Evaluation of Various Treatment Modalities in the Management of Ameloblastoma – A Clinical Study

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Abstract:

Aim: To evaluate various treatment modalities in the management of ameloblastoma is to achieve complete eradication of the lesion, reconstruction of the defect and restore the normal jaw functioning and to prevent recurrence. **Materials and Methods:** A total of 11 cases (4 male, 7 female) aged 12 to 45 years were evaluated and treated based on clinical, radiological and histopathological findings. Treatment options included enucleation with curettage, peripheral osteotomy, segmental resection and hemi-mandibulectomy. **Results:** All cases of ameloblastoma, treated with various modalities, with no recurrence till date. However, further follow-up needed for a minimum of five years to ensure long-term outcomes. **Conclusions:** Successful treatment of ameloblastoma ensures an acceptable prognosis with minimal disfigurement, considering the tumor's behaviour, growth patterns, location, size, and histology. Treatment is determined by the patient's age, health, and the need for complete lesion eradication and defect reconstruction. This aggressive yet curable neoplasm remains a subject of global interest in the literature, with treatment options ranging from enucleation and curettage to more extensive resections, based on its biological behaviour.

Key-words: Ameloblastoma, Mandible, Odontogenic tumor, Segmental reconstruction.

Introduction:
The aim of this study is to evaluate various treatment modalities of management of ameloblastoma is to achieve complete eradication of the lesion, reconstruction of the defect and restore the normal jaw functioning and to prevent recurrence.

Subjects and methods:
The study was carried out at the Department of Oral and Maxillofacial Surgery, Sibar Institute of Dental Sciences, Guntur. 11 cases were evaluated, diagnosed and treated, out of which four cases were male and seven cases were female, the age ranging from 12 to 45 yrs. The most common presenting symptom was swelling and facial asymmetry. Patients who required surgery were advised for surgical profile tests and screened for general anaesthesia.

Case reports:
Case 1:
A 21-yr old male presented with a history of pus discharge from the left lower back tooth region for 3 months. Extra orally, diffuse, hard, and non-tender swelling was palpated over the angle of the mandible. On intra oral examination, vestibular obliteration seen with expansion of the buccal and lingual cortical plates in relation to left lower first and second molars with pus discharge.

Radiograph revealed single unilocular radiolucency extending from left lower first premolar anteriorly to angle of the mandible posteriorly and superoinferiorly from crest of the alveolar bone to lower border of the mandible (Figure 1a). Incisional biopsy was performed and diagnosed as “Follicular Ameloblastoma” (Figure 1b).

Under adequate general anaesthesia enucleation with thorough curettage and chemical cauterization with carnoy’s solution was a choice of treatment through an intra oral approach (Figure 1c). Extraction of lower left canine, premolars and molars was performed. Mucoperiosteal flap reflected and enucleation with curettage done. The surgical area was thoroughly irrigated and a sterile ribbon gauge soaked in betadine was placed in the cavity. Check-up was done at regular intervals and after one week cavity was closed with 3-0 silk sutures. Follow up doneand no recurrence till date.

