



A Case Report on an Extensive Destructive Lesion of the Mandible: A Pathologist's Enigma and a Surgeon's Conundrum!

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Abstract

An extensive lesion of the jaw which is capable of destruction and hollowing out of the bone, is a major cause for concern, both, with regards to its correct diagnosis, as well as a timely institution of the most appropriate treatment procedure. A relatively aggressive lesion with considerable invasive and recurrence potential, such as an odontogenic tumor may radiologically and sometimes even histopathologically masquerade as a seemingly innocuous pathology such as an odontogenic cyst.

It is imperative to precisely diagnose and completely eliminate the lesion, while at the same time, ensure least possible morbidity for the patient, such as pathological fractures, persisting neurological deficits, esthetic deformity, functional debility, and of course, recurrence or persistence of the lesion.

A case of a large radiolucent lesion of the mandible is presented, in which Histopathological examination of the biopsy specimen was supplemented by Immunohistochemical analysis, using a Tumor Marker, namely, Calretinin and two Prognostic Indicators, namely, Ki-67 and Proliferating Cell Nuclear Antigen (PCNA). The use of Immunohistochemistry as an adjunct proved invaluable in correctly identifying the lesion as well as gaining an insight as to its likely prognosis, thereby aiding in its correct management.

Keywords: Immunohistochemistry (IH); Unicystic lesions; Dentigerous Cysts; Unicystic Ameloblastoma; Ki-67; Proliferating Cell Nuclear Antigen (PCNA); Proliferation Index (PI); Labelling Index (LI)

Introduction

The most common cause of a large lytic lesion of the jaws is the odontogenic cyst, and when seen in association with an impacted tooth, it is most likely to be a Dentigerous cyst [1]. This is the most common non-inflammatory odontogenic cyst which develops from the epithelial remnants of the dental follicle as a result of fluid accumulation between the follicular epithelium and crown of a developing or unerupted tooth.

Unless noticed on radiographs as an incidental finding, these cysts often remain undetected. They are capable of enlarging unobtrusively and asymptotically, attaining quite large sizes, causing considerable hollowing out of the jaws. It is usually only

when they are associated with pain, infection, inflammation or a visible bony expansion, that they are observed, investigated and diagnosed. A cause of concern is that these cysts may also transform into an odontogenic tumor such as Ameloblastoma and its variants [2], or even into Mucoepidermoid carcinoma [3] or Squamous cell carcinoma. Accurate and precise diagnosis is crucial in order to institute the correct surgical treatment modality and manage the pathology adequately.

When odontogenic tumors present as a radiolucency, they exhibit marked similarities to the odontogenic cysts, with even overlapping histological features. However, they vary considerably from the cysts in their biological behavior, in terms of invasiveness,

aggressiveness, tendency for local destruction, recurrence and malignant transformation; and hence require vastly different therapies and treatment modalities from the former [4]. In this way, what may appear as an innocuous Unicystic lesion, mimicking an odontogenic cyst, may in fact be an aggressive and destructive tumor, adding to its enigma and diagnostic dilemma for the Oral pathologist and a conundrum for the Maxillofacial surgeon as to its most appropriate and ideal management modality [5].

There is a need to make an accurate diagnosis, precisely distinguishing a cyst from a tumor, and also have a clear idea as to the likely prognosis of the lesion, prior to embarking upon instituting the management. Immunohistochemistry serves as a valuable tool in both these respects, guiding both the Oral Pathologists as well as the Clinician to form an informed decision as to the ideal treatment modality to be employed so as to achieve the best overall esthetic and functional outcome for the patient.

Case Report

A 23-year-old male patient reported with the complaint of a swelling on the left side of the face in the region of the lower jaw, for the past five months, which over the past three days, had been accompanied by a dull, deep seated pain in the region. Clinical examination showed a diffuse, firm and tender swelling in the region of the left angle and ramus of the mandible, extending below to involve the inferior border of the mandible, and above, almost up to the temporomandibular joint region (Figure 1A-1C). On intraoral examination, all three left lower molar teeth were missing and the alveolar mucosa in the region appeared swollen and inflamed (Figure 1D). There was no sinus opening or purulent discharge noted intra- or extraorally. There was mild regional lymphadenopathy, and the patient was mildly febrile.

