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College of Dentistry

Management of Local Aggressive Benign Odontogenic Neoplasms

A Project Submitted to The College of Dentistry, University of Baghdad, Department of Oral and Maxillofacial Surgery in Partial Fulfilment for the Bachelor of Dental Surgery

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Certification of the Supervisor

I certify that this project entitled " Management of Local Aggressive Benign Odontogenic Neoplasms " was prepared by Makarem Ismail Hussien under my supervision at the College of Dentistry/University of Baghdad in partial fulfilment of the graduation requirements for the bachelor's degree in dentistry.

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Supervisor’s Dedication

This is to clarify that the organization and the preparation of this graduation project have been made by the under graduated student Makarem Ismail Hussien under my supervision in the college of dentistry, University of Baghdad/ Department of oral and maxillofacial surgery.

Acknowledgment

Firstly, all gratefulness, faithfulness to ALLAH.

For providing me with patience, perseverance, and the ability to undertake and complete this project

I would like to extend my deepest respect and gratitude to dean of College Of Dentistry, University Of Baghdad Assist. Prof. Dr. Raghad Al-Hashimi.

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My deepest gratitude and my heartfelt thanks to my supervisor Dr. Mohammed W. Al-Gailani.

Because it is difficult to compensate for the fatigue, effort and sacrifices that they make . Donating the best effort is the only expression of thanks and gratitude for their presence . For the secret of my success and progress in this difficult life, the source of my inner strength . My father Ismail Hussein and My mother Feryal Hekmat .

At the time that my graduation project come to an end, my appreciation to who helped me and work with me during the hard times , my oldest sister Maryem Ismail and my oldest brother Mustafa Ismail Hussein

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Thank you , for being in my life and making it batter.

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Abstract

Odontogenic neoplasms encompass a group of lesions with a varied clinical picture and biological behavior ranging from indolent hamartomatous proliferation to locally aggressive benign tumors and their very aggressive malignant counterparts. Their biology and clinical expression can often be destructive and ominous. An appropriate treatment protocol needs to be followed to combat the high recurrence rate and aggressiveness of these entities. This project aims to give an understanding of the locally aggressive benign odontogenic neoplasms, their biologic behaviour and the therapy strategies employed to treat them.

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List Of Abbreviations :

ABON : Aggressive Benign Odontogenic Neoplasms
CEOT : Calcifying Epithelial Odontogenic Tumor
CS : Carney's Solution
KCOT: Keratocystic Odontogenic Tumor
Mm : millimeter
Min: Minute
Cm : Centimeter
RR : Recurrence Rates
SMA : Solid Multicystic Ameloblastoma

بسم الله الرحمن الرحيم

(تَعَالَى اللَّهُ الْمَلِكُ الْحَقُّ وَلَا تَعْجَلْ بِالْقُرْآنِ مِنْ قَبْلِ أَنْ يُقْضَى إِلَيْكَ وَحْيُهُ وَقُلْ رَبِّ زِدْنِي عِلْمًا)

صدق الله العظيم

طه (١١٤)

Chapter 1

Introduction:

Odontogenic neoplasms encompass a group of lesions with a varied clinical picture and biological behavior ranging from indolent hamartomatous proliferation to locally aggressive benign tumors and their very aggressive malignant counterparts. The benign neoplasms are normally slow growing, indolent with no invasive potential. However, there exists a few locally aggressive benign odontogenic tumors that have a tendency to invade and deform the surrounding structures. The exact reason for the aggressiveness of these benign neoplasms remained an enigma until recently but with the ongoing research and the tremendous progress in the molecular biology of tumors, great strides have now been made in our understanding of their pathogenesis. Their biology and clinical expression can often be destructive and ominous. An appropriate treatment protocol needs to be followed to combat the high recurrence rate and aggressiveness of these entities. **(Pratyusha P Gaonkar et al., 2016)**

The jaws are host to a wide range of cysts and neoplasms which are mainly of odontogenic origin traced back to various defects in odontogenesis. The ectomesenchymal and epithelial tissue interaction during odontogenesis is a complex process that may also lead to the development of lesions commonly derived from odontogenic epithelium that reside in the jaw bones or adjacent soft tissues and are collectively referred to as odontogenic tumors. They are the derivatives of epithelial, ectomesenchymal and/or mesenchymal elements of the tooth-forming apparatus . Also , the developmental stages of teeth formation are emulated in these tumors. Odontogenic neoplasms include a spectrum of heterogenous group of lesions ranging from tumor like malformations to benign neoplasms and their malignant counterparts, some with metastatic potential. Though they are broadly classified into benign and malignant types, there are odontogenic tumors that are described as benign lesion but display locally

aggressive behavior. The word aggressive is often associated with the malignant neoplasms which have the ability to invade the adjacent tissue thus subsequently resulting in metastasis and finally death if left untreated. On the other hand, the benign neoplasms exhibit a very characteristic slow, progressive and self-limiting growth . They are noninvasive, histologically benign with few mitotic cells and high differentiation of cells. The locally aggressive benign tumors are characterized by their inherent potential of local tissue destruction and deformation with severe morbid results**. (Pratyusha P Gaonkar et al., 2016)** .

The benign odontogenic tumors that exhibit local aggressiveness are ameloblastoma, odontogenic myxoma and the Pindborg tumor. **(Pratyusha P Gaonkar et al., 2016)** .

1.1 Aim of project

This project aims to give an understanding of the locally aggressive benign odontogenic neoplasms, their biologic behaviour and the therapy strategies employed to treat them .

Review Of Literature :

Odontogenic tumors represent a surprisingly diverse group of pathologic lesions of the jaws and overlying soft tissues. A basic understanding of the histology and embryology of tooth formation can help in understanding the development and histopathology of these lesion.Tooth formation is a complex process that involves both epithelial and connective tissues **(Kusukawa J et al.,1992)** . There are three major tissue components involved in odontogenesis: the enamel organ, the dental papilla, and the dental follicle .The enamel organ is an epithelial structure that is derived from oral ectoderm. The dental papilla and dental follicle are connective tissue structures that are considered ectomesenchymal in nature because they are also partly derived from cells from the neural crest. **(Philipsen HP , Reichart PA 2004)**

For each tooth, odontogenesis begins with the downward proliferation from the oral surface mucosa of the epithelium known as the dental lamina. This epithelium gives rise to the enamel organ, a cap-shaped structure that subsequently evolves into a bell shape corresponding to the future shape of the crown of the tooth. After the formation of the enamel organ, the cord of dental lamina epithelium from the surface mucosa will normally fragment and degenerate. However, small islands of this epithelium (rests of the dental lamina) will remain after tooth formation and may be found within the gingival soft tissues and superficial alveolar bone. These primitive dental lamina remnants are believed to be capable of giving rise to several types of developmental odontogenic tumors **(Philipsen HP , Reichart PA 2004)** see (table 2.1)

(Table 2.1) The Next Edition Of The WHO's Classification Of Odontogenic Tumors And Maxillofacial Bone Tumors Was Published In Early 2017 .(John M. Wright and Marilena Vered,2017)

WHO Classification of Odontogenic tumors

Malignant odontogenic tumors

1. Ameloblastic carcinoma
2. Primary intraosseous carcinoma
3. Sclerosing odontogenic carcinoma
4. Clear cell odontogenic carcinoma
5. Ghost cell odontogenic carcinoma
6. Odontogenic carcinosarcoma
7. Odontogenic sarcomas

Benign odontogenic tumors

1. Ameloblastoma
2. Ameloblastoma, unicystic type
3. Ameloblastoma, extraosseous/ peripheral type
4. Metastasizing (malignant) ameloblastoma
5. Squamous odontogenic tumour
6. Calcifying epithelial odontogenic tumour
7. Adenomatoid odontogenic tumour
8. Ameloblastic fibroma
9. Primordial odontogenic tumour
10. Odontoma
11. Odontoma, compound type
12. Odontoma, complex type
13. Dentinogenic ghost cell tumour
14. Odontogenic fibroma
15. Odontogenic myxoma/myxofibroma
16. Cementoblastoma
17. Cemento-ossifying fibroma

The benign odontogenic tumors that exhibit local aggressiveness are ameloblastoma, odontogenic myxoma , the Pindborg tumor **. (Post Graduate et la.,2016)**

