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Dr. Kanchan Shah
MDS in Oral and Maxillofacial
Surgery Professor and Head of
department, Department of Oral
and Maxillofacial Surgery,
Government Dental College and
Hospital, Ghati Medical Campus,
Chh. Sambhaji Nagar,
Maharashtra, India

Dr. Anjali A Meshram
Pursuing MDS in Oral and
Maxillofacial Surgery Lecturer
Department of Oral and
Maxillofacial Surgery, Government
Dental College and Hospital, Ghati
Medical Campus, Chh. Sambhaji
Nagar, Maharashtra, India

Dr. Jayant Landge
MDS in Oral and Maxillofacial
Surgery Associate Professor,
Department of Oral and
Maxillofacial Surgery, Government
Dental College and Hospital, Ghati
Medical Campus,
Chh. Sambhaji Nagar,
Maharashtra, India

Dr. Manisha Ambhore A
MDS in Oral and Maxillofacial
Surgery, Department of Oral and
Maxillofacial Surgery, Government
Dental College and
Hospital, Ghati Medical Campus,
Chh. Sambhaji Nagar,
Maharashtra, India

Dr. Anjali Meshram
Department of Oral and
Maxillofacial Surgery, Government
Dental College and Hospital, Ghati
Medical Campus, Chh. Sambhaji
Nagar, Maharashtra, India

Corresponding Author:
Dr. Anjali Meshram
Department of Oral and
Maxillofacial Surgery, Government
Dental College and Hospital, Ghati
Medical Campus, Chh. Sambhaji
Nagar, Maharashtra, India

Ameloblastoma Revisited: Classification updates, treatment modalities, and outcomes

**Kanchan Shah, Anjali A Meshram, Jayant Landge, Manisha Ambhore A
and Anjali Meshram**

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Abstract

Background: Ameloblastoma is the most common odontogenic tumor arising from odontogenic epithelium, accounting for 19.3-41.5% of all odontogenic tumors. Although it generally exhibits slow growth, certain variants are locally aggressive with high recurrence potential. The tumor shows higher prevalence in Asian and African populations and most frequently involves the posterior mandible.

Objective: To evaluate the clinical presentation, histopathological subtypes, surgical management, and treatment outcomes of ameloblastoma.

Methods: Literature on ameloblastoma was reviewed, emphasizing WHO classification changes, epidemiology, imaging features, histopathology, and therapeutic approaches. Variants including conventional, unicystic, peripheral, desmoplastic, and metastasizing types were discussed, along with their age, site distribution, and growth characteristics. Diagnostic modalities such as CT, MRI, OPG, and histopathology were highlighted.

Results: Clinical presentation most often includes slow-growing, painless mandibular swelling, with radiographic appearances ranging from unilocular to multilocular radiolucencies. Histologically, follicular and plexiform patterns predominate, with multiple described variants. Conservative management is associated with recurrence rates up to 40%, particularly in solid/multicystic forms. Radical resection with adequate bony margins remains the gold standard, while unicystic and peripheral lesions may be amenable to conservative surgery. Reconstruction typically involves vascularized free bone grafts. Adjuvant radiotherapy and chemotherapy are reserved for aggressive, recurrent, or metastatic disease.

Conclusion: Optimal management of ameloblastoma requires accurate diagnosis, appropriate selection of surgical modality, and long-term follow-up to minimize recurrence while preserving function and aesthetics. A thorough understanding of its clinicopathological spectrum is essential for preventing local and systemic complications.

Keywords: Ameloblastoma revisited, systemic complications, clinicopathological, adjuvant radiotherapy and chemotherapy

Introduction

Odontogenic tumors develop slowly and are generally non-aggressive, while some tumors exhibit aggressive behavior. Ameloblastoma is the most frequent odontogenic tumor that arises from the odontogenic epithelium. It accounts for 19.3-41.5% of all odontogenic tumors [1, 2]. Most typically seen in the second and fourth decades of life. Some authors claim no gender predilection; however, several studies show female predilection [5]. The frequency of ameloblastoma was significantly higher in Asian and African populations compared to European and American hospitals [7].