History revealed that he had been operated for a large cystic lesion of the left mandibular angle and body, 11 years ago. Case records revealed that a marsupialization procedure had been carried out when he was a 12-year-old child, and the left lower first and second molar teeth had been removed during the same surgical procedure, however, the third molar tooth germ had been left in situ. The reason given by the then treating surgeon was that the bone of the mandible had been excessively hollowed out and was extremely weak, vulnerable and liable to fracture had removal of the third molar or enucleation of the entire lesion had

been attempted in the young child. The patient had been reviewed for a year, but had not been taken up for surgical enucleation of the remaining pathology and the remnant cyst lining. The patient had thereafter not reported back for follow up until three years ago, when an Orthopantomogram had been taken. It did not reveal any obvious pathology or lesion within the bone, other than the horizontally impacted 38 lying in the angle region of the mandible (Figure 1E).

An Orthopantomogram was taken (Figure 1F), which revealed a large radiolucency involving the left angle and ramus of the mandible extending posteriorly almost up to the tip of the coronoid process and anteriorly up to the missing first molar region. A horizontally impacted third molar lay within the radiolucent space. Non Contrast Computed Tomographic Scans (NCCT) of the maxillofacial region (Figure 1G-1R and Figure 2) showed extensive destruction and hollowing out of the bone in the region of the angle and ramus on the left side with buccal as well as lingual cortical perforation noted at various locations. On corroborating the clinical and radiographic findings with the history, a provisional diagnosis of a persisting and progressing cystic lesion of the left mandibular angle and ramus, most likely, a Dentigerous cyst in relation to the impacted mandibular third molar tooth, with secondary infection, was made. Differential diagnosis included odontogenic tumors such as Ameloblastoma or Keratocystic odontogenic Tumor (KCOT).

The patient was put on Oral Antibiotics and Anti-inflammatory medication for five days, to which he responded very well with a complete resolution of the pain and reduction in size of the swelling. An incisional biopsy was carried out removing a small window of bone through the buccal cortical plate. Histopathological examination of the tissue sample revealed features of a Dentigerous cyst with a hyperplastic epithelium (Figure 1S-1U). Immunohistochemical examination revealed positive expression of Calretinin by the epithelial cells lining the cyst, forming a brownish band-like appearance (Figure 1V and 1W). This was suggestive of a Unicystic Ameloblastoma with no luminal or mural proliferation of the tumor cells. There was positive Ki-67 expression by few of the basal cells of the epithelial lining of the cyst (Figure 1X and 1Y). The Ki-67 Labelling Index was very low LI = 0.9, indicating a tumor of mild aggressive or invasive potential. PCNA labelling index was low as well LI = 0.5 (Figure 1Z).