2.1 Ameloblastoma

Ameloblastoma was defined by Robinson as unicentric, non-functional, intermittent in growth, anatomically benign and clinically persistent. It was as early in the late eighteenth century that ameloblastoma was first recognized and described under the name adamantinoma' by Broca and Malassez. It was later named ameloblastoma by Churchill. It accounts for almost 1 percent of all the oral tumors. It is the second most common benign epithelial odontogenic tumor. The ameloblastoma is a locally aggressive , unencapsulated, but benign odontogenic tumor composed of proliferating odontogenic epithelial nests within a fibrous stroma. Based on the clinical, radiographic, behavioral and prognostic factors, they are classified into: solid multicystic, unicystic, desmoplastic and peripheral ameloblastoma. The unicystic variety shows an indolent behavior incomparison to the more aggressive solid multicystic (SMA) type and hence lower recurrence rate. The SMA shows local infiltration into the bone marrow. **(Morgan PR, 2000)** . The maxillary SMA usually presents with facial swelling and expansion of both the buccal and lingual plates, sometimes along with nasal obstruction, otalgia, proptosis and diplopia. If the ameloblastoma remains undetected lesions in the ascending ramus can penetrate into the paracranial structures **(Barnes L,2000)**.Marx and Stern categorized ameloblastomas into three broad groups: ameloblastoma in situ, micro invasive ameloblastoma and invasive ameloblastoma. As the name suggests, the invasive ameloblastoma is the most aggressive variety which invades bone and sometimes invades and grows within the soft tissues. It exhibits cell replication and growth but seldom metastasizes. The exact nature of pathogenesis of ameloblastomais still unclear but the recent advances in research have revealed some key molecules that play a role in the genesis of odontogenic tumors. In the past numerous studies have been conducted to explore the tumor biology of ameloblastoma . **(Post Graduate et la.,2016)** see (figure 2.1)

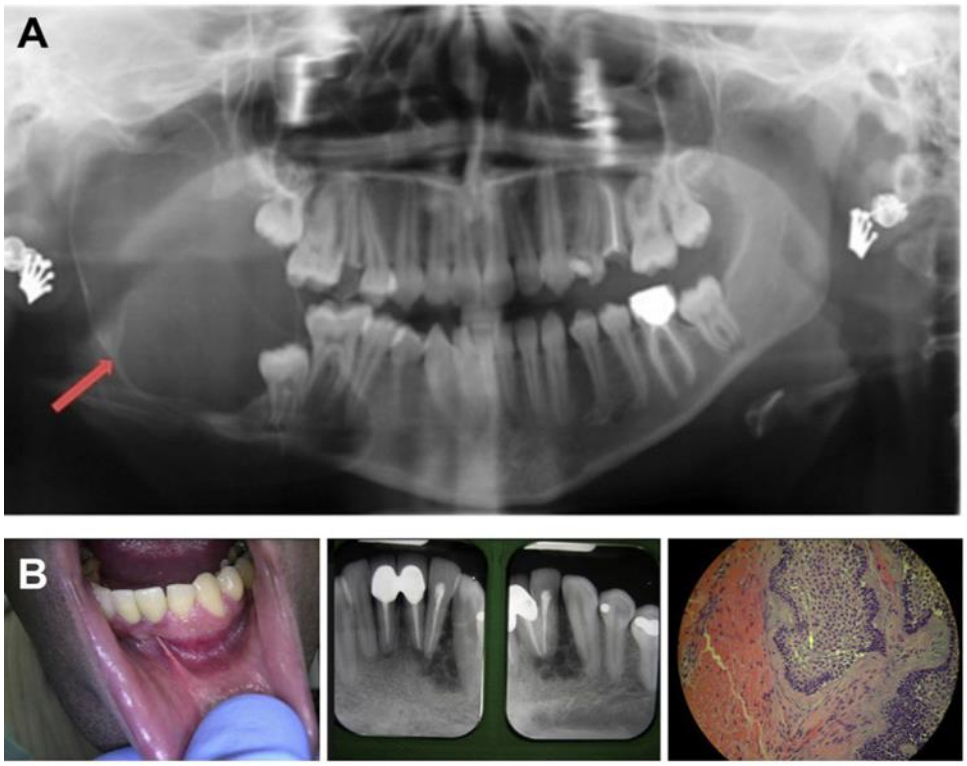

Figure 2.1 (A) Panoramic radiograph showing a large radiolucent defect involving right mandibular body. (B) Asymptomatic swelling and labial cortical plate expansion of lower anterior region. The intraoral periapical radiograph showing small multilocular radiolucent defect (honeycomb appearance) in lower left central incisor to canine region. The histopa- thology specimen showing follicular ameloblastoma with peripheral ameloblast-like cells and central stellate reticulum-like cells. ([A] (Almajid EA et la.,2019)and [B] (Courtesy of Earl I. Clarkson, DDS, and Orrett E. Ogle, DDS, Woodhull Hospital, Brooklyn, NY.)

2.2 Odontogenic Myxoma

Odontogenic myxoma in the jaw was first reported and described by Goldman and Thoma in 1947. It is classified by WHO (2005) as a benign neoplasm arising from odontogenic ectomesenchyme with or without odontogenic epithelium. It is a benign yet locally aggressive tumor with a recurrence rate of about 10 to 33%. Clinically it may present with tooth displacement and sometimes root resorption, displacement of the inferior alveolar canal which is suggestive of its benign process . Microscopically, odontogenic myxoma presents with spindle shaped or angular cells scantily distributed in loose mucoid intercellular material. It is believed that these cells are myofibroblasts and they give rise to the stroma rich in acid mucopolysaccharides like hyaluronic acid and chondroitin sulfate. It is postulated that this mucopolysaccharide rich stroma is responsible for its infiltrative behavior **(Nayak MT et la., 2013)** see figures (2.2 and 2.3) .

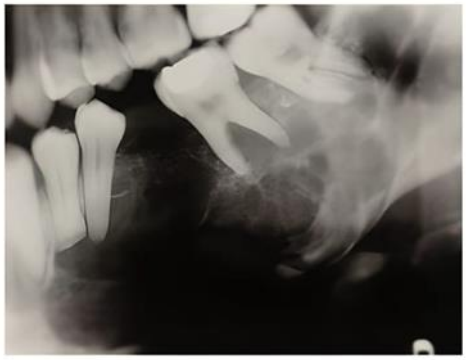

Figure 2.2 Odontogenic myxoma. Multilocular expansile radiolucency of the posterior mandible. (Courtesy of Dr. T.R. Kerley.)

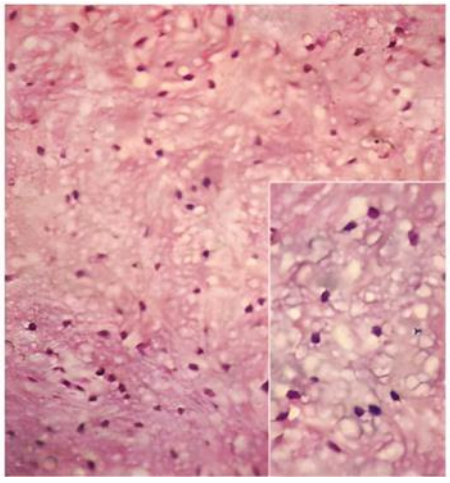

Figure 2.3 Odontogenic myxoma. Low-power photomicrograph showing a pale, myxomatous lesional cell proliferation. High-power photomicrograph showing stellate lesional cells set in a myxoid background with delicate collagen fibers (Courtesy of Dr. T.R. Kerley.)