In the 2005 classification, ameloblastomas were categorized into four subtypes: solid/multicystic, unicystic, extrasosseous/peripheral, and desmoplastic. The 2017 classification simplified this, narrowing it down to conventional ameloblastoma, unicystic ameloblastoma, and extrasosseous/peripheral types and metastasizing ameloblastoma [6].

Clinical Presentation

Most cases of ameloblastoma present as slow-growing, painless swelling of the maxilla or mandible, leading to facial disfigurement.

Nearly 80% of ameloblastomas arise in the posterior mandible [5]. Maxillary ameloblastoma also mostly occurs in the posterior molar region. The desmoplastic variant of ameloblastoma often occurs in the anterior mandible or maxilla. The pediatric age range is where the unicystic form of ameloblastoma most frequently manifests. Because of its frequent dentigerous relationship with an unerupted tooth, it may originate from a dental follicle or from a pre-existing dentigerous cyst. Accordingly, unicystic ameloblastoma most commonly occurs in the third molar region [6]. In adults, the peripheral form of ameloblastoma typically manifests as a gradual, painless gingival enlargement. The mean age of occurrence of metastasizing ameloblastoma is 43±16 years with a slight male predilection [7, 8]. Solid multicystic-type ameloblastoma has the highest predicted growth rate, while peripheral ameloblastoma has the lowest [8].

Diagnosis

Diagnosis of ameloblastoma requires imaging [usually a CT scan] as well as a biopsy. A CT SCAN most commonly shows a well-defined, UNI- or multilocular radiolucent expansile lesion. A CT SCAN also provides details on cortical destruction or soft tissue extension.

Orthopantomograms (OPGs) and plain film frequently show ameloblastoma originating within bone, although the degree of soft tissue or bone invasion is frequently not precisely recorded. The more common multilocular ameloblastoma shows up on X-rays as the recognizable "soap bubble". An MRI can better describe any extension to the orbit, paranasal sinuses, or base of the skull than a CT scan, which is less helpful for ameloblastoma originating from the maxilla. Additionally, because desmoplastic ameloblastoma has soft tissue borders that are not clearly defined and might be mistaken for a fibro-osseous lesion, MRI is the preferred imaging modality for this condition.

The unicystic ameloblastoma appears as a thinly corticated unilocular radiolucency on imaging modalities like CT or MRI. This radiolucency is typically associated with an unerupted tooth and frequently causes the jaw to enlarge.

A positron emission scan is typically the preferred method for detecting distant metastases in cases of metastasizing ameloblastoma.

Both clinically and radiologically, unicystic ameloblastoma resembles an odontogenic cyst; hence, a histopathologic investigation is typically required to make the diagnosis. Only by biopsy can ameloblastoma be definitively diagnosed because none of the radiological signs are pathognomonic. Histopathology aids in distinguishing ameloblastoma from myeloma, sarcoma, giant cell tumor, osteomyelitis, ossifying fibroma, and cystic fibrous dysplasia. In malignant ameloblastoma cases, preoperative staging is also determined by biopsy. Peripheral ameloblastoma can be easily biopsied since it is not covered by bone.

Histopathological Findings

Ameloblastoma, when viewed histologically, is composed of two distinct cell types: the peripheral 'basal cells' that resemble ameloblasts and the central suprabasal 'epithelial cells' that are similar to stellate reticulum. The basal cells exhibit hyperchromasia, have a columnar shape with a palisaded arrangement, possess vacuolated cytoplasm, and display nuclei that are distanced from the basement membrane (known as reversal of polarity). The epithelial cells appear

relatively bland cytologically and contain few mitotic figures, which correlates with their gradual growth rate. In classical ameloblastoma, these basal and epithelial cells are organized into two distinct arrangements: follicular and plexiform. In the follicular arrangement, the epithelial cells form islands or follicles that are enveloped by connective tissue in contrast, the plexiform arrangement features the epithelial cells organized in a crisscrossing network surrounding the connective tissue. Various other histological variants of multicystic ameloblastoma have been described, such as desmoplastic, acanthomatous, basal cell, granular cell, and keratopapillary ameloblastoma. The unicystic ameloblastoma consists of two histological types: luminal and mural. In the luminal type, the cyst wall presents as a consistent sac lined with ameloblastoma epithelium. Occasionally, thickened regions formed by ameloblastoma cells may protrude into the lumen. In the mural type of ameloblastoma, tumor islands invade the fibrous wall in a manner similar to that of conventional ameloblastoma.