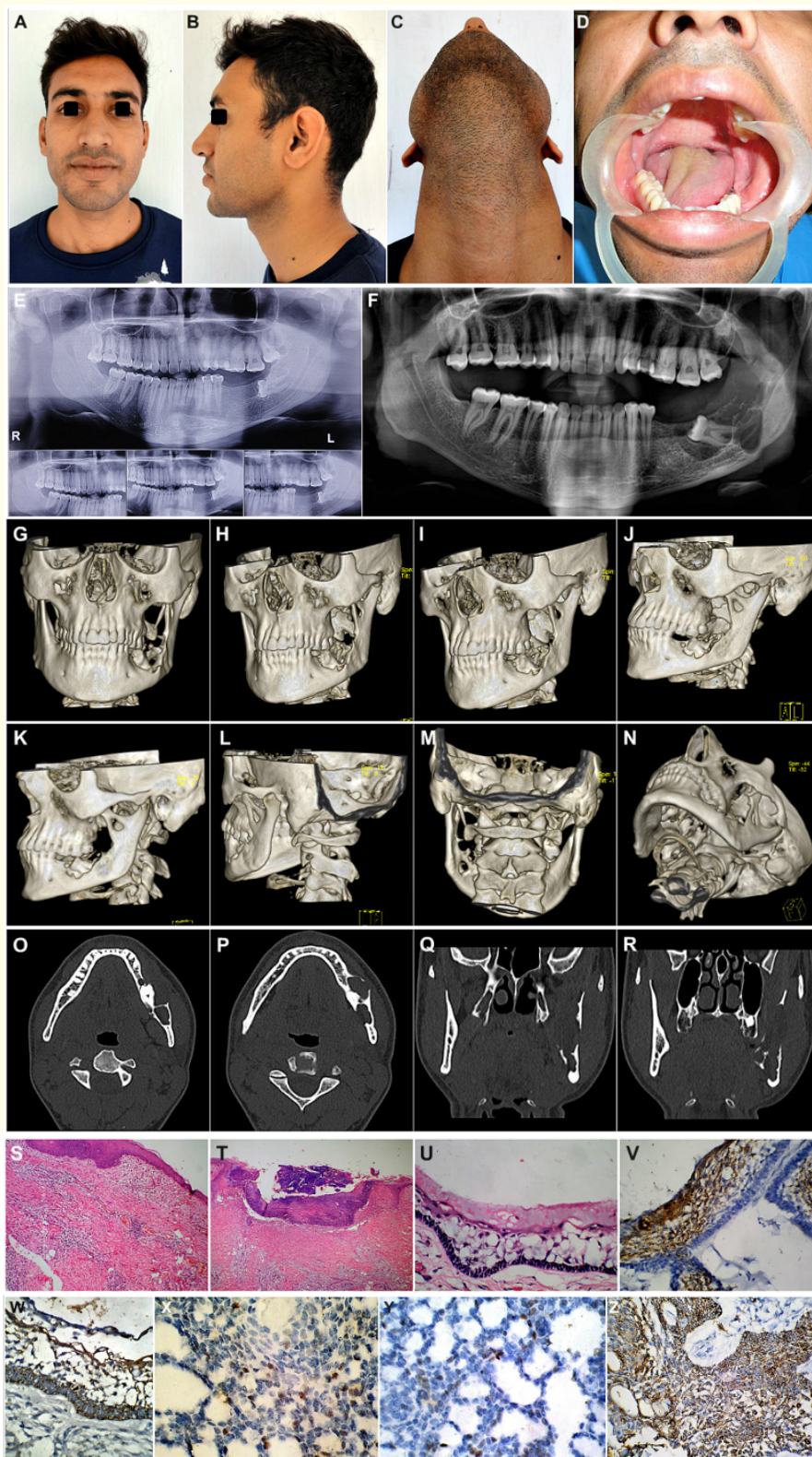


Figure 1: (A-D) 23 yr old male patient who reported with complaints of pain and swelling in the region of left angle of mandible. On intraoral examination, all three molars were missing on the left side. (E) OPG taken at 3 yrs ago, showing no evidence of the radiolucent lesion at that time, but revealing the presence of an impacted mandibular third molar in the region. (F-R) Present Radiographs revealed an extensive unilocular radiolucency involving the left angle and ramus of the mandible extending posteriorly almost up to the tip of the coronoid process. A horizontally impacted third molar lay within the radiolucent space. (S-U) Histopathological examination of an incisional biopsy revealed features of a Dentigerous cyst with a hyperplastic epithelium. (V, W) IH examination revealed positive expression of Calretinin by the epithelial cells lining the cyst forming a brownish band-like appearance. This was suggestive of a Unicystic Ameloblastoma with no luminal or mural proliferation of the tumor cells. (X, Y) There was positive Ki-67 expression by few of the basal cells of the epithelial lining of the cyst. The Ki-67 Labelling Index was very low LI=0.9, indicating a tumor of insignificant aggressive or invasive potential. (Z) PCNA labelling index was low as well LI = 0.5.