2.3 Calcifying Epithelial Odontogenic Tumor (CEOT)

(CEOT) first described by Pindborg in 1955 as a rare benign epithelial odontogenic tumor with a variable biologic nature ranging from mild to moderate invasiveness. It normally presents as a slow growing swelling and grows by infiltration resulting in cortical expansion, tooth displacement and root resorption **(Kaplan I et la 2001)** . CEOT is said to arise from enamel organ's stratum intermedium. It is reduced invasive property as opposed to ameloblastoma can be credited to the reduced activity of the stratum intermedium compared to the tissue of origin of ameloblastoma. The histopathology of CEOT comprises of sheets and islands of polyhedral epithelial cells with little stroma. Eosinophilic masses may be found within these tumor sheets and can undergo calcification giving rise to Liesegang rings. A characteristic finding of clear cell variant of CEOT is the presence of sheets or cords of clear cells with foamy cytoplasm containing glycogen in the matrix and is accountable for aggressiveness and higher recurrence rates as compared to the conventional CEOT **(Badreshetty D et la., 2013)** . see figures (2.4 and 2..5)

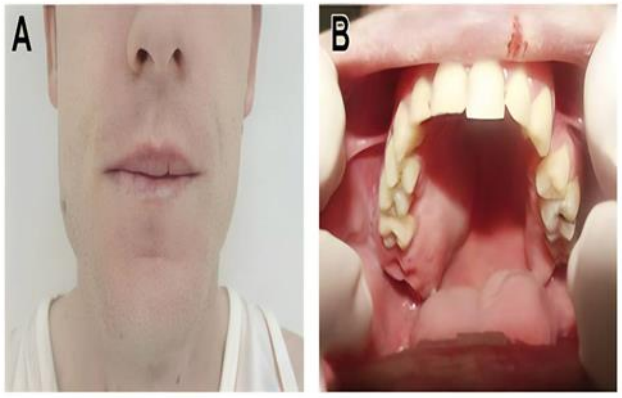

Figure 2.4 A) Extraoral swelling of the right side of posterior maxillae. (B) Intraoral appearance of swelling in posterior region of maxillae.(Gruber K et la.,2019)

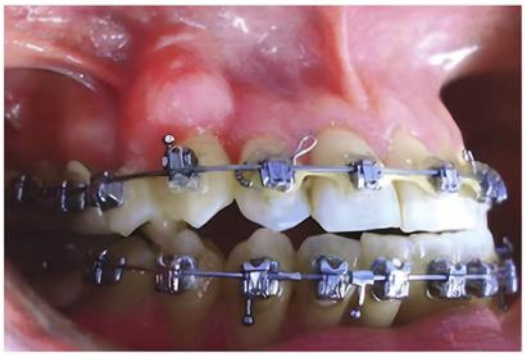

Figure2.5 Solitary swelling in the gingival area of maxillary canine region. (From Rahman N, et la., 2013)

2.4 Keratocystic Odontogenic

The odontogenic keratocyst first described by Philipsen in 1956 has been termed keratocystic odontogenic tumor (KCOT) by the most recent WHO classification (2005). This change in terminology has been brought about to stress on the neoplastic nature of this entity and it is attributed to its aggressive clinical behavior, histologically high mitotic rate and association with genetic and chromosomal abnormalities which is not typical of other cysts. Also, the recurrence rate of this tumor is variable ranging from 2.5 to 62% **(Nayak MT et la., 2013)** . KCOTs tend to grow quickly within medullary bone, while bony expansion becomes clinically evident only when the lesion reaches large size. Increased aggressiveness in the form of proptosis of the eye due to involvement of the maxillary sinus and the floor of the orbit has been reported. However, KCOT cannot infiltrate into the soft tissue unless seeded into it **(Marx RE et la.,2012)** . It is defined as "a benign unicystic or multicystic, intraosseous tumor of the odontogenic origin, with a characteristic lining of parakeratinized stratified squamous epithelium and potential for aggressive, infiltrative behavior **(Barnes L et la.,2005)** .However this lesion shows some features of a cyst one of them being response to decompression and so the controversial topic of its neoplastic nature prevail **(Bilodeau EA et la 2014)** . The next edition of the who's classification of odontogenic tumors and maxillofacial bone tumors was published in early 2017 that didn't mention about being keratocystic odontogenic tumor which main it is considerable cyst . The long paried in naming the keratocystic odontogenic tumor make it important to mention that point , also the reclassification or appearance of new entities, and the fact that long- standing names are subjects for renaming or changing categories such as cyst to tumor or tumor to cyst through academic discussions. However, regardless of reclassifications and name changes the fundamental concepts on diagnostics and

clinical presentations remain the same. Another thing should be focus on that the psychological effect on patient regarding to the name make different on the patient **(Post Graduate et la.,2016)** .See figures(2.7 and 2.6)

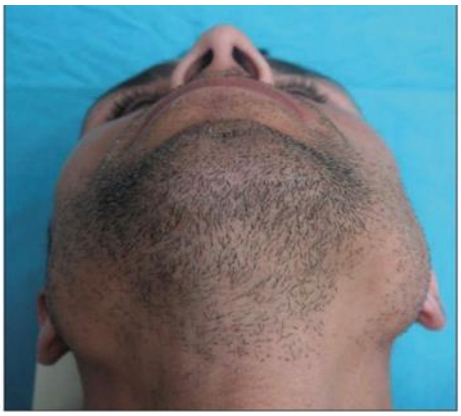

***Figure 2.* 7 Pre-operative extra-oral photograph showing swelling over the lower border of the mandible on the left side**

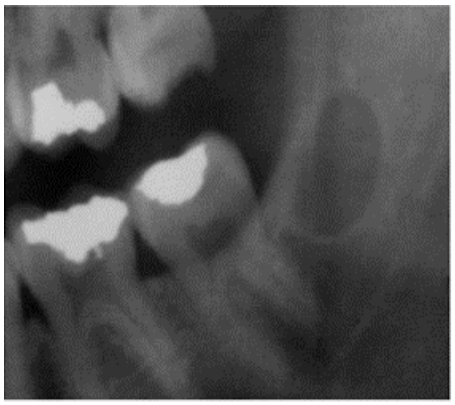

Figure 2.6 Odontogenic keratocyst. Small unilocular radiolucency distal to the left mandibular second molar

A discussion of the surgical management of jaw tumors is made easier by the fact that many tumors behave similarly and therefore can be treated in a similar manner. The three main modalities of surgical excision of jaw tumors are (1) enucleation (with or without curettage), (2) marginal (i.e., segmental) or partial resection, and (3) composite resection see (table 2.2). Many benign tumors behave non-aggressively and are therefore treated conservatively with enucleation, curettage, or both . Another group of benign oral tumors behaves more aggressively and requires margins of uninvolved tissue to lessen the chance of recurrence. Marginal (i.e., segmental) or partial resection is used for removal of these lesions . The last group of tumors includes the malignant varieties. These tumors require more radical intervention, with wider margins of uninvolved tissue . Surgery may include the removal of adjacent soft tissues and dissection of lymph

nodes. Radiotherapy, chemotherapy, or both, alone or in addition to surgery, may be used. Thus maxillary tumors have a poorer prognosis than those within the mandible . **(James R. Hupp et la., 2015)** (see table 2.3)

(Table 2.2) Types Of Surgical Operations Used For The Removal Of Jaw Tumors (James R. Hupp Et La., 2015) .

Types of Surgical Operations Used for the Removal of Jaw Tumors
• Enucleation and/or Curettage Removal of tumor by instrumentation in direct contact with the lesion; used for benign types of lesions. • Resection Removal of a tumor by incising through uninvolved tissues around the tumor , thus delivering the tumor without direct contact during instrumentation also known as en bloc resection **.** • Marginal (i.e., segmental) resection: Resection of a tumor without disruption of the continuity of the bone. • Partial resection: Resection of a tumor by removing a full-thickness portion of the jaw in the mandible; this can vary from a small continuity defect to a hemimandibulectomy jaw continuity is disrupted. Total resection: Resection of a tumor by removal of the involved bone e.g., maxillectomy and mandibulectomy**.** • Composite resection: Resection of a tumor with bone, adjacent soft tissues, and contiguous lymph node channels (an ablative procedure used most commonly for malignant tumors) .

