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**Richa Wadhawan**
Senior Lecturer, Department of Oral Medicine, Diagnosis & Radiology, Institute of Dental Education & Advance Studies, Gwalior, Madhya Pradesh, India

**Bhuvnesh Sharma**
Senior Lecturer, Department of Oral Medicine, Diagnosis & Radiology, Institute of Dental Education & Advance Studies, Gwalior, Madhya Pradesh, India

**Pulkit Sharma**
Oral & Maxillofacial Surgery, Institute of Dental Education & Advance Studies, Gwalior, Madhya Pradesh, India

**Dharti Gajjar**
Senior Lecturer, of Oral Medicine, Diagnosis & Radiology, Narsinhbhai Patel Dental College & Hospital, Visnagar, Gujarat, India

**Correspondence**
**Richa Wadhawan**
Senior Lecturer, Department of Oral Medicine, Diagnosis & Radiology, Institute of Dental Education & Advance Studies, Gwalior, Madhya Pradesh, India

# Unicystic ameloblastoma in a 23 year old male: A case report

**Richa Wadhawan, Bhuvnesh Sharma, Pulkit Sharma and Dharti Gajjar**

**Abstract**
Ameloblastomas are infamous for their invasive growth and their tendency to recur. It is a common and aggressive odontogenic epithelial tumor and is rarely metastatic. Radiographically, it appears as an expansile radiolucent, with thinned and perforated cortices, and is known to cause root resorption. As it shares common radiographic features with other lesions such as the giant cell tumor, aneurysmal bone cyst, and renal cell carcinoma metastasis, a definitive diagnosis can only be made with histopathology. Differential diagnosis prior to definitive treatment is mandatory and necessitates a tissue biopsy as this lesion requires to be treated more aggressively than other benign periapical lesions. Moreover, recurrence of Unicystic ameloblastoma may be long delayed and a long-term post-operative follow up is essential for proper management of these patients. Here we are presenting a case of Unicystic ameloblastoma in a 23 year old male patient.

**Keywords:** Mandible, unicystic ameloblastoma, plexiform ameloblastoma, odontogenic tumour

## 1. Introduction
Mandibular swellings can be caused by many benign lesions of odontogenic or non-odontogenic origin. The most common tumor of odontogenic origin is ameloblastoma which develops from epithelial cellular elements and dental tissues in various phases of development. It is a slow-growing, persistent and locally aggressive neoplasm of epithelial origin, affecting the posterior area of lower jaw in 80% of cases. Ameloblastoma is a true neoplasm of the odontogenic epithelium. It is an aggressive benign neoplasm that arises from the remnants of the dental lamina and dental organ (odontogenic epithelium) and patients usually present late in life after the tumor has achieved considerable size, to cause facial disfigurement [1]. The ameloblastoma is a true neoplasm of enamel organ- type tissue which does not undergo differentiation to the point of enamel formation. It is described by Robinson (1937) as a benign tumor that is 'usually unicentric, nonfunctional, intermittent in growth, anatomically benign and clinically persistent.'70% of ameloblastomas develop in the molar-ramus region of the mandible and are occasionally associated with an unerupted third molar teeth [2]. Radio graphically an ameloblastoma can be a unilocular or multilocular radiolucent lesion with a honeycomb or soap bubble appearance. According to the World Health Organization, ameloblastomas are classified into the following types: conventional, Unicystic, and peripheral [3]. Unicystic ameloblastoma refers to those cystic lesions that show clinical, radiographic or gross features of a jaw cyst but on histologic examination show a typical ameloblastomatous epithelium lining the cyst cavity, with or without luminal and/or mural tumor proliferation Unicystic ameloblastoma is a less encountered variant of the ameloblastoma and believed to be less aggressive. It appears more frequently in the second or third decade with no sexual or racial predilection. It is almost exclusively encountered asymptomatically in the posterior mandible [4].
The clinical and radiological simulation of a Unicystic ameloblastoma with mandibular cyst often leads to simple enucleation of lesion. Unicystic ameloblastoma accounts for 10-15% of all extra osseous ameloblastomas in various studies. Whether Unicystic ameloblastoma originates de novo as a neoplasm or whether it is a result of neoplastic transformation of non-neoplastic cyst epithelium has long been debated. It is usually asymptomatic, although a large tumor may cause painless swelling of the jaws with facial asymmetry.