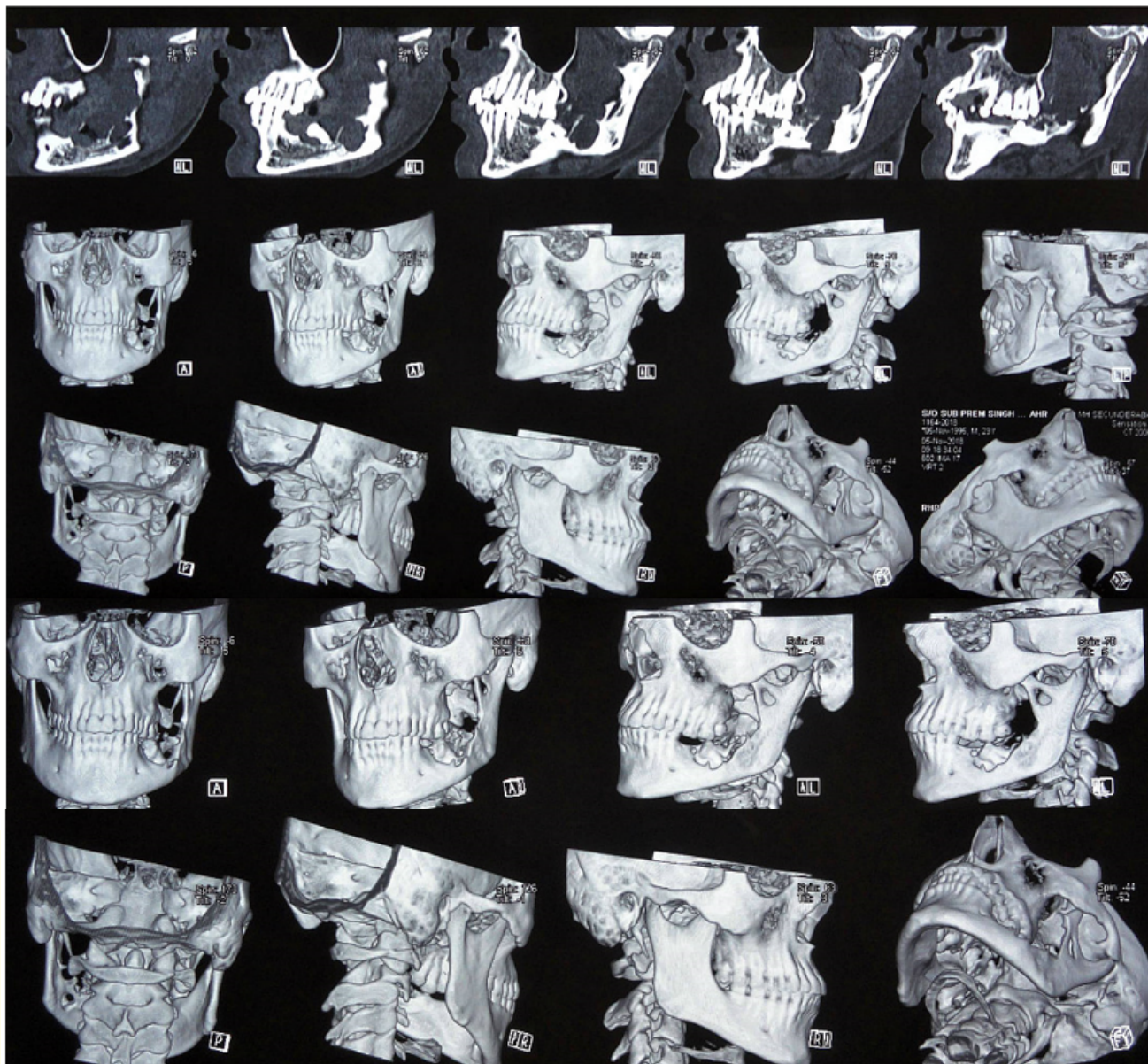


Figure 2: Non Contrast Computed Tomographic Scans (NCCT) of the Maxillofacial region with 3-Dimensional reformatting, showing the extensive hollowing out and destruction of the left angle and ramus of mandible caused by the pathology. A displaced and impacted third molar tooth was evident within the lesion.