(Table 2. 3) Types Of Jaw Tumors And Primary Treatment Modalities (Odontogenic Tumors) (James R. Hupp Et La., 2015)

Enucleation and/or Curettage	Marginal or Partial Resection	Composite Resection
Odontoma Ameloblastic fibroma Ameloblastic fibro-odontoma Adenomatoid odontogenic tumor Calcifying odontogenic cyst Cementoblastoma	Ameloblastoma Calcifying epithelial lignant odontogenic tumor Myxoma Ameloblastic Odontoma Squamous odontogenic tumor	Ameloblastoma Ameloblastic fibrosarcoma Ameloblastic Odontosarcoma Primary intraosseous carcinoma

2.5 Basic Surgical Goals.

1. Eradication of Pathologic Condition . (EDWARD ELLIS III, 2018)
2. Functional Rehabilitation of Patient . (EDWARD ELLIS III, 2018)

2.6 Jaw Tumors Treated With Enucleation ,Curettage, or Both

Most jaw tumors with a low rate of recurrence can be treated with enucleation or curettage—for example, most of the odontogenic tumors, including odontomas, ameloblastic fibromas, ameloblastic fibro-odontomas, keratinizing and calcifying odontogenic cysts , adenomatoid odontogenic tumors, cementoblastomas, and central cementifying (i.e., ossifying) fibromas. lesions that are treated in this manner to enucleate is “to remove whole or clean, as a tumour from its envelope.” Curettage is defined as “the removal of growths or

other material from the wall of a cavity **(Giuliani et al., 2006).** Enucleation with and without various adjuncts has been utilized for many years. Although enucleation/curettage has the advantage over marsupialization of providing a complete specimen for histopathologic analysis, it shows recurrence rates as high as 62.5%, which is no longer an acceptable treatment modality. This high incidence of recurrence is explained by the thin, friable wall of the tumor , which is often difficult to enucleate from the bone in one piece, and the small satellite cysts within fibrous wall. Regarding curettage, clinicians have advocated mechanical techniques (hand, rotary) alone or in combination with a chemical solution (Carnoy's) **(Stoelinga, 2003)** or cryosurgical agents (liquid nitrogen) **(Jensen et al., 1988).** See (figures 2.8,2.9and 2.10) which explain a case for Surgical management of odontogenic myxoma . **(Kawase-Koga et al.,2014)**

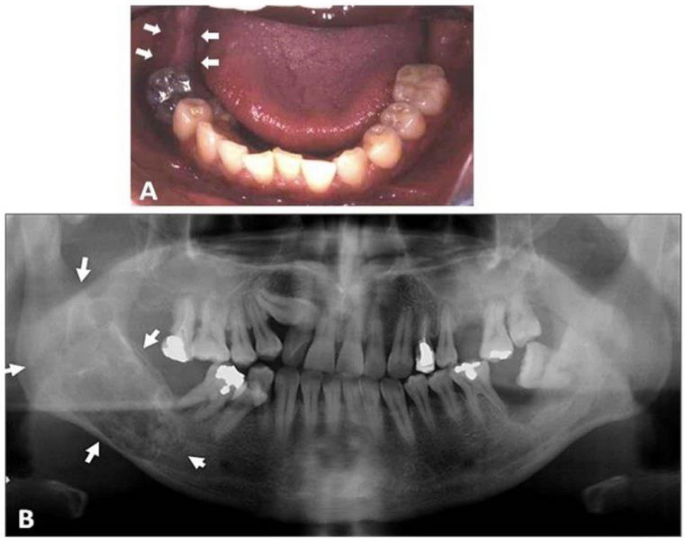

Figure 2. 8 The patient reported no symptoms in his mouth including the mandibular area, and on clinical examination no swelling could be detected on the right side of the jaw, and the oral mucosa appeared normal (Figure 1A) . a pano- ramic radiograph revealed an extensive radiolucent and multilocular area with imprecise borders that extended from the right posterior mandibular body to around the root of tooth #46, and exhibited a "soap bubble" appear- ance (Figure 1B) . (Kawase-Koga et al.,2014)

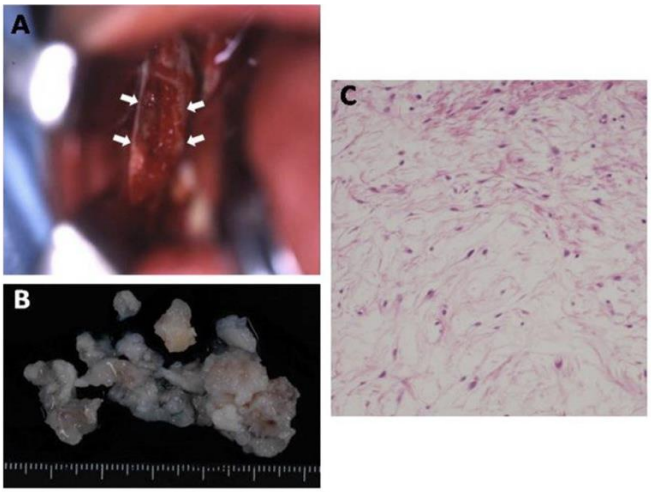

Figure2.. 9 incisional biopsy showed loosely arranged spindle-shaped cells in a myxoid fibrous stroma. On the basis of these histological findings, a provisional diagno- sis of odontogenic myxoma was made.We performed extraction of tooth #46, and an enucle- ation and wide curettage of the normal surrounding tissue to preserve the inferior alveolar nerve, the jaw, and oral function under general anesthesia with nasopharyngeal in- tubation (Figure 2A) The surgical specimen revealed benign-looking spindled and stellate cells in the mucinous stroma (Figure 2 B, C).(Kawase-Koga et al.,2014)

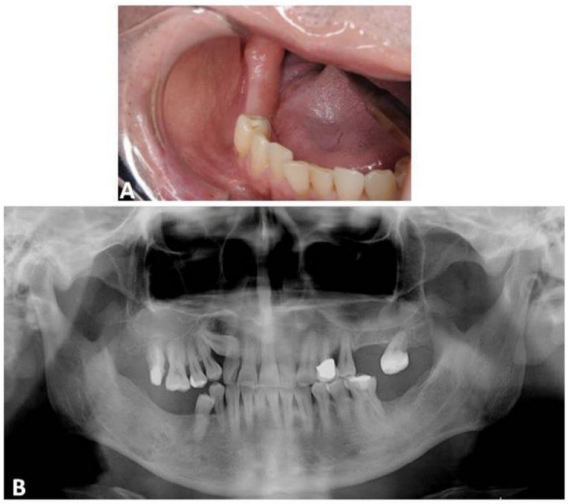

Figure1. 10There have been no clinical or radiological signs of recurrence over 10 years follow-up (Figure 3 A, B). (Kawase-Koga et al.,2014)

2.7 Enucleation and treatment of the bony defect with Carnoy's solution

As a result of the difficulty of enucleating the thin, friable wall of the some tumors due to the thin wall of it or the present of daughter cell, therefore, treatment should aim to eliminate the possible vital cells left behind in the defect. For this reason a mild, not deeply penetrating, cauterizing agent is used such as Carnoy's solution {consists 3 ml of chloroform, 6 ml of absolute ethanol, 1 ml of glacial acetic acid and 1 g of ferric chloride} **(Morgan et al., 2005)**. This should be enough to do cauterization of the remaining cells.

Other studies showed that, although the defect was treated with Carnoy's solution. Microcysts and epithelial islands were always seen in the overlying attached mucosa. And so recurrence took place. So, the authors of these studies recommended the complete excision of the overlying mucosa to decrease the recurrence **(Stoelinga, 2005). (Morgan et al.,2005)** also reported in their study that the treatment with Carnoy's solution did not show a significant association with recurrence. Yet, **(Voorsmit et al.,1981)** reported a decreased recurrence rate following treatment with enucleation and Carnoy's solution (2.5%) compared with enucleation alone (13.5%) .

The solution can be applied inside the tumor lesion or, more commonly, directly over the remaining bone bed after the lesion has been removed. The success of the application of this agent after enucleation was thought to be due to both of its penetration and fixation action. The usual practice is to apply Carnoy's solution with cotton applicators or ribbon gauze for 3–5 min, rinse the bony defect, and pack the wound open for healing by secondary intention. Some investigator reported some complication resulting from the use of Carnoy's solution although that some doubt still remains regarding them, this complications include infection, dehiscence, bone sequestrum formation, and

neuropathy.**(Frerich et al., 1994)** suggested that the application of Carnoy's solution should not exceed 3–5 min. They showed that the critical time to nerve impairment of the rabbit inferior alveolar nerve was 3–5 min, and that Carnoy's solution should not be applied directly over the nerve. It is concluded that any damage happened to the blood vessels is reversible when the exposure times are <5 min . **(Alchalabi et la., 2017)**

The effects of Carnoy's solution on the inferior alveolar nerve were first reported by **(Frerich et al. ,1994).** The authors did not observe axonal damage during the first three minutes of direct application. In contrast, another important study, **(Wolgen et al.,1999),** noted that the alterations in neural conductivity developed after 2 min of direct application, with few signs of recovery after two weeks of follow-up. However, (**Júnior et al.,2007),** reported that when a proper protocol is followed, the chemical treatment of the nerve can be accomplished without permanent functional damage. (Figure 1.11)