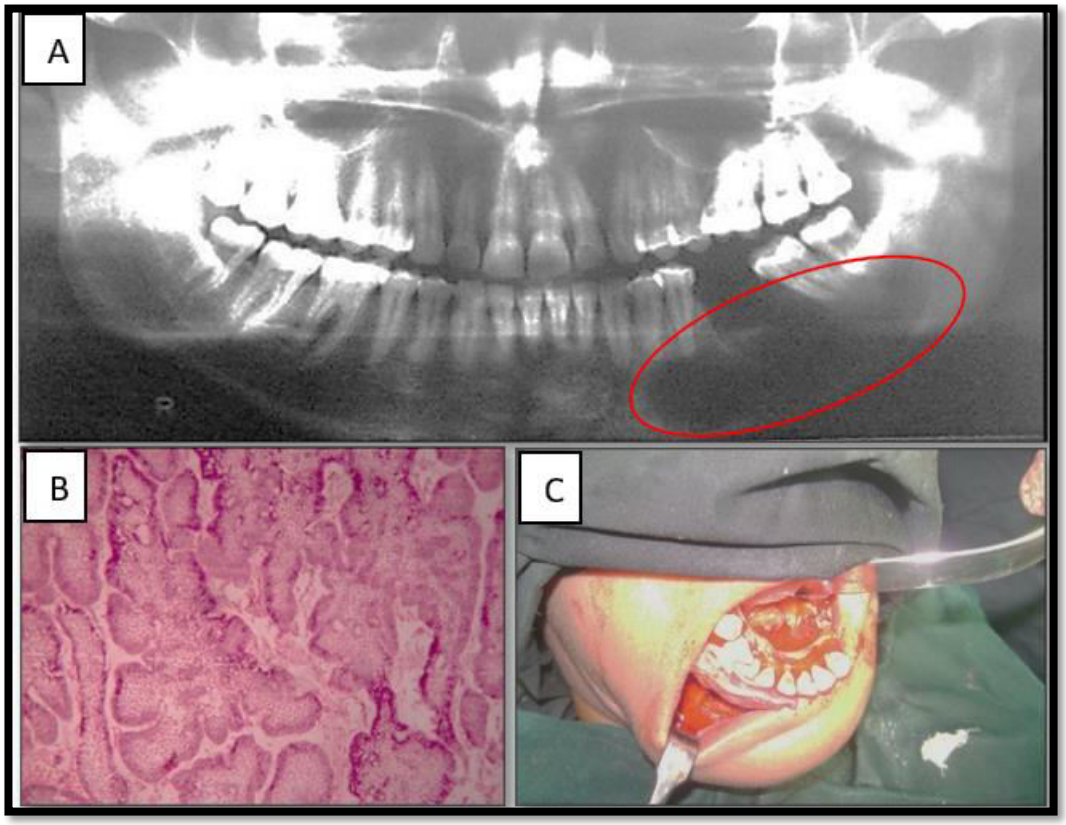

Figure 1. A) Single unilocular radiolucency
B) Follicular Ameloblastoma
C) Enucleation with curettage and chemical cauterization

Case 2:

A 35yr old female presented with a chief complaint of swelling in the lower front region of the jaw for 5 months. Intra oral examination revealed single diffused swelling of 5×3 cms in size situated in the symphysis region, extending from the left lower first premolar to right lower first premolar and supero-inferiorly from gingival margin to the depth of the vestibule with deranged occlusion anteriorly. Radiograph revealed multilocular radiopaque and radiolucent appearance extending from left first premolar to right second premolar with displaced root position (Figure 2A). Incisional biopsy was performed and diagnosed as “Plexiform Ameloblastoma” (Figure 2B).

Under general anaesthesia, peripheral osteotomy was a choice of treatment through intra oral approach (Figure 2C). Sublabial vestibular incision given from left lower second premolar to right lower second premolar, mucoperiosteal flap reflected. Extraction of lower second premolars done bilaterally. Bilateral vertical osteotomy cuts given from extraction socketsjoining the horizontal cut, bone removed involving the tumor. Sharp edges trimmed, Irrigation done with betadine, hydrogen peroxide and saline. Flaps repositioned and suturing done. Follow up done and no recurrence till date.