Treatment

The goal of surgical treatment of ameloblastomas is to minimize recurrences and restore good function and aesthetics with minimum morbidity in the donor area. Conservative surgery has also been tried, which includes marsupialization, enucleation, curettage, enucleation combined with Carnoy's solution, enucleation combined with curettage, and curettage combined with cryotherapy [9]. However, these conservative approaches lead to a high recurrence rate, which has been reported to be 40% in a recent meta-analysis [9]. 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. Radical surgery leads to aesthetic deformities, functional impairments, and psychological distress. For mandibular reconstruction, vascularized free bone grafts (from the fibula, ilium, scapula, or radius) are the standard; the flap of choice is the fibular free flap, which has the added advantage of reconstructing long segment mandibular defects. He extraosseous/peripheral ameloblastoma is mostly treated with wide local excision, and a recurrence rate of 9%-20% following treatment has been reported [10]. For unicystic ameloblastomas, both the radical as well as the conservative surgical approach, including excision, marsupialization, chemical electrocautery, curettage, radiation therapy, or combined surgery and radiation, may be employed [10,11]. However, there remains an ongoing discussion regarding the best management approach that can achieve a cure while minimizing unnecessary impact on appearance and function. Therefore, it is crucial to have a comprehensive understanding of the clinicopathological characteristics of this tumor to prevent local complications due to recurrence and the risk of malignant transformation or metastasis arising from insufficiently treated cases.

This study aimed to analyze the clinical presentation, surgical treatment, and outcomes in patients with different variants of ameloblastoma.

Benign epithelial odontogenic tumours	Frequency	Histological variants
Ameloblatoma	91%	Follicular, Plexiform, Acanthomatous, Granular Cell, Basal Cell, Keratopapillary, Desmoplastic
Ameloblastoma, unicystic type	6%	Luminal, Mural
Ameloblatoma, extraosseous/peripheral type	2%	
Metastasizing ameloblastoma	1%	

Methods

This retrospective study was conducted on patients who underwent treatment for ameloblastoma in the Department of Maxillofacial Surgery between January 2021 and May 2025. The study aimed to assess surgical outcomes, recurrence rates, and any associated complications.

Patients treated for ameloblastoma during this period were recalled, and all available cases were reviewed on an outpatient basis. Data including age, gender, tumor location, preoperative diagnosis, histopathological subtype, and type of surgical intervention were retrieved from patient records. Routine follow-up evaluations were performed, comprising

radiological investigations (orthopantomogram [OPG], paranasal sinus [PNS] view, and computed tomography [CT] scans, when indicated) and comprehensive clinical examinations. Clinical assessments focused on signs and symptoms such as pain, swelling, presence of a draining sinus, fracture or exposure of the reconstruction plate.

Additional analysis was carried out to evaluate the age, gender tumor's site, surgical techniques used, and the incidence of recurrence.

Preoperative clinical, radiograph intraoperative and postoperative photograph are mentioned in Figure 1, Figure 2 and Figure 3.