The lesion is often asymptomatic, although a large lesion may cause painless swelling of the jaws. In a clinicopathologic study of 57 cases of Unicystic ameloblastoma, Ackermann classified this entity into the following three histologic groups [5]: Group I—luminal Unicystic ameloblastoma (tumor confined to the luminal surface of the cyst); Group II—intraluminal/plexiform Unicystic ameloblastoma (nodular proliferation into the lumen without infiltration of tumor cells into the connective tissue wall); Group III—mural Unicystic ameloblastoma (invasive islands of ameloblastomatous epithelium in the connective tissue wall not involving the entire epithelium). According to this classification, our case study belongs to Group III. This report highlights the importance of clinicopathologic analysis of any pathology in jaws even if it seems innocuous in clinical as well as radiological examination.

**2. Case report:** A 23-year-old male reported to department of Oral Medicine, Diagnosis & Radiology, Institute of Dental Education & Advance Studies, Gwalior presented with massive swelling of floor of mouth since one month. The general health and medical history of the patient were not relevant. Extra oral clinical examination of the patient was notable for facial asymmetry and a firm swelling in submental region extending to the base of the mandible (Figure 1).

Intra oral examination demonstrated dome shaped bosselated swelling extending to left & right molar region measuring approximately 8 × 8 × 10 cm with overlying undulating skin pinkish red in color displacing 31 32 41 42 (Figure 2). Swelling in the anterior mandible causing obliteration of labial vestibule & floor of mouth. Intraorally, palpation revealed a firm, non-tender swelling with regular borders and teeth 31 32 33 34 41 42 43 44 45 46 had grade-III mobility. There was no nerve deficit in the head and neck. Patient had lymphadenopathy of submental lymph nodes. Vitality testing of the teeth revealed the entire dentition to be vital. Panoramic radiograph (Figure 3) revealed a well-defined, large, expansile, multilocular radiolucent lesion, involving the entire mandible with lateral displacement of the teeth & resorbed roots irt 36 & 47. It also revealed distoangularly impacted 38 48 & mesioangularly impacted 18 28. Hence provisional diagnosis was made as central giant cell granuloma. Subsequently, the patient underwent excisional biopsy of the mandibular mass & extraction of 31 32 33 34 41 42 43 44 45 46. The excised mass was sent for histopathology examination. It revealed a cystic lumen lined by tall, columnar hyper chromatic ameloblastoma like cells. The overlying epithelial cells are stellate reticulum like. The cystic lining is supported by thick fibrous capsule which is infiltrated with plexiform form of ameloblastoma & islands of follicular ameloblastoma showing acanthomatous changes. Some of the follicles are showing micro cyst formation also. The fibrous capsule is dense showing chronic inflammatory infiltrate with numerous blood vessels suggestive of mural type of Unicystic ameloblastoma with predominant plexiform and acanthomatous changes.

**3. Discussion**

The neoplasm was first described by Cusack in 1827 [6]. Etymologically, the name derives from the old French word ‘‘amel,’’ which means enamel, and the Greek word ‘‘blastos,’’ meaning germ or bud.

Over time, this tumor has been referred to by many different names including ‘‘cystosarcoma,’’ ‘‘adamantine epithelioma,’’ ‘‘adamantinoma,’’ and finally ‘‘ameloblastoma’’ [7]. Ameloblastoma shows variable geographic prevalence, being the most common benign odontogenic tumor in China [8] and Africa [9], while it is the second most common in the United States and Canada [10]. African Americans have an overall fivefold increased risk of disease as compared to Caucasians [11]. Global incidence has been estimated at 0.5 cases per million person years, and most cases are diagnosed in patients 30–60 years of age. It is characterized by slow growth and local infiltration into the adjacent tissues [12]. Ameloblastoma is a benign odontogenic tumour usually located in the jaw bone. It arise from either neoplastic transformation of odontogenic cyst epithelium or from residual epithelial rests left over from the formation of teeth, such as remnants of the enamel organ (reduced enamel epithelium) found over the crown of an unerupted tooth, remnants of Hertwig’s epithelial root sheath (rests of Malassez) in the periodontal ligament or remnants of the dental lamina (rests of Serres). Clinically, ameloblastoma appears as an aggressive odontogenic tumour, often asymptomatic and slow growing, with no evidence of swelling. It can sometimes cause symptoms such as swelling, dental malocclusion, pain and paresthesia of the affected area. It spreads by forming pseudopods in marrow spaces without concomitant resorption of the trabecular bone. There are three forms of ameloblastomas, namely peripheral, Unicystic and multicystic tumors. Unicystic ameloblastoma, a variant of ameloblastoma first described by Robinson and Martinez [13] in 1977 is believed to be less aggressive, tends to affect patients at a younger age and its response to enucleation or curettage is more favorable than the classic solid or multicystic ameloblastomas.