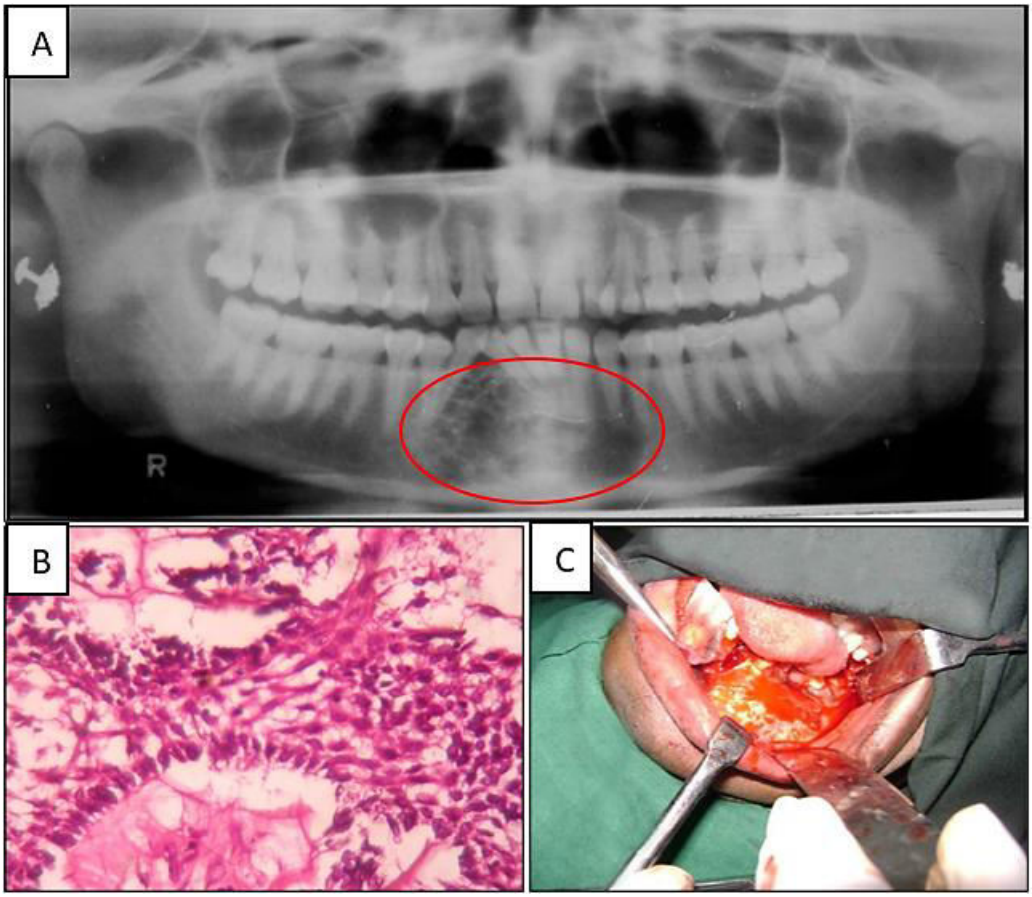

Figure 2. A) Multilocular radiopaque and radiolucent
B) Plexiform Ameloblastoma **C)** Peripheral Osteotomy

Case 3:

A 31yr old male was presented with a history of swelling in lower jaw for 3 yrs. Extra oral examination revealed an irregular swelling of around 12 × 6 cms in size. Intra oral examination revealed an irregular swelling extending from right lower second premolar to left lower second molar crossing the midline. Swelling was around 12 × 4 cms in size firm in consistency.

Radiograph revealed ill-defined multilocular radiopaque and radiolucent appearance extending from right lower first molar to left lower second molar crossing the midline (Figure 3A). Incisional biopsy was performed and diagnosed as "Acanthomatous Ameloblastoma" (Figure 3B).

Under general anaesthesia Segmental resection was a choice of treatment with an extra oral approach (Figure 3C). An extra oral Apron incision was given 2 cms below the lower border of the mandible. Mucoperiosteum along the muscle attachments were separated from left angle to right angle of the mandible. Resection of the bone was done from left

angle to right angle of the mandible including the tumor mass using gigli saw. All the bleeders were cauterized. A stainless-steel reconstruction plate was placed from left angle to right angle of the mandible using 2.5 × 8mm screws 6 in number. The deep skin layers were closed in layers using 3-0
catgut and superficial skin layer closed using 3-0 vicryl. Intra oral mucosa closed with 3-0 vicryl. Follow up done and no recurrence till date.

