of Malassez and the odontogenic epithelium which plays essential role in tooth development.[3] The deregulation of several genes related with the mitogen-activated protein kinase, sonic hedgehog, and WNT/-catenin signalling pathways is significantly connected to the neoplastic transition of odontogenic epithelium to ameloblastoma. [4] About 2% of ameloblastomas undergo metastasis. [5] Nonspecific irritational causes such as extraction, caries, trauma, infection, inflammation, or tooth eruption; nutritional deficiency diseases; and viral infection have all been implicated as etiologic factors for these cystic ameloblastomas.[6] A few early investigations have revealed the presence of HPV, mostly in peripheral ameloblastomas. A research found HPV at low and high risk in samples of intraosseous ameloblastomas. HPV positive was more prevalent in unicystic cases than solid kinds, with HPV-6 being the most common genotype. [7] The epithelial-mesenchymal transition (EMT) has a role in tooth growth and tumour invasion. By activating -catenin and its downstream transcription factor zeb1, IL-8 may induce EMT in ameloblastoma tumour cells. [8] Only two incidences of ameloblastoma in pregnant women have been described in the scientific literature. The potential role of pregnancy hormones in the formation and development of tumours in general, and ameloblastoma in particular, remains unknown. However, in a case report from Brazil, a lady had an en bloc resection and her foetus was delivered with alobar holoprosencephaly.[9] According to the 5th edition of World Health Organization (WHO) Classification of Head and Neck Tumors, there are **five types of Ameloblastoma**: ameloblastoma; unicystic ameloblastoma; extraosseous/peripheral ameloblastoma; and metastasizing ameloblastoma and adenoid ameloblastoma.[10] 'Solid/multi-cystic' for conventional ameloblastoma as well as desmoplastic ameloblastoma have been removed from the 2005 Classification.

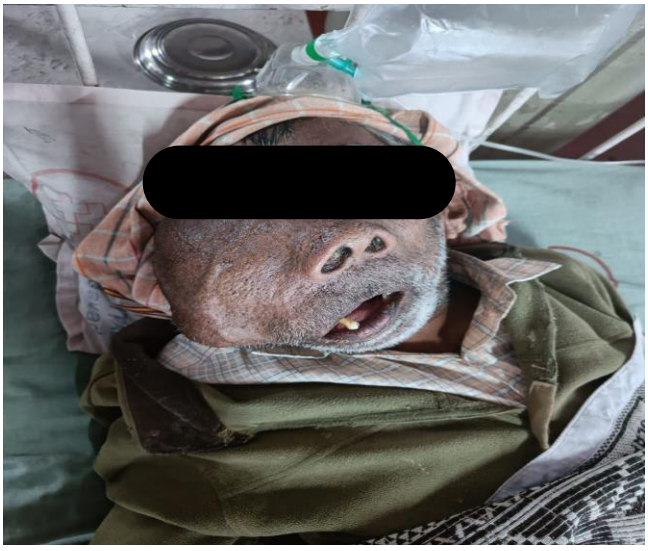
Benign epithelial odontogenic tumors	Frequency	Histological Variants
Ameloblastoma	91%	Follicular, plexiform, acanthomatous, granular cell, basal cell, keratopapillary
Ameloblastoma unicystic type	6%	Luminal, Mural
Ameloblastoma extraosseus/peripheral type	2%	
Metastasizing ameloblastoma	1%	
Adenoid ameloblastoma	40 cases recorded so far	

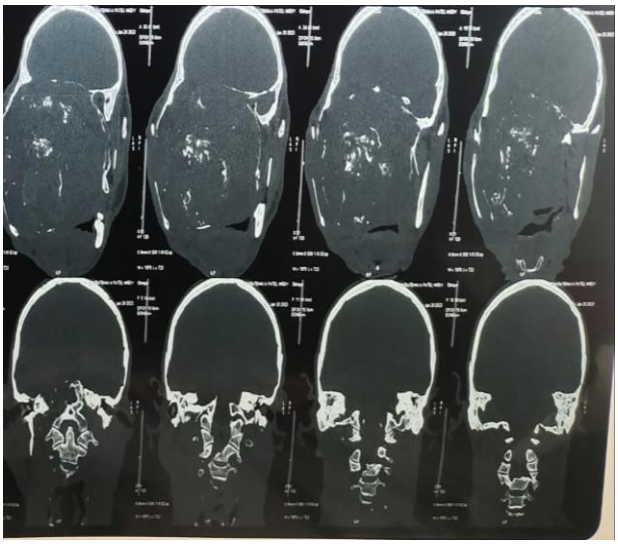
Table from 5th WHO 2022 Classification of Head and Neck Tumors