Based on the character and extent of tumor cell proliferation within the cyst wall, several histologic subtypes of Unicystic ameloblastoma are recognized, which include those of simple cystic nature, those with intraluminal proliferative nodules and those containing infiltrative tumor islands in the cyst walls. While the first two groups of lesions may be treated successfully by enucleation or curettage, it has been suggested that recurrence following conservative surgery is more likely to occur in the third group and that these lesions should therefore be treated in the same manner as solid ameloblastomas. Unicystic ameloblastoma requires separate consideration based on clinical, radiographic and pathologic features and its response to treatment. Because of its slow growth, recurrences of ameloblastoma generally present many years and even decades after primary surgery. When treated inadequately, malignant development is a possibility. In most cases ameloblastoma has a characteristic but not diagnostic radiographic appearance. Resorption of the adjacent tooth roots is not uncommon [14].

**4. Radiological Features:** The radiographic appearance of an ameloblastoma varies from characteristic soap bubble loculations, to Unicystic and multicystic radiolucencies, to subtle appearances such as expanded follicles of erupting teeth. The most common location is the posterior mandible associated with impacted teeth and follicular cysts, causing expansion of the cortical plates with scalloped margins and perforations with resorption of the involved teeth in advanced stages. Radiographically an ameloblastoma may be mistaken for an odontogenic keratocyst, aneurysmal bone cyst, fibrosarcoma, or a giant cell tumor [15]. Radio logically, the lesions are expansile, with thinning of the cortex in the buccal–lingual plane. The lesions are classically multilocular cystic with a “soap bubble” or “honeycomb” appearance. On occasion, conventional radiographs reveal unilocular ameloblastomas, resembling dentigerous cysts or odontogenic keratocysts [16].

The radiographic appearance of ameloblastoma can vary according to the type of tumour. Computed tomography (CT) is usually helpful in determining the contours of the lesion, its contents and its extension into soft tissues. In a patient with a swelling in the jaw, the first step in diagnosis is panoramic radiography. However, if the swelling is hard and fixed to adjacent tissues, CT is preferred. Although the radiation dose is much higher in CT, the necessity of identifying the contours of the lesion, its contents and its extension into the soft tissues, makes it preferable for diagnosis. Plain radiographs do not show interfaces between tumour and normal soft tissue; only interfaces between tumour and normal bone can be seen. The axial view in contrast-enhanced CT images and the coronal and axial views in magnetic resonance imaging (MRI) clearly show both types of interface. Although there are no appreciable differences between MRI and CT for detecting the cystic component of the tumour, for visualizing papillary projections into the cystic cavity, MRI is slightly superior to provide information regarding edge definition and tumor consistency [17].

**5. Clinicopathological features:** The early ameloblastic changes within the cyst wall were first described by Vickers and Gorlin in 1970, and their histologic criteria for the diagnosis of Unicystic ameloblastoma includes a cyst lined by ameloblastic epithelium with a tall columnar basal layer, subnuclear vacuoles, reverse polarity of hyperchromatic nucleus, and a thin layer of oedematous, degenerating stellate reticulum-like cells on the surface.

The mural extension into the cystic wall is the frequently seen feature, and the term mural Unicystic ameloblastoma is used when the thickened lining (either plexiform or follicular) penetrates the adjacent capsular tissue [18]. A definitive diagnosis of Unicystic ameloblastoma can only be done by histological examination of the entire lesion and cannot be predicted preoperatively on clinical or radiographic grounds. As preoperative incisional biopsy is not representative of the entire lesion, it may result in an incorrect classification. The epithelial lining of a Unicystic ameloblastoma is not always uniformly characteristic and is often lined partly by a nonspecific thin epithelium that mimics the dentigerous cyst lining. Thus, true nature of the lesion becomes evident only after enucleation when the entire specimen is available for microscopy [12]. The pathogenesis of cystic ameloblastomas remains obscure. Whether lesion originates de novo as a neoplasm or whether it is a result of neoplastic transformation of non-neoplastic cyst epithelium has long been debated. Some investigators believe that it arises from preexisting odontogenic cysts, in particular a dentigerous cyst, while others maintain that it arises de novo. Ameloblastomas arise in dentigerous cysts or in others in which the neoplastic ameloblastic epithelium is preceded temporarily by a nonneoplastic stratified squar rence of Unicystic ameloblastoma may be long delayed. Several attempts have been made in the past to distinguish the lining of the Unicystic ameloblastomas from that of odontogenic cysts. However, immunohistochemical markers like lectins (Ulex europaeus agglutinin I and *Bandeiraea simplicifolia* agglutinin I) and proliferating cells (proliferating cell nuclear antigen (PCNA) and Ki-67) may assist in their differential diagnosis. However, Eversole *et al*. contend that currently unaided histologic assessment for Unicystic ameloblastoma remains the gold standard for diagnosis, because of a variable response of neoplastic lesion to tissue markers.