The patient was taken up for Enucleation and Curettage of the cystic lesion of the left angle and ramus of the mandible (Figure 3A-3D), via an intraoral approach, removal of the horizontally impacted third molar tooth lying within the lesion (Figure 3E and 3F) and peripheral ostectomy of the residual bony walls. This was followed by chemical cauterization of the walls of the bone defect using Carnoy's solution (Figure 3G and H3), in order to

completely eliminate any persisting or residual tumor cells in the vicinity. Autologous Platelet Rich Fibrin was then placed within the bony cavity (Figure 3I-3L) to accelerate both soft tissue healing in the operated site as well encourage and hasten bone fill with the residual large bony defect of the mandible, so as to facilitate an early rehabilitation of the young patient subsequently with dental prostheses for the missing molar teeth.

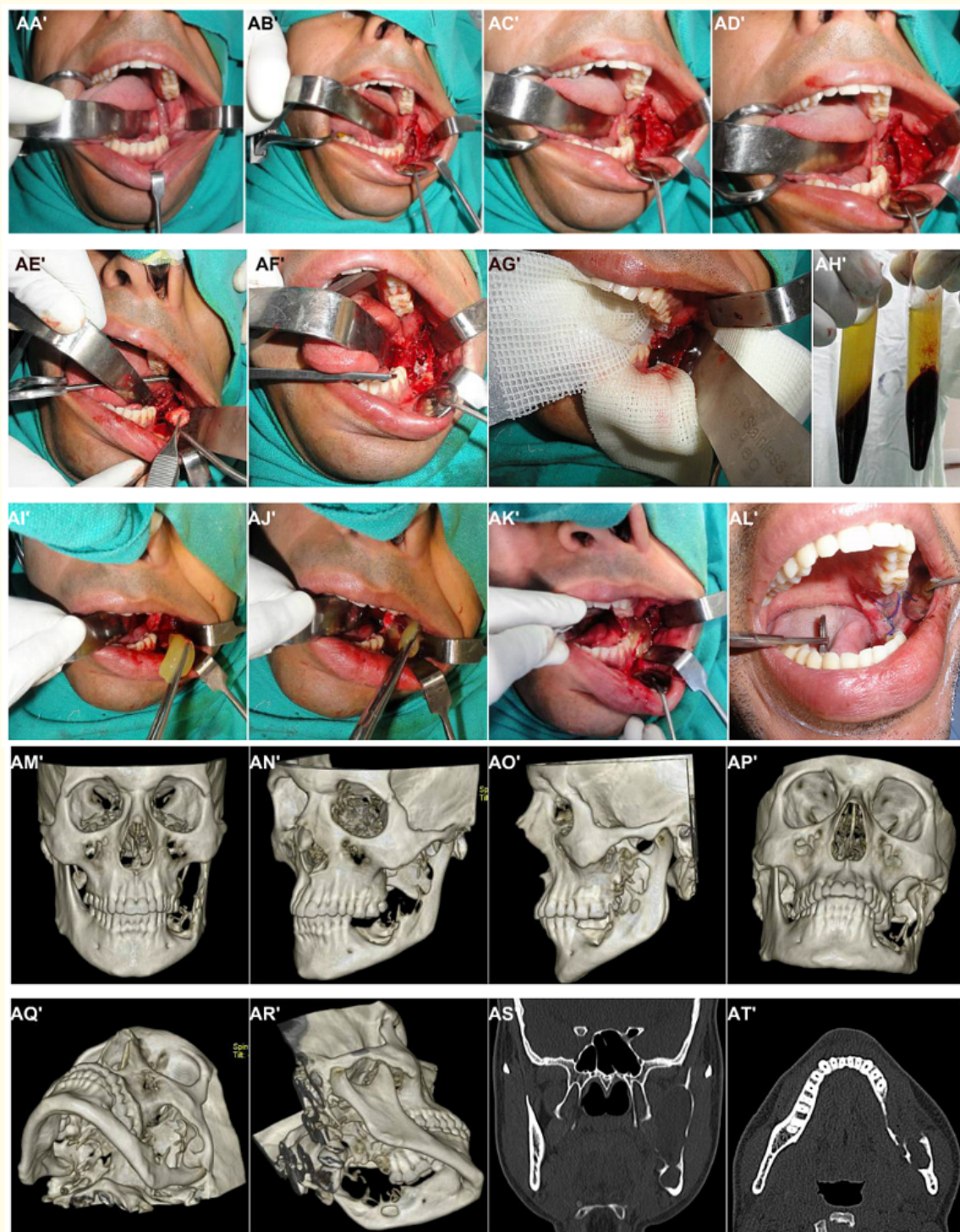


Figure 3: (AA'-AF') Enucleation and curettage of the lesion carried out, along with removal of the impacted third molar tooth. (AG') This was followed by Chemical cauterization of the walls of the bony cavity with Carnoy's solution, taking care to protect the neighboring tissues from the highly caustic substance. (AH' -AL') Fresh autologous Platelet Rich Fibrin harvested from the patient, was placed within the residual cavity to encourage subsequent bone fill and promote quicker reossification of the bone defect. This was followed by watertight closure of the mucoperiosteal flap. (AM' -AT') Postoperative NCCT.