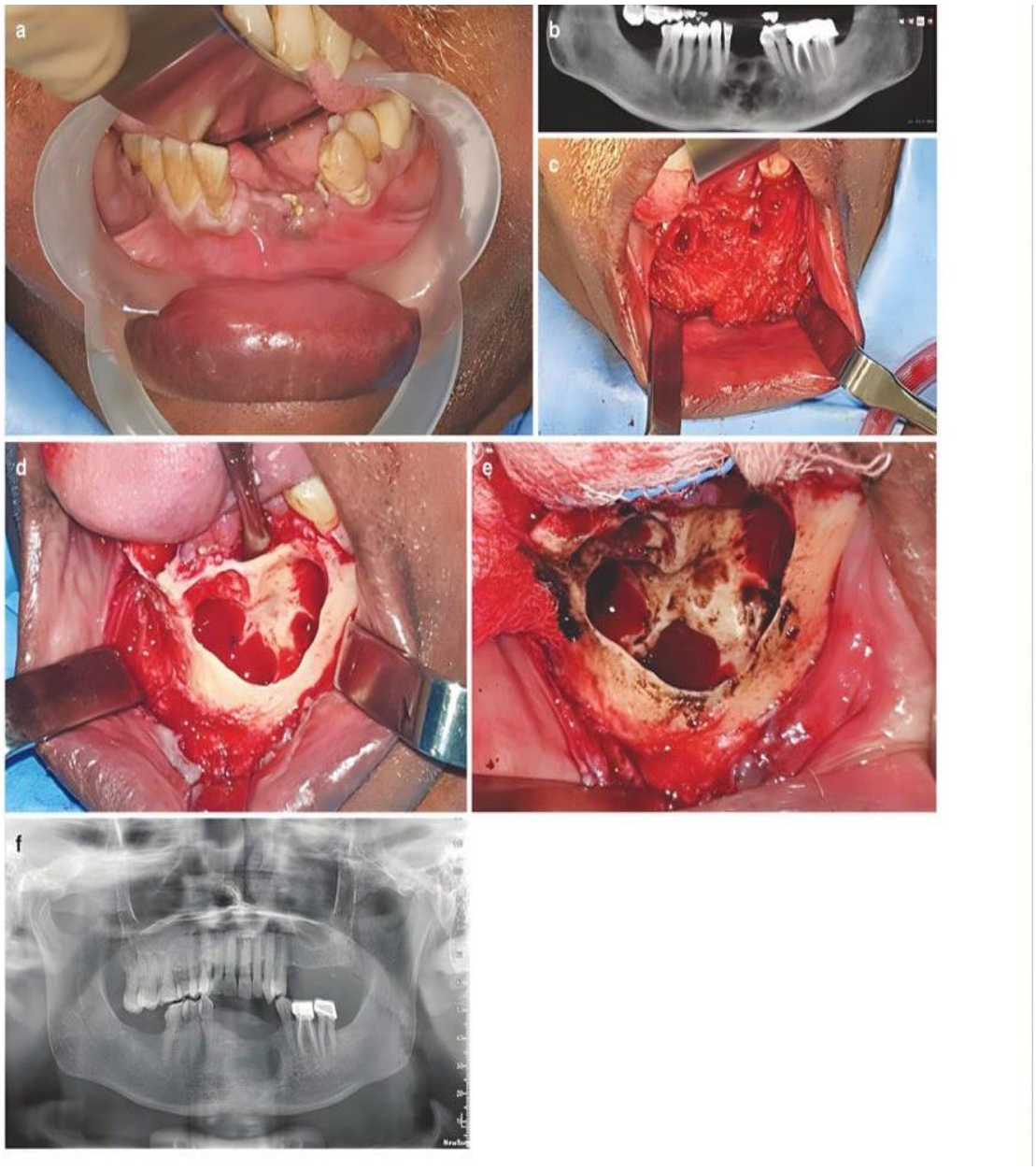

Figure 2. 11(a) loosening of teeth and expansion of the gams in the anterior lower mandible . (b) A OPG and CBCT showing multilocular radiolu cency in the anterior mandible . (e) Lesion exposed (d) lesion excised and peripheral ostectomy done (e) carnoys solution applied to surgical bed . (f sixteen month post operative OPG (Anjan K. M. , 2021)

2.8 Enucleation and liquid nitrogen cryotherapy

Liquid nitrogen has the ability to devitalize bone in situ while leaving the inorganic framework untouched, as a result of this, cryotherapy has been used for a number of locally aggressive jaw lesions, including ameloblastoma and ossifying fibroma **(Pogrel, 1993).** Cell death with cryosurgery occurs by direct damage from intracellular and extracellular ice crystal formation plus osmotic and electrolyte disturbances **(Schmidt and Pogrel, 2001)** .

According to **(Schmidt and Pogrel, 2001)** the standardized technique is as follows, the initial step in management of the lesion is enucleation of the tumor . The surrounding tissues are then protected with sterile wooden tongue blades and gauze, and the cavity is sprayed with liquid nitrogen twice for 1 min, with a 5-min thaw between freezes. Bone graft can inserted in the defect simultaneously, and then mucosa is closed with watertight sutures.

Figure 2.12 A typical portable liquid nitrogen cryospray. The technology can also be used with a probe (Pogrel MA,2013)

The advantages of liquid nitrogen over alternative methods of devitalizing the tissue beyond the visible lesion of the margin are that (1) the bone matrix is left in place to act as a clean scaffold for new bone formation, (2) a bone graft can be placed immediately to accelerate healing and minimize the risk of a pathologic fracture, and (3) decrease of bleeding and scarring. However, because of the difficulty in controlling the amount of liquid nitrogen applied to the cavity, the resultant necrosis and swelling can be unpredictable **(Salmassy and Pogrel, 1995)**.

The recurrence rate following enucleation and liquid nitrogen cryotherapy has been reported at 3–9% . **(Pogrel, 2005)** (figure 2.12)

When the liquid nitrogen cryotherapy is given around the inferior alveolar nerve, it is affected, and patients will suffer paraesthesia or anaesthesia. However, the axon sheaths are left intact and nerve regrowth is normal such that most patients obtain partial or complete return of sensation in 3 months **(Schmidt, 2003)** . see (figure2.13)

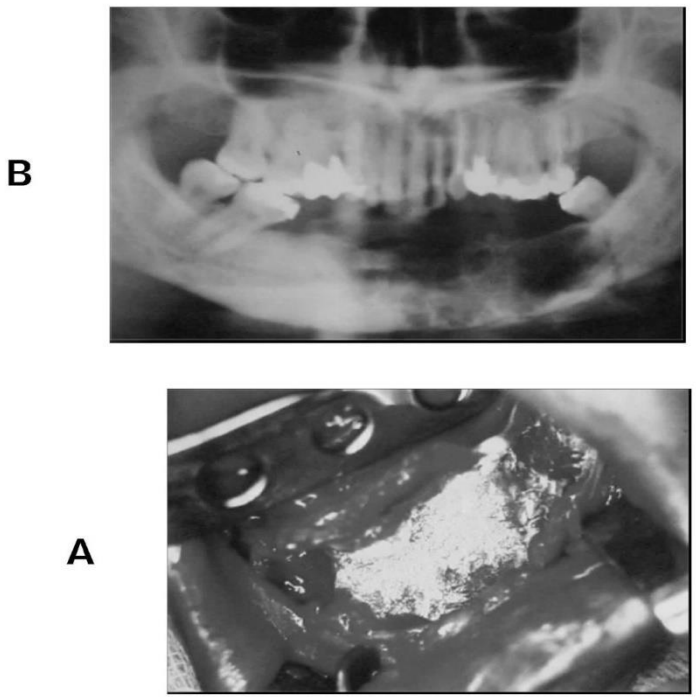

Figure 2.13 A) Frozen bone after liquid nitrogen application. And Panoramic radiograph 10 weeks after the surgery. B)Image suggestting pathological fractures in the left molar region Teeth within the lesional area were extracted . (André Caroli Rocha et la.,2009)

2.9 Jaw Tumors Treated With Marginal or Partial Resection

When the lesion is determined to be aggressive, by histopathologic determination or by its clinical behavior, or if it is of such a consistency that total

removal by enucleation, curettage, or both would be difficult, removal may be facilitated by resecting the lesion with adequate bony margins. Odontogenic lesions treated in this manner are the ameloblastoma, the odontogenic myxoma (i.e ,.fibromyxomas), the calcifying epithelial odontogenic tumor (i.e ,.Pindborg), the squamous odontogenic tumor, and the ameloblastic odontoma. As a general principle, the resected specimen should include the lesion and 1-cm bony margins around the radiographic boundaries of the lesion. If this can be achieved with the inferior border of the mandible left intact, marginal resection is the preferred method .Reconstruction then is limited to replacing the lost osseous structure , including the alveolus .If the lesion is close to the inferior border, the full thickness of the mandible must be included in the specimen, which disrupts mandibular continuity .**(GNEPP R et la.,2015) .** Reconstruction in this instance is much more difficult because the remaining mandibular fragments must be secured in their proper relationship to one another for proper function and symmetry to be restored . **(GNEPP R et la.,2015)**