Sr. No	Age	Gender	Site	Clinical features	Treatment	Histopathological variant	Follow up period	Recurrence
1	24 yr.	M	Posterior mandible	Swelling over the angle of mandible	Enucleation followed by chemical cauterization	Follicular ameloblastoma	2 year	-
2	17 yr.	F	Posterior mandible	Swelling over the mandible and obliteration of buccal mucosa	Enucleation followed by chemical cauterization	Follicular ameloblastoma	1.5 yr.	-
3	16 yr.	F	Posterior mandible	No extraoral findings	Enucleation followed by chemical cauterization	<i>Haemangiomas</i> ameloblastoma	1.5 yr.	-
4	43 yr.	F	Posterior mandible	No extraoral findings	Enblock resection	Plexiform ameloblastoma	3 yr.	-
5	52 yr.	F	Anterior mandible	Swelling over the anterior mandible and obliteration of labial mucosa	Marginal resection	Desmoplastic ameloblastoma	6 months	-
6	30 yr.	F	Posterior mandible	Swelling over the mandible	Segmental resection with reconstruction with reconstruction plate	Follicular ameloblastoma	1yr	-
7	27 yr.	F	Posterior mandible	Swelling over the left side of mandible	Hemimandibulectomy with reconstruction	Follicular ameloblastoma	1 yr.	-
8	43 yr.	M	Posterior mandible	Swelling over the right side of mandible	Segmental resection with reconstruction with reconstruction plate	Follicular ameloblastoma	2.5 yr.	-
9	37yr.	M	Anterior mandible	Asymotamatic	Segmental resection with reconstruction	Follicular ameloblastoma	3 yrs.	-
10	36 yr.	F	Posterior mandible	Asymotamatic	Segmental resection with reconstruction	Follicular ameloblastoma	3 yrs.	Hard ware failure
11	17 yr.	F	Posterior mandible	Swelling over the left side of mandible	Enucleation followed by chemical cauterization	Plexiform ameloblastoma	2 yrs.	-
12	30 yr.	F	Posterior mandible	Left	Hemimandibulectomy with reconstruction	Plexiform ameloblastoma	2 yrs.	-
13	30 yr.	M	Posterior mandible	Left	Enucleation followed by chemical cauterization	Unicystic Ameloblastma	1.5 yr.	-
14	22 yr.	M	Posterior mandible	Left	Hemimandibulectomy with reconstruction	Acanthomatous ameloblastoma	1.5 yr.	-

15	47 yr.	F	Posterior mandible	Left	Enblock resection	Follicular ameloblatoma	2 yr.
16	25	F	Posterior mandible	Left	Enucleation followed by chemical cauterization	Unicystic ameloblatoma	2.5 yr.
17	65	M	Posterior mandible	Right	Enucleation followed by Chemical cauterization	Follicular ameloblatoma	2 yr.
18	40	F	Posterior mandible	Left	Enucleation followed by chemical cauterization	Follicular ameloblatoma	2 yr.
19	24	F	Posterior mandible	Left	Segmental resection	Mural ameloblastoma	2.5 yr.
20	30	M	Posterior mandible	Left	Enucleation followed by chemical cauterization	Unicystic ameloblastoma	6 Months
21	4	M	Anterior mandible	Left	Enucleation followed by chemical cauterization	Ameloblastic Fibroma	5 month

Results

A total of 21 ameloblastoma patients records were analyzed, operated and followed up for ranging from 6 months to 3 yrs.

follow up. The results are analyzed and summarised through graphs. The patients age varies from 4 yrs. to 65 yrs. Mean age is about 30.43 yrs.