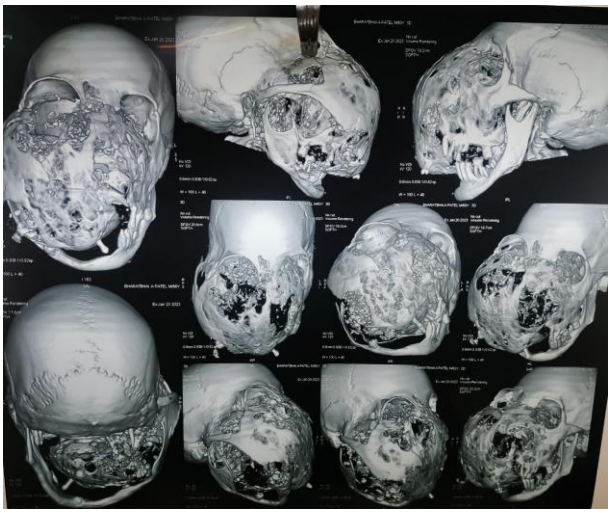
This report illustrates the case of ameloblastoma in 60 year old male patient who presented with complaints of lower respiratory tract infection.

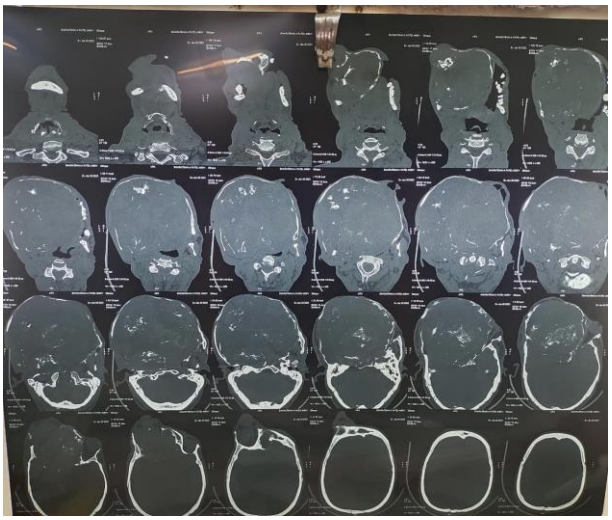
CASE REPORT:

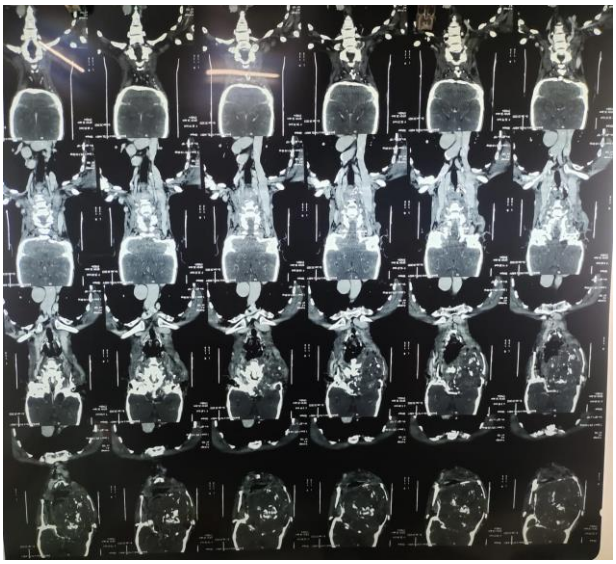
A 60 year old male presented to the Department of Medicine, with difficulty in breathing, chest pain, cough with expectoration since 2 days and a swelling over the right side of face causing massive facial deformity. On examination, the swelling appeared as a massive, painless swelling of about 14 x 16 cm. The swelling was present since the patient was 10 years old and had grown in size since the last 50 years. No history of trauma and birth deformity were present. Other symptoms that were found in association with swelling were: Absence of teeth due to delayed tooth eruption, multiple loose teeth, difficulty in speaking and obstruction of nasal airways, loss of vision and no perception of light in the right eye, ptosis in right eye and facial asymmetry. Patient was a tobacco chewer since 25 years.