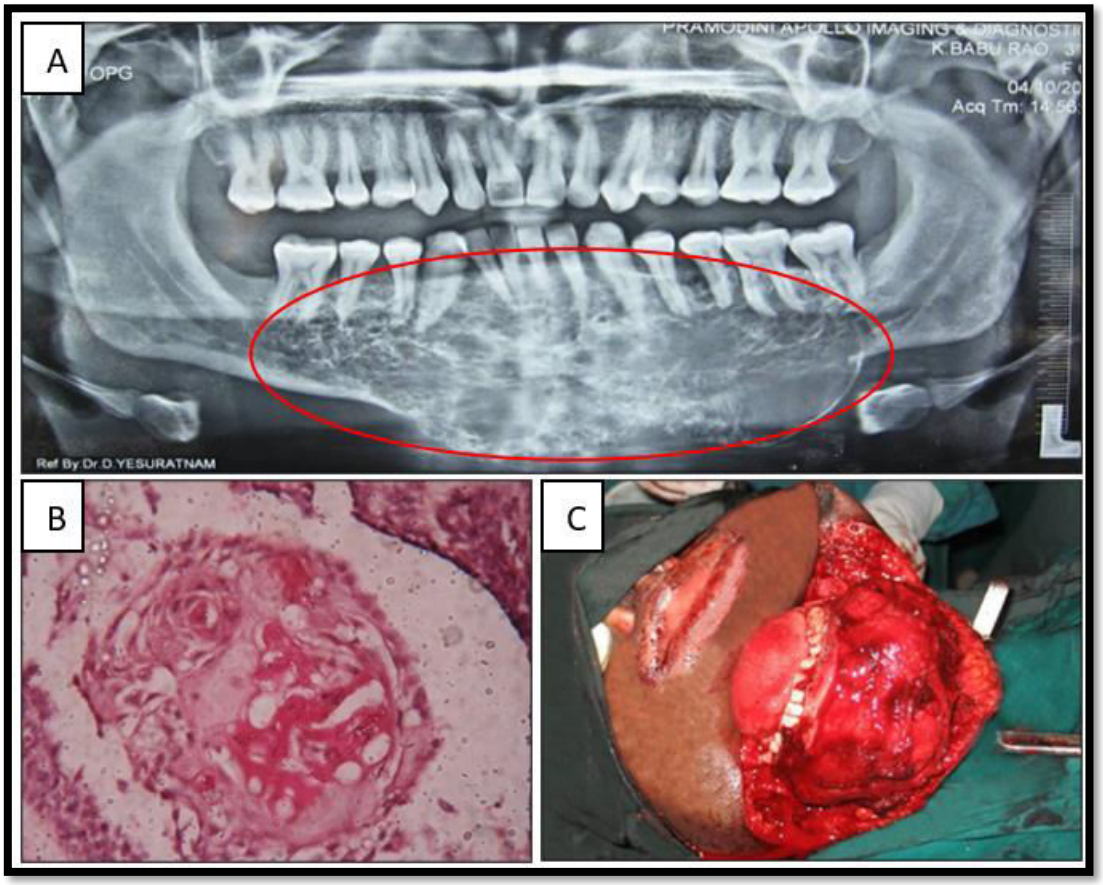

Figure 3. A) Multilocular radiopaque and radiolucent
B) Acanthomatous Ameloblastoma **C)** Segmental resection

Case 4:

A 28yr old female presented with a chief complaint of swelling in the left lower region of the mandible with a history of 8 months.

Extra oral examination revealed an irregular and diffused swelling of around 7 × 5cms in size extending antero-posteriorly from corner of the mouth to posterior border of the mandible and supero-inferiorly from ala tragus line to lower border of the mandible. Intra oral examination revealed vestibular obliteration and expansion of both buccal and lingual cortical plates.

Radiograph revealed well defined unilocular radiolucency with sclerotic border in the left mandible (Figure 4A). Resorption of the distal root of lower left first molar and

displacement of the second molar to the inferior border of mandible. Incisional biopsy was performed and diagnosed as "Follicular & Plexiform Ameloblastoma" (Figure 4B).

Under general anaesthesia, segmental resection with an extra oral approach and reconstruction with iliac crest bone graft with stainless steel reconstruction plate was a choice of treatment. Incision was given at the Iliac crest region. Deep dissection was carried out through skin, subcutaneous tissue and iliac bone was identified. 6cms iliac bone was obtained with the help of chisel and mallet, micromotor and bur. Sutures were placed in layers with 3-0 vicryl and 3-0 BBS. Local anaesthetic infiltration was given along the proposed line of incision in the left lower border of the mandible. Risdon's submandibular incision was given on left side with 15no. BP blade (Figure 4C). Deep dissection carried out; resection of mandible done from distal aspect of lower left canine to anterior border of ramus along with coronoid process with gigli saw. Later all the mucoperiosteum and muscle attachments were stripped off. All the bleeds were cauterized. The surgical site was thoroughly irrigated with betadine and normal saline. Iliac crest bone graft reconstruction done using stainless steel plate from lower right lateral incisor to posterior border of the ramus using 8mm screws. Intraoral mucosa sutured with 3-0 vicryl. The deep skin layers were closed using 3-0 vicryl and superficial skin layer closed using 3-0 silk. Follow up done and no recurrence till date.