The surgical technique for marginal (i.e., segmental) resection is straightforward. A full-thickness mucoperiosteal flap is developed and stripped from the bone to be removed. Air-driven surgical saws or burrs are then used to section the bone in the planned locations, and the segment is removed. Whenever marginal or partial resection is used, the clinician must determine whether the tumor has perforated the cortical plates and invaded adjacent soft tissue, in which case it is necessary to sacrifice a layer of soft tissue to eradicate the tumor, and a supraperiosteal dissection of the involved bone is performed. Immediate reconstruction is more difficult because enough remaining soft tissue may not be available to close over the bone grafts . If the clinician is concerned about the adequacy of the soft tissue surgical margins around a lesion when surgery is being performed in a hospital setting, specimens along the margins can be removed and sent immediately to the pathologist for histopathologic examination. This process

is performed in approximately 20 minutes by freezing the tissue in liquid carbon dioxide or nitrogen and then sectioning and staining the tissue for immediate examination. Frozen-section examination is accurate when used for detecting adequacy of surgical margins. However, such examination is less accurate when trying to diagnose a lesion histopathologically for the first time . **(GNEPP R et la.,2015)** (Figure 2.14 and 2.15)

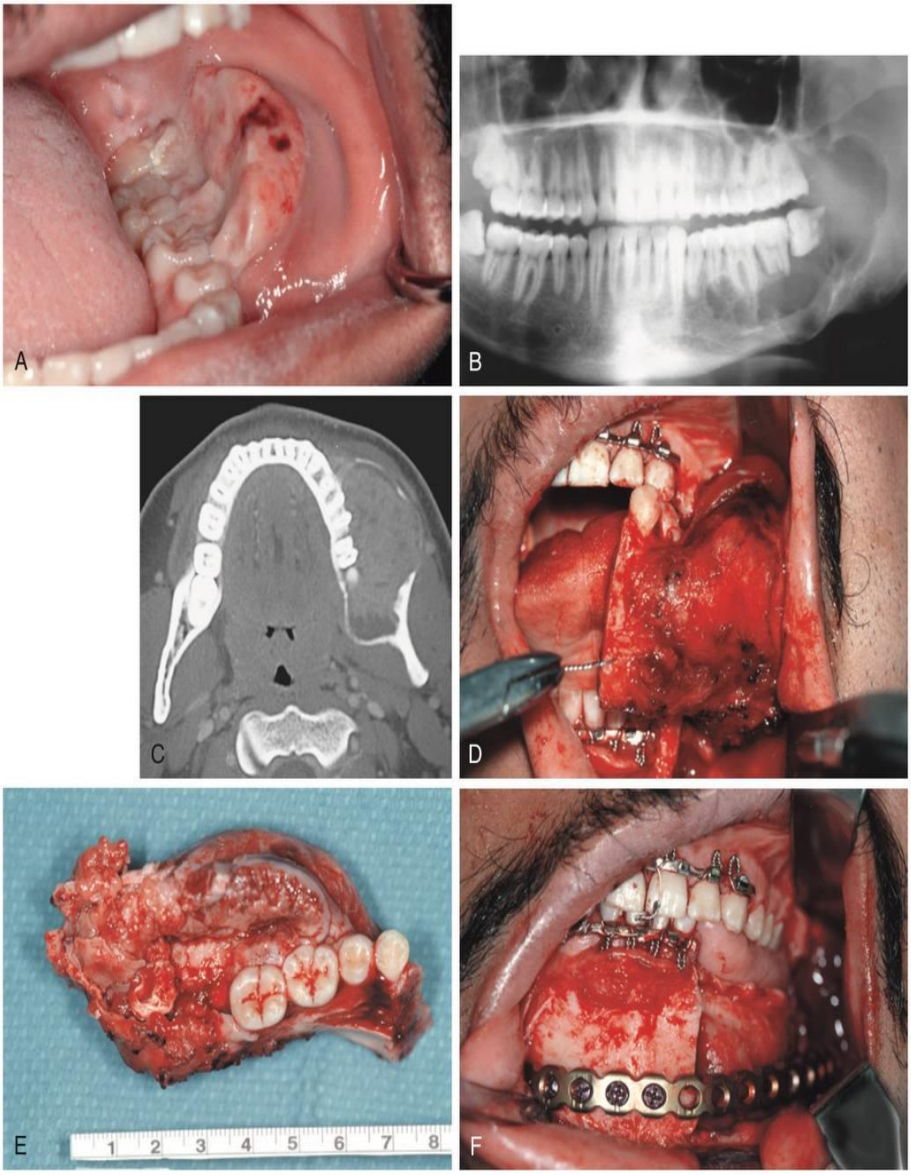

Figure 2.14 Partial resection of the lower jaw for ameloblastoma. (A) A lesion in the left molar region. (b) Panoramic radiograph at initial view showing multi-ocular radiolucency associated with an impacted tooth. Incision biopsy confirmed the lesion to be a haematoblastoma. (C) CT scan showing the extent of the lesion. (D) Excision of the intraoral tumor. (E) The surgical specimen. (f) Reconstruction of the lower jaw with a large bone plate • (EDWARD ELLIS III, 2018)