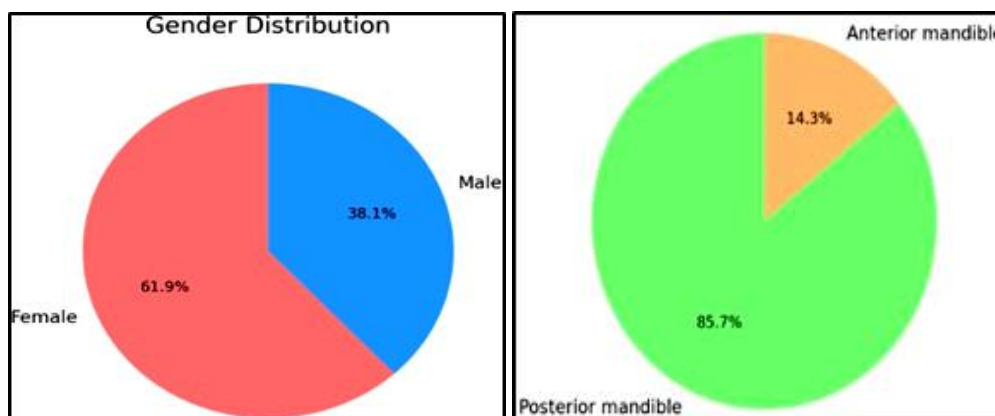


Fig 1: The graphical representation showing the gender and site distribution for your ameloblastoma cases

On analysis of radiographic features: Multilocular (78.4%) and unilocular (32.2%). We found that impacted teeth involved were common with mandibular third molar teeth.

Histopathological Variant Distribution

Variant	Number of Cases	Percentage (%)
Follicular ameloblastoma	9	42.9%
Plexiform ameloblastoma	3	14.3%
Unicystic ameloblastoma	3	14.3%
Desmoplastic ameloblastoma	1	4.8%
Haemangiomas ameloblastoma	1	4.8%
Acanthomatous ameloblastoma	1	4.8%
Mural ameloblastoma	1	4.8%
Ameloblastic fibroma	1	4.8%

The most common variant was Follicular ameloblastoma, comprising nearly 43% of all cases.

Treatment Plan	No of Cases	Percentage (%)
Enucleation + chemical cauterization	11	52.4%
Segmental resection + reconstruction plate	3	14.3%
Hemimandibulectomy + reconstruction	3	14.3%
Enblock resection	2	9.5%
Marginal resection	1	4.8%
Segmental resection (unspecified reconstruction)	1	4.8%

Final Treatment Plan Summary (N=21)

The most frequently used treatment was Enucleation with chemical cauterization used in more than half of the cases.

- Surgical resection procedures (segmental, hemimandibulectomy, enblock) were used in ~ 43% of patients, likely indicating more aggressive or extensive lesions.

Recurrence Status	Number of Cases	Percentage (%)
No recurrence ("-")	20	95.2%
Complication (hardware failure)	1	4.8%
Total Recurrence Events	0	0%

No true recurrence was observed in any of the cases. This suggests that the treatments employed particularly surgical resection and enucleation with chemical cauterization were effective in preventing recurrence over the recorded follow-up periods (up to 3 years).

Discussion

Ameloblastoma of the mandible is a benign, but locally aggressive, tumor that develops in the jawbone, specifically the lower jaw (mandible). It originates from cells that are involved in tooth enamel formation.

Robinson in 1937 described ameloblastoma as a benign tumor that is usually “unicentric, nonfunctional, intermittent in growth, anatomically benign and clinically persistent”.

In our study, patient's age ranged from 4 to 65 years with a mean value of 30.43 ± 3 years which is in corroboration with Ismail BR *et al.* [6] stating that the mean age of 29.5 years. According to Reichert *et al.* Men and women are equally affected. Women are 4 years younger than men when ameloblastomas first occur, and the tumours appear to be larger in females [3]. In our study there is female predominance. As far as side distribution is concerned left side was affected more than the right side even Meshram M, *et al.* [13]. Noted the same prevalence. In our study, almost 90% cases occur in angle and ramus region (out of 36 patients), 1 case occur in anterior mandible and 5 cases occur in body region of mandible. Other studies also suggested that the incidence of ameloblastoma higher in the mandibular posterior region (ramus region) [10, 6, 11, 12]. Reichert and Philipsen [3] observed that the incisor region and mandibular ramus were more frequently involved in females, whereas the premolar region and maxillary sinus were predominantly affected in males. Conversely, the molar region demonstrated a comparable distribution between both sexes. Our study suggests that 73% cases are present with multilocular radiolucency and rest unilocular radiolucency if the tumour occur involving the ramus region mostly associated with impacted tooth. Characteristic Soap bubble appearance and honey Comb Appearance seen in multilocular cases. There is a pronounced tendency for ameloblastomas to cause extensive root resorption, either blunting of root apex/knife-edge root resorption or multiplanar or sharp root edges [13, 14].