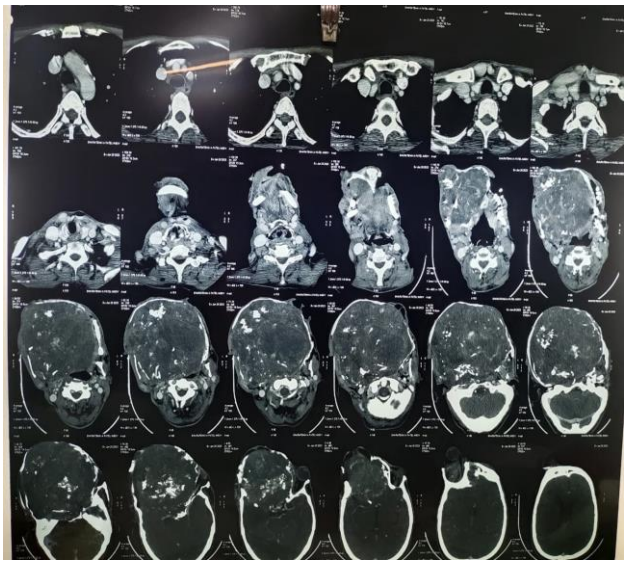


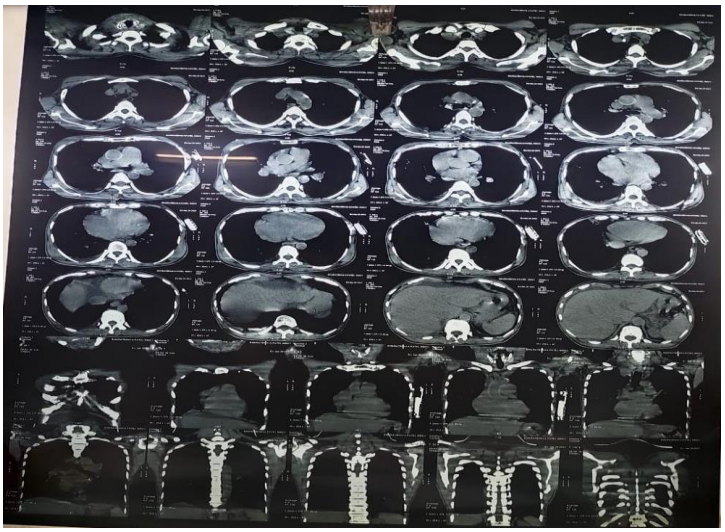












The patient was vitally unstable on admission and had oxygen saturation spo2 of 88%. Patient was treated for 10 days with intravenous antibiotics and was on an 8L/min simple NRBM mask. Sputum was mucopurulent and Gram stain revealed the presence of a few gram positive cocci in chains. Modest elevation in white blood cells was seen predominantly neutrophilia. Erythrocyte sedimentation rate was markedly increased. Hrct thorax examination revealed ground glass haziness with interlobular septal

thickening in right upper lobe, medial and lateral segment of right middle lobe. Right side pleural effusion and minimal free fluid in right perihepatic region were noted. Multiple subcentimeter sized nodes in subcarinal, upper and lower paratracheal regions were noted.

CECT imaging was performed using submillimeter thin contiguous plain and contrast axial scan of neck and thorax from base of skull. CECT Scans of Neck, Thorax and Face, reveal the presence of a large expansive, lytic lesion arising from the body and ramus of mandible on the right side. It extends superiorly up to the roof of right orbit and right frontal bone involving all sinuses resulting in marked thinning of bone. It also extends into the right retro-orbital and pushes the globe causing marked ptosis. The lesion has multiple internal and solid components and large amounts of internal calcification. Histopathological examinations of the Ameloblastoma could not be performed as the patient had critically low oxygen saturation and succumbed to lower respiratory tract infection.

DISCUSSION:

Cusack is considered the first person to identify an Ameloblastoma in 1827. The first histological description was provided by Weld in 1853 and Wagstaffe gave the histological drawing. Malassez in 1885 introduced the term 'adamantine epithelioma ' and Derjinsky gave the term 'adamantioma . In 1930 Ivy and Churchill coined the term 'Ameloblastoma'.[2] Ameloblastoma are benign and locally aggressive. They are believed to spread their pseudopods into the marrow spaces without concomitant resorption of trabecular bone. Thus the tumors margins are not clear in radiographic investigations causing a high recurrence rate after surgery.[11]

Site of Occurrence:

80% of the Ameloblastoma occur in mandible and other 20 % in maxilla of which most occur in the posterior maxilla than the anterior maxilla. In the mandible, most tumors occur frequently in the body and posterior mandible .