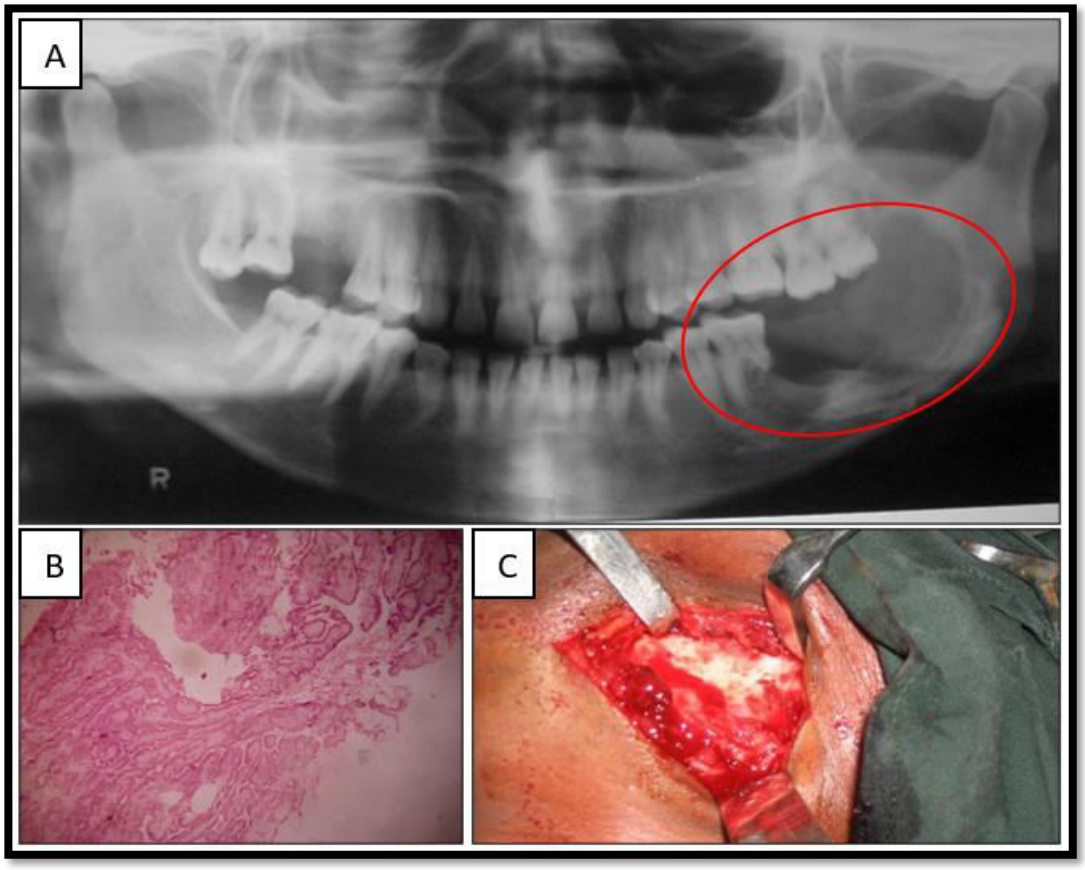

Figure 4. A) Unilocular radiolucency with sclerotic border
B) Follicular & Plexiform Ameloblastoma **C)** Risdon's submandibular

Results:

A total of eleven cases (four male, seven female), in which four were unicystic and seven were multicystic ameloblastoma treated with various treatment modalities. Out of 4 cases of unicystic ameloblastoma, one case was treated by peripheral osteotomy, two were treated by enucleation and curettage and one by segmental resection.

Out of 7 cases of multicystic ameloblastoma, one case was treated by enucleation and curettage, one by peripheral osteotomy, two were treated by segmental resection and three by hemi-mandibulectomy (Table-1). All these cases of different types of ameloblastomas treated by various modalities had no recurrence till date. However further evaluation, at least for five years must be done.

Type of Ameloblastoma	Treatment modalities	Number of cases (n=11)	Recurrence
Unicystic ameloblastoma	Peripheral Osteotomy	1	No
	Enucleation and Curettage	2	No
	Segmental Resection	1	No
Multicystic ameloblastoma	Enucleation and Curettage	1	No
	Peripheral Osteotomy	1	No
	Segmental Resection	2	No
	Hemi-Mandibulectomy	3	No

Table 1: Different types of ameloblastomas treated by various modalities and there have been no recurrences till date.

Discussion:

Robinson 1937 defined Ameloblastoma as a true epithelial odontogenic tumor usually, unicentric, nonfunctional, intermittent in growth. It originates in the mandible in 80% of cases and 75% of these cases have occurred in the molar ramus area. Ameloblastoma is diagnosed by thorough complete history, physical examination, radiological examination and histopathological study. Differential diagnosis of ameloblastoma includes Odontogenic keratocyst, Aneurysmal bone cyst, Hemangioma, Central giant cell granuloma, Adeno ameloblastoma, Calcifying epithelial odontogenic tumor, Hyperparathyroidism and Fibrous dysplasia[1].