Conventional ameloblastoma (67.35% was the most common type of ameloblastoma documented in our study. This results are in consistent with Ramakant *et al.* [14]. Other authors have also started a similar pattern which ranges from 80 to 92%, whereas unicystic ameloblastoma ranges from 4.6% to 20% [12, 6, 14]. Since its initial description in 1977, unicystic ameloblastoma has been regarded as a unique kind. It can be distinguished by its early onset age, unilocular radiographic appearance, macroscopic cystic appearance, and above all better response to conservative treatment. Histologic characteristics allow unicystic ameloblastoma to be divided into luminal, intraluminal, and mural subtypes, each of which has implications for prognosis and treatment. The majority type of histological pattern in the conventional group observed was follicular ameloblastoma (55.2%). It was followed by plexiform (21.3%), which is in corroboration with other studies ranging from 33 to 44.9% [14, 15]. The other histopathological variant reported are haemangiomas

ameloblatoma, desmoplastic ameloblastoma and ameloblastic Fibroma. Hemangiomatous ameloblastoma (2%), an uncommon variant of ameloblastoma, shares clinical characteristics with plexiform ameloblastoma. Nevertheless, radiographic examination reveals a well-defined mixed radiolucent multilocular lesion with a few septae arranged like a tennis racket, leading to a differential diagnosis between central haemangioma and odontogenic myxoma. The specimen showed plexiform ameloblastoma upon histological analysis, with a notable vascular component in the form of anastomosing cords and an odontogenic epithelial sheath in a loosely structured stroma of vascular connective tissue. Because the vascular component is made up of blood-filled, differently sized compartments that are lined by epithelial cells, its diagnosis is confirmed. Surgical removal of tumour is the standard treatment for ameloblastoma. But the extent of the resection has always been controversial, ranging from conservative to radical approach [9, 10, 15]. Selecting the most appropriate therapy is a crucial step that must prioritize the removal of the lesion while considering the potential morbidity associated with the chosen method, as well as its impact on the patient's life and rehabilitation. Various options are available, from curettage to extensive bone resections, with reconstruction able to be performed using plates and pins [19]. Desmoplastic ameloblastoma as it shows higher rate of recurrence, radical treatment is preferred in our case managed by segmental resection followed by chemical cauterization. Whereas enucleation provided a recurrence rate of 21.1%, resection reduced this rate remarkably to 3.1% [24].

Conservative treatment comprises of enucleation, physiochemical treatment (cryotherapy or Carnoy's solution), Marsupialization and decompression and cryosurgery. Radical treatment includes marginal resection, segmental resection, and hemi mandibulectomy with the reconstruction of the jaw using reconstruction plate or bone grafts. The aesthetic and functional rehabilitation of a segmental defect in the mandible is a challenge to be overcome by a multiplicity of combined procedures.

Treatment according to age

In patients younger than 20 yrs. of age, conservative approach is more preferable. In 2010 protocol given on treatment on ameloblastoma it was suggested that conservative surgeries would interfere less in facial developing. The idea regarding the necessity of steering clear of extensive procedures was emphasized, as these could jeopardize facial structures crucial for the development of the skeleton and teeth. It was advised that more aggressive procedures be conducted only when patients showed signs of recurrence. The results are in corroboration with [18-20]. The management of solid/multicystic ameloblastomas should initially evaluate anatomical barriers, including cortical bone, periosteum, muscles, and mucous membranes that may have been compromised. If these tissues are involved, resection will be necessary. Furthermore, the authors recommend that these resections should include a bone margin of no less than 1.5 cm separating the lesion from healthy tissue [20, 21].