The post-operative recovery of the patient was smooth and uneventful. There was excellent soft tissue healing of the operated site, with negligible postoperative pain, swelling or trismus. Orthopantomogram (OPG) taken before surgery (Figure 4A) showed the extent of bone destruction caused by the ameloblastomatous lesion. OPG taken immediately following surgery (Figure 4B) revealed the extent of bone loss caused by the peripheral ostectomy procedure carried out following the enucleation and curettage, to remove a safe margin of 1mm of bone all along the periphery of the lesion, so as to eliminate all remnants of the tumors cells in order to prevent a possible recurrence of the tumor. OPG at 4 months following surgery (Figure 4C), showed an excellent reossification and bone fill of the large defect.

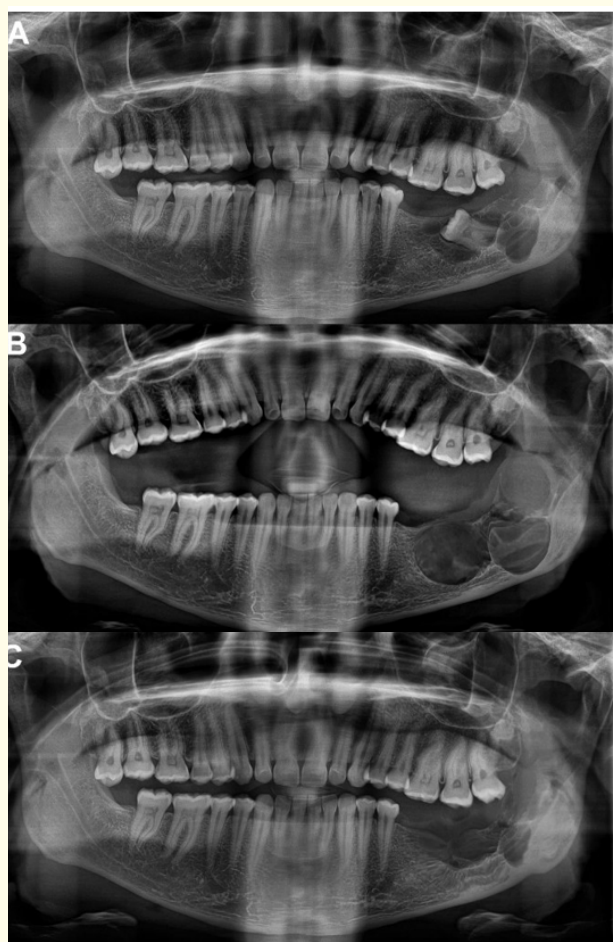


Figure 4: Orthopantomograms (OPG) (A) Before treatment, showing the degree of bone involvement and destruction by the ameloblastomatous lesion. (B) Immediate postoperative OPG, showing the extent of bone loss following the peripheral ostectomy carried out to remove a safe margin of 1cm from all along the periphery of the lesion to prevent possible recurrence of the Ameloblastoma. (C) OPG taken at 4 months following surgery, showing radiographic evidence of a good bone fill and reossification within the bony cavity, bringing about a marked reduction in size of the defect. No evidence of tumor recurrence or extension was noted.

The patient was followed up for a period of two years, with regular clinical and radiological evaluation, and there was no evidence of recurrence of the lesion.