Age of Occurrence:

Ameloblastoma is found to be the most common Odontogenic tumor. Most studies indicate that they occur in the 30-60 years of age group with a slight male preponderance and most commonly found in the mandible. Racial diversity in occurrence was also noted with high occurrence in Asian and African races as compared to American and European races.[12]

Clinical Presentation:

Clinical Features that May be Present are:

A growth that is abnormal in the jaw or sinus area, jaw swelling that is not painful, bone pain can be constant or intermittent, tooth eruption is delayed,difficulty speaking due to loose mobility of numerous teeth, airway obstruction in the nose, ulceration in the mouth, the teeth are not properly aligned. Patients may not have any symptoms or may just have a few of the ones listed. Nonetheless, it is critical that this tumour be discovered early, as ameloblastomas can develop to vast sizes and become progressively difficult to treat if left untreated.

Diagnosis:

Diagnosis comprises of clinical examination along with radiological investigations and biopsy.

Radiological findings:

A radiolucent expansile lesion which may be uni or Multilocular can be seen on CT Scan. It also shows degree of cortical destruction and soft tissue expansion. Other three dimensional methods used are cone-beam computed tomography (CBCT) or magnetic resonance imaging (MRI). Malignant potential is evaluated on positron emission tomography combined with CT(PET/CT).[13] X-ray appearance of unicystic Ameloblastoma is a lytic lesion with scalloped margin, may be associated with a mandibular third molar and cortical perforation may be present while the multilocular one appears as a classic "soap bubble appearance".[14] However, MRI is a more useful tool for Ameloblastoma arising from the maxilla.

Histopathological Findings:

Histopathological examination reveals presence of two varieties of cells: peripheral 'basal cells' and central 'epithelial cells'. Basal cells appear hyperchromatic, columnar, vacuolated, having reversal of polarity resembling ameloblasts. The epithelial cells resemble Stellate reticulum. The classic Ameloblastoma further shows these two cell layers in two different patterns: Follicular and plexiform. Follicular pattern shows the follicles in connective tissues and plexiform pattern shows an interlacing pattern. Other histological variants are formed as a result of superimposing of these two primary patterns. The unicystic Ameloblastoma lacks the classical diagnostic features. Membranous parts of cyst wall are present but the nuclear palisading is often negligible. This unicystic Ameloblastoma is further classified as mural and luminal on the basis of histological differences. Luminal variant shows the cell invaginations in the lumen and mural variant shows the fibrous wall infiltrated by tumor islands. Peripheral Ameloblastoma bone or periosteum involvement is absent, stellate

reticulum is inconspicuous. Metastasizing possesses the histology of a classical Ameloblastoma along with the presence of another tumor foci at distant sites, of which lung is the most commonly involved. Histology commonly found of the foci is follicular Ameloblastoma.[13]

Staging:

Yang et el Classified Stages of Ameloblastoma into:

Stage 1: diameter 6cm

Stage 2: diameter of≤tumor>6cm or tumor invasion into maxillary sinus or orbital floor

Stage 3: Invasion into skull and metastasis to lymph nodes.[15]

Immunohistochemistry:

BRAF VE1 is an efficient tool for diagnosing mandibular ameloblastoma but has limited value in the maxilla, where it is less prevalent and the BRAFV600E mutation is much less common.[16]

TREATMENT:

Surgical Management:

Surgical management of ameloblastoma includes two approaches the- conservative approach (for small lesions) and an en bloc or radical approach which involves wide bone resection and secondary defect reconstruction (for large tumours). Owing to the high recurrence rate, the radical surgery is performed with a margin of safety. This is further classified into segmental or marginal Osteotomy in case of mandible and partial maxillectomy in case of maxilla. Radical surgery, however possesses certain drawbacks such as aesthetic deformities, functional impairments and psychological distress.[12] Conservative methods include enucleation, curettage, physiochemical treatment, marsupialization and decompression. The advantage of this approach is preservation of adjacent healthy tissue, avoidance of facial disfigurement and thereby increased quality of life postoperatively. It is ideal treatment of choice in paediatric population.[11] The radical approach involves resection with a 1.5 cm margin of healthy bone around the lesion and immediate or delayed reconstruction. [17] The latter can help improve aesthetics and it's functioning postoperatively.

There are Two Types of Grafts:

- Non-vascularised bone grafts from iliac crest [17] and split rib graft [3] when the total resection defects were smaller than 6 cm in length and located within one mandibular region. Here the defects were still surrounded by healthy bone and well vascularised soft tissues for better graft uptake.
- Vascularised bone grafts which include STFF and FFF. Performing FFF inevitably prolonged the stay in terms of number of fibulae fragments used.