"All benign tumors are not completely innocent just as all malignant tumors are not completely evil". Based on origin they are classified into Ectodermal, Mesodermal and Endodermal tumors[2].

The various treatment modalities of ameloblastoma include Curettage, Enucleation, Marginal resection, Cauterization, Cryotherapy, Radiotherapy, Segmental resection and Hemi-section. The selection of treatment for an individual ameloblastoma depends to a large extent on its clinical type that is intra-osseous solid multicystic ameloblastoma, Unicystic ameloblastoma or Peripheral ameloblastoma. Other factors of importance are its location in the jaws and its size, the age of the patient and patient's availability for follow-up examination.

The goal of surgical treatment of ameloblastomas is to minimize recurrences and restore good function and aesthetics with minimum morbidity in the donor area. The currently recommended surgery for classic ameloblastoma (solid/multicystic type) is complete en bloc resection (radical surgery) with an adequate margin of safety, which is classified as segmental or marginal osteotomy for the mandible and partial or total maxillectomy for the maxilla. Due to the high recurrence rate after conservative surgery, particularly for solid/multicystic ameloblastomas, a wide resection with a 1 to 1.5 cm bony margin is recommended[3].

when the lesion confined within the bone enucleation or marginal resection often can be successful. However, when there is a bony perforation full thickness resection should be done. Because of late recurrence of some lesions long term follow-up is indicated in all patients[4].

"If the person is free from disease for 5 years postoperatively, he is considered as relieved from the disease". In the present study though the patients are disease free for 2 years postoperatively, they have to be kept under observation for another 3 years in accordance with Shigeru Ueno[5].

Incases of unicystic ameloblastoma with enucleation followed by Carnoy's solution and stated that carnoy's solution is probably able to fix residual ameloblastoma tissue often enucleation of unicystic ameloblastoma and distinguished the risk of rate of recurrence[6].

Recurrence is attributed to the infiltration of tumor cells into the cancellous bone beyond the periphery of radiographic margins[7]. Immediate or delayed bone reconstruction and dental rehabilitation have to be ensured to help with speech and swallowing and improve patient outcomes[8].

Radiotherapy in advanced, inoperable ameloblastoma of jaw is a definite therapeutic option. It warrants that advanced, inoperable ameloblastoma be subjected to definitive megavoltage radiation therapy[9].

Newer technologies for radiotherapy such as image-guided radiotherapy, stereotactic radiotherapy, intensity-modulated radiotherapy, and proton beam therapy may be beneficial for patients with extensive maxillary ameloblastomas extending to the skull base to effectively treat the tumor without significant dose to the CNS and visual apparatus[10].

It is to investigate the presence of EGFR in ameloblastoma in order to consider using newly developed anti- EGFR therapeutic agents in cases of unresectable tumors. Currently extensive surgery is the most acceptable treatment modality[11].
Primary unicystic ameloblastomas were histochemically stained with PCNA and Ki67 antisera. Cellular proliferative activity varied within ameloblastoma types. The unicystic ameloblastoma showed statistically, significantly higher PCNA and Ki67 labeling indices than solid and multicystic variants[12].

Recently, with the elucidation of molecular markers of ameloblastoma, there have been attempts for the treatment of ameloblastoma with molecular targeted therapy. These tumors have highly recurrent somatic mutations in the signalling pathways of mitogen-activated protein kinase (MAPK) and sonic hedgehog (SHH), which are known to be activated during tooth development. Within the MAPK pathway, the BRAFV600E mutation is found in 57% of ameloblastomas, while within the SHH pathway, smoothened (SMO) mutations have been identified in 24% of ameloblastomas[13].

The upfront treatment with BRAF inhibitors resulting in substantial tumor regression has enabled non-mutilating complete surgical removal, ad integrum bone regeneration, and organ preservation. Most patients show a marked radiologic and clinical response to medical treatment, enabling successful conservative surgery. Face preservation therapy could be achieved in pediatric patients presenting with BRAF V600E mutated ameloblastoma[14].

Treatment and prognosis, including cure rates, are all dependent upon the variant of the ameloblastoma, the solid and multicystic variant is believed to be the most aggressive of the three variants, with relatively less aggressive behaviour associated with the unicystic variants[15].

Conclusion:
All these cases of different types of ameloblastomas treated by various modalities, there have been no recurrences till date. However, further evaluation needed.

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