Discussion

The importance and value of the correct diagnosis as well as an indication of the likely prognosis of a destructive jaw lesion cannot be stressed enough. Immunohistochemistry is of immense value, both, as a diagnostic indicator as well as a prognostic indicator, guiding the ideal management protocol to be employed, on a case to case basis [6].

Enucleation is the procedure of choice for removal of most cysts and other benign pathology of the oral and maxillofacial region and involves complete removal of the entity. It is suitable for those pathologies which are surrounded by a capsule, that is anatomically distinct and cleaves easily from the surrounding tissue and is thus amenable to this type of therapy. Physical or chemical curettage may be added to the enucleation procedure in certain pathologies that require additional removal of surrounding bone suspected to have microscopic invaginations of the lesion or satellite cysts/tumours, to help ensure their complete removal and to decrease the persistence and recurrence of the lesion [7]. Curettage may be completed with a sharp curette or a round diamond/tungsten carbide bur with copious cool irrigation to remove 1 to 2 mm of bone containing any pathology remnants.

Meticulous technique in the procedure of enucleation and curettage is particularly important in the surgical management of lesions that tend to have high recurrence or persistence rates, in which case, the addition of Carnoy's solution to curettage or peripheral ostectomy has been shown to be even more effective in decreasing the recurrence rate than are the enucleation procedures alone [8]. This procedure was employed, in this case of Dentigerous cyst showing histopathological evidence of ameloblastomatous change, which by means of corroborating the histopathological as well as Immunohistochemical findings, was precisely diagnosed as Unicystic Ameloblastoma of the luminal subtype.

Immunohistochemical analysis helped in diagnosing the presence of Ameloblastoma by means of the positive expression of Calretinin which is a tumor marker specific for Ameloblastoma and its variants [9]. This diagnosis could have been missed entirely, had histopathological examination alone been relied upon. Further, the low Labelling Index of the Immunohistochemical Proliferative Markers (Ki-67 and PCNA) [10], also helped prevent overtreatment in the form of Jaw resection in this young patient. Institution of additional measures in terms of a vigorous and thorough curettage with peripheral ostectomy of a 5mm margin of bone all along the periphery of the lesion, in addition to chemical cauterization of the bony walls of the residual defect to destroy any remnant tumor cells, would help prevent future recurrence of the lesion [11].

The enucleation and curettage procedure is limited in the treatment of multicystic lesions [12], for which the treatment of choice might otherwise be the Unicystic counterpart [13]. Benign multicystic lesions of the oral and maxillofacial region may have numerous loculations and invaginations that would make access extremely difficult using even an extraoral approach and almost impossible if using an intraoral approach [14]. In addition, the enucleation process may not remove the pathology in its entirety, and physical and chemical curettage may not be able to access or remove all remnants of the lesion. This will invariably lead to persistence of the lesion, particularly a high-recurrence lesion like the Keratocystic odontogenic tumor, or in aggressive benign lesions such as the solid/multicystic Ameloblastoma [14].

Conclusion

In cases of extensive destructive lesions of the jaws, where ambiguity often exists in both diagnosis and appropriate treatment plan, Immunohistochemistry can serve as an invaluable tool in establishing the precise diagnosis, guiding the treatment plan, as well as indicating the likely prognosis of these lesions. Thus, it is of utmost importance to correlate histopathologic findings with clinical and radiographic features as well as Immunohistochemical analysis, to arrive at a correct definitive diagnosis as all such lesions may have prognostically different biologic behaviors and the final diagnosis may alter the therapeutic decision significantly.

Disclosure of Potential Conflicts of Interest

The author of this article has not received any research grant, remuneration, or speaker honorarium from any company or committee whatsoever, and neither owns any stock in any company. The author declares that she does not have any conflict of interest.

Research Involving Human Participants and/or Animals

All procedures performed on the patients (human participants) involved were in accordance with the ethical standards of the institution and/or national research committee, as well as with the 1964 Helsinki declaration and its later amendments and comparable ethical standards.

Ethical Approval

This article does not contain any new studies with human participants or animals performed by the author.

Informed Consent

Informed consent was obtained from all the individual participants in this study.

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