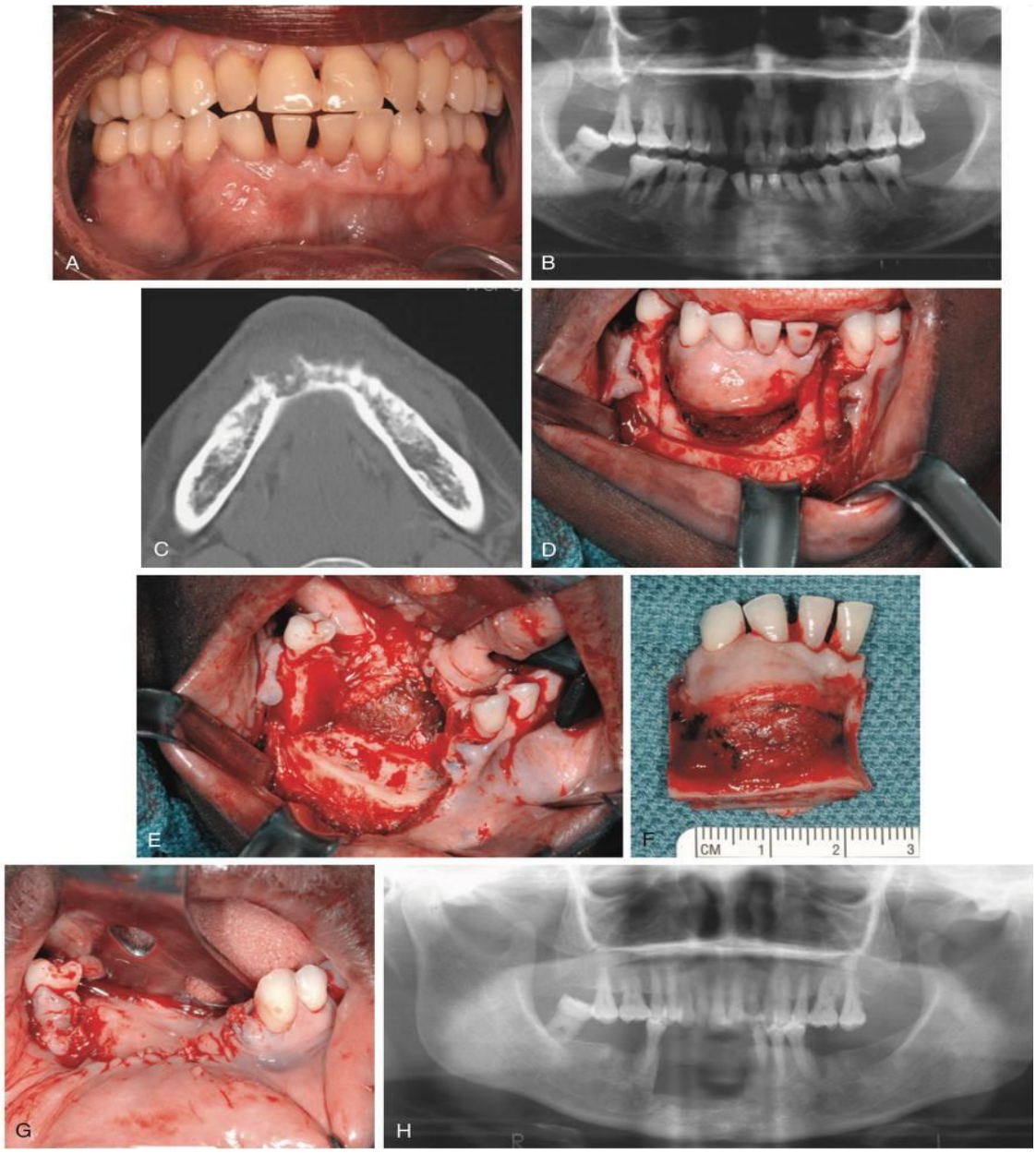

Figure 2.15 Marginal (or segmental resection) of ameloblastoma. (A) Preoperative photograph showing swelling of anterior mandible around roots of teeth. (B) Panoramic radiograph shows spacing of the roots from an ill-defined radiolucency. (C) Computed tomography scan shows an exophytic lesion that seems to be coming out of bone. (D) Intraoral exposure of mandible and osseous cuts made around lesion. The inferior border was left intact. (E) Intraoral defect after removal of lesion. Height of bone along the inferior border was sufficient to maintain continuity of the mandible. Bony reconstruction of the alveolar process was delayed until a later date. (F) Surgical specimen. (G) Appearance of the defect after soft tissue closure. (H) Panoramic radiograph taken after surgery (EDWARD ELLIS III, 2018)

2.10 Treatment Modalities for Malignancies

Malignancies of the oral cavity are treated with surgery, radiation , chemotherapy, or a combination of these modalities. The treatment for any given case depends on several factors, including the histopathologic diagnosis, the location of the tumor, the presence and degree of metastasis, the radiosensitivity or chemosensitivity of the tumor, the age and general physical condition of the patient ,the experience of the treating clinicians, and the wishes of the patient. In general, if a lesion can be completely excised without mutilating the patient, this is the preferred modality. If spread to regional lymph nodes is suspected, radiation may be used before or after surgery to help eliminate small foci of malignant cells in adjacent areas. If widespread systemic metastasis is detected or if a tumor such as a lymphoma is especially chemosensitive, chemotherapy is used with or without surgery and radiation . Currently malignancies are often treated in an institution where several specialists evaluate each case and discuss treatment regimens .These "tumor boards" include at least a surgeon, a chemotherapist ,and a radiotherapist. Most head and neck tumor boards also include a general dentist, a maxillofacial prosthodontist, a nutritionist, a speech pathologist, and a sociologist or psychiatrist . **(GNEPP R et la.,2015)**

2.11 Prognosis

When appropriately treated with surgical excision, benign tumors have a low recurrence rate except for ameloblastoma, which has a recurrence rate of 10 to 20% according to histological subtypes. While the majority of malignant odontogenic tumors are either malignant ameloblastoma or odontogenic carcinoma. The improved survival rate is associated with an age of under 57 years, lack of comorbidities, surgical resection, and absence of nodal disease. The 5- year overall survival for surgical excision is around 88% compared with 26.6% for non-surgical management. The presence of lymph node metastases is always

associated with a poor prognosis. **(Amir M. Labib1and Roger E. Adlard, 2022)**

2.12 Complications And Failure

The complications can be either related to the tumor or surgical management. Gradual expansion of the tumor may lead to mandibular maxillary distortion leading to facial asymmetry, pain, teeth displacement, malocclusion, or recurrence. Distant metastases can be seen in cases of malignant tumors. Lungs and cervical lymph nodes are the most affected sites **(Amir M.et la.,2022)**

At the same time, surgical complications may be in the form of postoperative bleeding, which may be quite significant as it will endanger the airway patency, infection, neurosensory disturbance due to inadvertent injury of the inferior alveolar nerve. Other general complications may also occur, including aspiration, deep venous thrombosis (DVT), and pulmonary embolism. All necessary postoperative measures should be taken to avoid the occurrence of these complications. **(Goldenberg D et la.,2004)**

Enucleation in combination with chemical agents or their combinations, for example, Carnoy's solution ,represents an option for surgical treatment of aggressive tumor like ameloblastomas. The use of Carnoy's solution helped to reduce the recurrence risk of ameloblastoma from 60–80 to 1–10%. **(Haq, J.et la.,2016)** . Carnoy's solution was first used as a medicament in surgery by Cutler and Zollinger in 1933 **(Cutler et la.,1933)**. It is a potent fixative, hemostatic, and cauterization agent that penetrates cancellous spaces in the bone (the average penetration depth is approximately 1.54 mm 5 min after application on the bone tissue) and ensures removing the remaining cells of the tumor lining **(Pitak-Arnnop et la.,2010)** . Most surgeons do not use chloroform in the

composition of Carnoy's solution since chloroform triggers malignant transformation of cells and causes infertility **(Ecker, Jet la., 2016)** .

Since Carnoy's solution is a nonselective fixative, its effect involves both tumor cells and the surrounding tissues, including blood vessels and nerves. Evaluation of the fixative effect on the neurovascular bundles is essential for detection of the postoperative course and late complications . **(Amir M.et la.,2022)** .

Carnoy's solution (CS) is a chemically cauterizing agent that has been used to treat various tumors of aggressive nature in the oral and maxillofacial surgery area . Although many studies indicated that the use of CS is effective to reduce the recurrence of various tumors in the oral and maxillofacial surgery area, such unicystic ameloblastoma (UAM) **(De Molon, R.S. et la.,2014)**. The penetration of this solution into tissues results in rapid local fixation and denaturation **(Ljubenović et la.,2007)** . CS has been reported to have systemic toxicity that can cause local damage to anatomical structures, especially nerves **(Leger, M.et la.,2011)**. However, Blanas et al. **(Soufir, N et la ., 2006).** suggested that there would be no damage to the nerves if the inferior alveolar nerve (IAN) is not exposed to CS for more than 3 min .

It is important to educate patients on the natural history of different odontogenic tumors and highlight the red flags to look for, such as rapid growth, neurosensory changes, pain, and neck masses. In addition, educating the patients on how to examine themselves and keeping regular follow-up is crucial for early detection of any possible recurrence or malignant transformation. **(Amir M. Labib1and Roger E. Adlard, 2022)**

The radical approach comprises segmental or marginal resection involving healthy bone 1.5-2 cm beyond the radiological margin .The recurrence rate after

conservative treatment is higher than that following aggressive treatment. Nakamura et al. reported a 7.1% recurrence rate after radical surgery and 33.3% after conservative treatment in 78 ameloblastoma cases. Despite the relatively high recurrence rate associated with conservative methods. Sampson and Pogrel reported that curettage of ameloblastomas resulted in high recurrence rates and indicated that during the first operation, soft-tissue spread should be prevented to reduce or eliminate the need for further extensive surgery in the event of recurrence. The solid/multicystic subtype, representing more than 80% of all cases, is more aggressive and more commonly recurrent than the unicystic subtype . **(Onur Yilmaz et la.,2020)**

Tumor cells remaining in areas of osteotomy after inadequate resection can lead to tumorigenesis in the graft. Periosteum invasion may cause tumor cells to spread to soft tissue. For this reason, the free margins should be determined histologically before reconstruction . We performed soft-tissue resection and conducted histopathological evaluation before reconstruction in all cases. **(Onur Yilmaz et la.,2020)**

The use of liquid nitrogen has been shown to have the ability To devitalize hard and soft tissues in the maxillofacial region. The Advantages of cryotherapy are easy application, little discomfort and absence of bleeding. Disadvantages, therefore, include an Unpredictable postoperative symptomatology and extensive Necrosis at the time of application . In the late postoperative Period, pathological fracture of the mandible was observed after Unrecommended masticatory exertion. **(LEBEDEV and BUTSAN,2019)**

Pathological fracture is a known risk when cryosurgery is Applied to the mandible. It appears to be secondary to necrosis and Demineralization by weakening the bone, reaching a maximum of 8 Weeks after treatment **(Daniel E Sampso et la.,2004)** . When bone is weakened by cryotherapy May have

the risk of pathological fracture, a phenomenon clinically And experimentally shown by Fisher and Pogrel . Some authors have suggested placing autogenous graft simultaneously in large cavities to promote, as soon as possible, a stimulus in osteogenesis as an attempt to correct the period of bone weakening The study by **(Rosenstein., et al.2001)** .