Treatment depending on the anatomical site

Maxillary ameloblastomas are more aggressive and have more unfavorable prognosis in addition to the greater difficulty in treating them. Unlike compact bones that compose the mandible, the maxilla has a much thinner bone tissue, which facilitates faster advancement of the lesion. In that case, it is possible that the lesion reaches the orbital sinus

area and the cranial base. This way, a more radical approach is necessary when choosing the initial surgery. The choice of radical procedures is almost certain, because the spongy characteristic of maxillary bone facilitates the spread of the lesion.

Crawley and Levin [18] proposed that the initial management of ameloblastoma should involve conservative treatment. This recommendation stems from the fact that tumor cells only invade the medullary bone while causing minimal erosion of the compact bone. Consequently, it is advisable to excise only the medullary bone. The medial and lateral cortical plates, as well as the inferior border of the mandible, should be preserved to the greatest extent possible. In their research, they conservatively treated four cases. Upon follow-up of these patients, ranging from 21 months to seven years after the initial treatment, they noted significant bone regeneration. The management protocol proposed in 2010 recommends that unicystic ameloblastomas should initially be approached with marsupialization, followed by a careful radiological assessment to determine whether the lesion is decreasing. Otherwise, enucleation should be performed in the case of solid/multicystic ameloblastomas. On the other hand, in case of recurrence, the protocol indicates a radical treatment with security margins of 1.5 to 2 cm. Post-operative follow-up with annual assessments should be performed during the first five years, followed by biannual assessments during the next ten years. Peripheral ameloblastoma is another entity successfully treatable with conservative therapy. It is most frequently present in the gingival tissues and the conservative approach with narrow margins of unaffected tissue is treatment of choice. According to several authors, smaller and unicystic lesions can be treated with enucleation and curettage, which can also be associated with other ancillary procedures, such as peripheral osteotomy, application of Carnoy's solution, and cryotherapy. Carnoy's solution is a fixative initially proposed by Stoelinga and Bronkhorst. It has ability to penetrate cancellous bone to a depth of 15 mm, so it is ideal for application after enucleation.

It was concluded that conservative treatment was preferable due to better postoperative quality of life, despite a slightly higher recurrence rate. Huang *et al.* [45] also claim that radical treatment should be reserved for recurrent and more aggressive types of ameloblastoma, with important statement that recurrence is probably not a major consideration for pediatric patients and should not be considered as equivalent to failure. The main identified mutations are found in MAPK and SHH signaling pathways. These include BRAF, RAS and FGFR2 genes from MAPK pathway and SMO gene from SHH signaling pathway. Drugs approved by US Food and Drug Administration which are predominantly used for treatment of metastasizing, unresectable or recurrent ameloblastoma are vemurafenib, dabrafenib and trametinib. Both authors [22] recommended single agent therapy over dual therapy in ameloblastoma patients. However, adverse reaction to vemurafenib including arthralgia, nausea and rash has been reported after 12 months of therapy [63]. Adverse reaction to vemurafenib including arthralgia, nausea and rash has been reported after 12 months of therapy. Adverse effects can be controlled by decreasing the dosage without adversely affecting outcomes of therapy. It has been found that neoadjuvant treatment with dabrafenib significantly reduces size of the primary tumor which could reduce the extent of the subsequent surgery. In our research, we handle cases involving individuals aged 20 to 30 years with enucleation followed by chemical cauterization, as this approach does not

affect growth and facial development. For larger lesions, based on their size and location, we pursue more extensive management strategies such as segmental resection, en bloc resection, and hemimandibulectomy, followed by reconstruction using titanium plates.

Conclusion

Ameloblastoma is a benign but locally aggressive odontogenic tumor with a high tendency for recurrence if inadequately treated. Accurate diagnosis through imaging and histopathology is crucial for distinguishing it from other jaw lesions. Treatment choice depends on the histological subtype, with radical resection offering the lowest recurrence rates for solid/multicystic variants, while some unicystic and peripheral forms may be managed conservatively. Advances in surgical reconstruction and adjuvant therapies have improved functional and aesthetic outcomes. A clear understanding of its clinicopathological features is essential to guide optimal management and long-term follow-up.

Conflict of Interest

Not available

Financial Support

Not available

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