To improve cosmetic and functional outcomes plus patient satisfaction often dental rehabilitation with Osseointegrated implants and inferior alveolar nerve repair with nerve allografts are added to the treatment. [17] Potential complications of the surgery include bleeding, hematoma, infection, thrombotic events [17] and aspiration (the head of the bed should be elevated). Prophylaxis is commonly provided to prevent the occurrence of DVT and stress ulcers. [3] The major setback of this disease is its high recurrence rates which occurs mainly because of insufficient local excision. [17] The recurrence rates for aggressively treated tumours is about 12% while that with conservative treatment is 30%.[13] Ameloblastoma cells express markers of dental epithelial cells which are SOX 2 and BMI1 due to which they can transform into cancer stem cells and this can be responsible for tumor relapse. Fragmentation during conservative surgical procedures leading to seeding of ameloblastoma cells in wound bed can also lead to the increasing recurrence rates. [17] Some other aspects which should be assessed after the surgeries include feeding as oral tissues can take weeks or months to heal, oxygenation, breathing and oral suctioning. Also as it is a major surgery involving aesthetic changes, mental health counselling should be provided to the patient.[3]

Non-Surgical Management:

Non-surgical methods include radiotherapy and/ or chemotherapy. However, they have played no significant role in the treatment of the tumor. Although radiation may reduce the size of an ameloblastoma, it does not appear to be an effective treatment for operable ameloblastoma. Its primary application is in inoperable situations, most notably in the posterior maxilla. [18]

Molecular Targeted Therapies:

Recent discoveries in the molecular signalling pathways related with ameloblastoma pathogenesis have resulted in the development of targeted treatments for ameloblastoma management.Several MAPK-specific medicines specifically block the actions of mutant BRAF and MEK to prevent ameloblastic cell growth and differentiation. These include vemurafenib and dabrafenib, which block the mutant BRAF gene; trametinib, which blocks the mutated MEK gene; and ponatinib and regorafenib, which block the mutated FGFR2 gene. Unfortunately, vemurafenib therapy for ameloblastoma has been linked to resistance mechanisms such as compensatory activation of the MAPK kinase pathway by the epidermal growth factor receptor. This raised the possibility that mutated MEK inhibitors would be

preferable to mutant BRAF inhibitors for treating ameloblastoma .[4]

RECURRENCE:
There are presently no biomarkers or diagnostic techniques available other than biopsy. This makes determining proper resection margins during surgery challenging, contributing to the high recurrence rate. Accurate tumour margin evaluation with precise, non-invasive imaging would result in the preservation of healthy tissue and improved long-term local tumour management, lowering the chance of recurrence. To increase the accuracy of tumour margin evaluation, new methodologies for targeted imaging should be developed. The majority of ameloblastomas have been proven to be epidermal growth factor receptor (EGFR) positive as a possible biomarker. One study that looked at 193 instances with AB discovered that 85-100% of them had EGFR3 expression. The use of EGFR as a biomarker for ameloblastoma might allow tumour distinction from normal tissue.Previous studies have employed FDA-approved antineoplastic antibodies that can be modified for use in fluorescence-guided surgery, such as the anti-EGFR medicines cetuximab and panitumumab. These FDA-approved medications can target the EGFR in cancer and are authorised for treatment of head and neck malignancies as well as colorectal cancer using cetuximab and panitumumab, respectively.89Zr-panitumumab, a radiolabeled anti-EGFR antibody, may be utilised to efficiently detect ameloblastoma tumour tissue in vivo. This was proven by 89Zr-panitumumab's substantial localisation to ameloblastoma PDX tissue as evaluated by biodistribution and SUV. This approach capitalises on the EGFR expression seen in ameloblastoma tumours while providing the feasibility of using advanced imaging for ameloblastoma detection. This will allow surgeons to more confidently excise ameloblastomas by accurately assessing the tumour location and preserving normal tissue, thereby improving long-term local tumour control and, ultimately, patient outcomes. [19]

CONCLUSION:
Radiological and clinical investigations of our case are consistent with those of Ameloblastoma.

DECLARATION:
ETHICS APPROVAL AND CONSENT TO PARTICIPATE:
Not applicable

CONSENT FOR PUBLICATION:
Not applicable as the subject is deceased and has no family or legal guardian.

COMPETING INTERESTS:
Authors declare that they have no competing interests.

FUNDING:
No role of funding.

ACKNOWLEDGEMENT:
We sincerely acknowledge with immense gratitude the support and guidance provided by Dr. Chitralekha Vora , Department of Medicine Civil Hospital Ahmedabad.

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