It is mandatory to treat odontogenic tumors in an interprofessional team approach to ensure proper treatment and outcome. The team should include an oral surgeon and head and neck surgeon with proper expertise in neck dissection. Having a plastic surgeon in the team is also important in cases when possible reconstruction might be needed. Postoperative care is crucial for optimal outcomes. Nursing staff should look after the airway make sure it is clear and patent by frequent suctioning to prevent aspiration and maintain good oxygenation. **(Onur Yilmaz et la.,2020)**

Although reports of bone regeneration through the use of tissue engineering appear promising, the limitations regarding the appropriate size of defect amenable to this approach is poorly defined. Furthermore, the additional challenge of salivary contamination of a nonvascularized reconstruction technique and higher risk for infection remains a real issue. **(Joseph S Solomkin et ia.,2013)**

Prophylactic measures should also be taken to avoid potential risks of deep venous thrombosis (DVT) or stress ulcers. Pain team involvement in the early postoperative period can significantly improve the overall patient treatment experience. Dietitian may be needed for early postoperative care for patients struggling with oral feeding or who have been instructed not to eat to heal the surgical site. **(Onur Yilmaz et la.,2020)**

Discussion

Local aggressive benign odontogenic tumors though benign possess an inherent tendency to invade and deform. With a higher rate of their recurrence and aggressiveness as compared to other benign tumors , it is crucial to decide upon an effective treatment modality. **(Post Graduate et la.,2016)**

Numerous surgical methods have been practiced in the management of odontogenic tumor , the confusion still exists as to which methods provide the lowest recurrence rates (RR) without causing significant morbidity. These methods are divided into conservative and aggressive/radical approaches or a combination of the two. Conservative methods include simple enucleation. Adjuvant methods such as peripheral ostectomy, cryotherapy (liquid nitrogen) and Carnoy's solution are considered aggressive forms of treatment which have shown more promising outcomes. Radical methods involve mainly resection which yields the lowest RR which causes significant morbidity .**(Al-Moraissi EA et la.,2017)**

The biologic behavior of the locally aggressive tumor determines the surgical technique that should be employed . The surgical approach is determined by size, patient age, proximity to vital structures, accessibility, soft tissue/cortical perforation, and if the lesion is recurrent . **(Post Graduate et la.,2016)**

Enucleation alone is an inadequate form of treatment and needs to be used in combination with adjuvant methods to lower RR. Epithelial remnants can easily be left behind after enucleation which leads to high RR 20.8%-26.1%**(Fadi Titinchi, 2020)**

Enucleation with peripheral ostectomy Cure rate, although not well studied, is believed to improve with the additional removal of 1–2 mm of bone beyond the visible margin of the lesion . Methylene blue or crystal violet can be

applied, allowed to penetrate, and used as a visual cue for the appropriate amount of bone removal with rotary Instrumentation .The recurrence rate which is approximately 20% with this procedure . **(Pogrel M, 2013).**

Enucleation with Carnoy's solution , carnoy's solution is a tissue fixative that is applied after enucleation. Classically, every 10 ml of solution contains 6 ml of 95% ethanol, 3 ml of chloroform, 1 ml of glacial acetic acid, and 1 g of ferric chloride **(Ribeiro Junior O et la.,2012)**. Carnoy's solution inhibits the osteogenic and osteoconductive properties of bone following application .The agent works by penetrating cancellous spaces in bone, devitalizing, and fixing remaining tumor cells. Depth of penetration has been reported up to 1.5 mm after 5 min **(Johnson NR et la., 2013)** . In theory, penetration is adequate to prevent recurrence caused by daughter cysts, budding of the cystic lining, or remnants of cystic epithelium. Following careful enucleation, the solution is applied to the cavity walls for 5 min, and then rinsed away . Dependent on operator preference, denatured bone is either left in place or removed by peripheral ostectomy down to healthy bone. The rate of cyst recurrence with this procedure is no more than 6.6% . . **(Chrcanovic et la.,2017)**

Enucleation with cryotherapy results in the formation of intracellular and extracellular ice crystals that disrupt normal osmotic and electrolytic balance within cells, ultimately resulting in cell death . **(Tonietto L et la.,2011)**. However, for cell death to occur, freezing must be rapid, thawing should be slow, and a temperature of less than -208 C must be achieved . Liquid nitrogen is an agent that is readily available and meets the necessary criteria. Following careful enucleation, liquid nitrogen is applied to the cavity walls for a minimum of 1 min. Once thawing occurs, the agent is reapplied until the provider feels all areas have been sufficiently covered. Studies have shown a depth of penetration for liquid nitrogen to reach at least 1.5 mm **(Pogrel MA,2013)** . The recurrence rate for

enucleation with cryotherapy is approximately 11 to 23%. liquid nitrogen preserves inorganic bone structures **(Tonietto L et la.,2011)** . The preservation of the inorganic bone matrix allows for improved repair and remodeling. However, cryotherapy has been reported to cause bone weakening, which peaks at 8 weeks following the procedure, putting the patient at risk for pathologic fracture **(Schmidt Bl and Pogrel MA, 2001)** . Also ,the recurrence rate when using liquid nitrogen is two times (or even more) higher compared to Carnoy's solution and its modifications . **(LEBEDEV and BUTSAN,2019)**

Care must be taken to ensure no damage to nearby structures such as teeth, nerves, and soft tissue . **(LEBEDEV and BUTSAN,2019)**

Marginal/segmental resection of the jaw together with a margin of surrounding healthy tissue is the most radical treatment for the aggressive types of benign tumors . The recurrence rate when using this technique is no more than 3% **(Chrcanovic B.R. and Gomez R.S, 2016)**. The implementation of such surgical interventions should be considered a main method of choice. The formed bone defect is eliminated by using the reconstruction titanium plate or bone autograft (preference is given to revascularized fibular bone autograft). Unfortunately , not all patients can qualify for this type of surgical treatment. For example, titanium plates cause patient disability (aesthetic and functional defects remain) Furthermore, this method requires a longer and more expensive anesthetic and surgical intervention as well as a longer postoperative period and rehabilitation periods than other types of treatment . **(LEBEDEV and BUTSAN,2019)**

Owing to their aggressive nature . extensive surgical treatment is recommended in solid multicystic ameloblastomas. A conservative local treatment is recommended for young patients to reduce the future growth

problems, as also in the indolent unicystic ameloblastoma. To avoid recurrence, radical resection including a healthy bone margin of at least 1cm is the most preferred therapeutic approach . The odontogenic myxoma is best treated using resection with 1 to 1.5 cm bony margins thus reducing the recurrence risk associated with enucleation and curettage. The CEOT though less aggressive than ameloblastoma shows recurrence when treated with enucleation and curettage and hence a resection using 1 to 1.5 cm margins in bone is recommended . **(Post Graduate et la.,2016)**

Therefore, enucleation with the use of Carnoy's solution should be considered the optimal method of choice in the treatment of aggressive odontogenic tumor it is simple and inexpensive and carries high chances to preserve the integrity of the jaw. A low rate of recurrence (up to 6.6%) and safety are the main criteria for using carnoy's solution , a follow-up period is clearly also necessary. It has been recommended that patients should be followed closely for at least the first 2 years after surgery, which represents the period during which the neoplasm is most likely to recur . Rocha et al. suggested that 5 years of surveillance is needed to confirm successful excision, but that ideally follow-up should be maintained indefinitely . **(Lo Muzio L et la., 1996).**

Conclusion

Management of ABON remains controversial, but in light of prior clinical trials, there is a general consensus recommending complete lesion eradication with radical surgical procedures, which may cause deformity. These deformities can have adverse psychosocial consequences, particularly for young patients. Therefore, the primary aim should be to preserve structural and functional integrity for a better postoperative quality of life for patients. Enucleation with or without Carnoy's solution application followed by iodoform gauze dressing can be recommended as a good conservative treatment option that has a low recurrence rate with uneventful secondary healing for ABON , also it recommends long clinical and radiographic follow-up due to the aggressive nature of ABON. Although the precise definition of aggressive behavior of odontogenic tumors have not been established, it is accepted that those lesions that are locally infiltrative with the potential for recurrence following enucleation and curettage are within this category.

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