Three clinicopathologic variants of Unicystic ameloblastoma have been described. In the first type (luminal Unicystic ameloblastoma), the tumor is confined to luminal surface of cyst; while the lesion consists of fibrous cyst wall, with a lining that consists partially or totally of ameloblastic epithelium. This demonstrates a basal layer of columnar or cuboidal cells with hyper chromatic nuclei that show reverse polarity and basilar cytoplasmic vacuolization. The overlying epithelial cells are loosely cohesive and resemble stellate reticulum. The finding thus seems to be related to inflammatory edema. In the second microscopic variant (intraluminal Unicystic ameloblastoma), one or more nodules of ameloblastoma project from cystic lining into lumen of cyst. These nodules may be relatively small or they largely fill the cystic lumen. In some cases, nodules of tumor that project into lumen demonstrate an edematous plexiform pattern that resembles plexiform pattern seen in conventional ameloblastoma. These lesions are referred to as plexiform Unicystic ameloblastoma. In the third variant (mural Unicystic ameloblastoma), the fibrous wall of cyst is infiltrated by typical follicular or plexiform ameloblastoma. The extent and depth of ameloblastic proliferation may vary considerably. With any presumed Unicystic ameloblastoma, multiple sections through many levels of specimen are necessary to rule out the possibility of mural invasion of tumor cell [19].

**6. Management:** Two therapy strategies are mentioned in literature: a conservative way of treatment and radical procedures. Non-radical surgical procedures like enucleation and curettage, combined with liquid nitrogen spray cryosurgery, or just drilling of the perilesional bone are mentioned to be useful in Unicystic ameloblastomas, especially in children and young patients. Other authors show high rates of recurrence of ameloblastoma after conservative treatment protocols and therefore recommend radical surgical treatment.

Authors suggest a “rational radical conservative” resection of the mandible with preservation of the lower border of the mandible to maintain the continuity of the lower jaw and the facial contours. In the previous reports, conservative treatments for ameloblastoma appeared to have failed to control local recurrences [20]. Sehdev *et al*, [21] reported recurrence after the conservative approach (curettage) in more than 90% of 92 ameloblastomas. Shatkin and Hoffmeister [22] reported that 86% of 20 mandibular ameloblastomas recurred after curettage compared with a 14% recurrence rate after en bloc resection. However, extensive tumours require a more radical approach. The amount of resection is variable and depends on the site and extension of the tumor. Wide resection of the jaw is usually the recommended treatment for ameloblastoma, should priority be given to the recurrence rate. However, radical surgery often means that the patients have serious complications including facial deformity, masticatory dysfunction and abnormal jaw movement. Considering the characteristics of ameloblastoma as a locally invasive but slow-growing and extremely rare metastasizing benign tumor, the priority of the treatment method should be discussed from the points of morbidity and quality of life of the patients, noting that the recurrence rate is not always the primary factor. When planning the treatment of ameloblastoma, it is important to understand the growth characteristics and to remove the full extent of the tumor, including the surrounding tissues. Otherwise, the remaining tumor cells may lead to multiple morbidities of recurrence. Recent advancements in the understanding of the biological behaviours of ameloblastoma have revealed that Unicystic lesions are well-localized by the

fibrous capsule of the cyst, with few tumors broaching peripheral tissues, whereas multicystic and solid lesions are characterized by an aggressive infiltration to adjacent tissue. Gardner [23] discussed the treatment of ameloblastoma on the basis of pathological and anatomical considerations.

He stated that the recommended treatment for solid and multicystic ameloblastoma was radical treatment, whereas Unicystic ameloblastoma was usually cured by curettage. The Unicystic type is the most benign and is further classified into intraluminal and intramural subtypes. The intraluminal Unicystic subtype does not exhibit invasion of the supporting connective tissue, has the lower recurrence rate of the two subtypes, and may be the only histology amenable to conservative surgical treatment. Cellular atypia and mitotic activity are rarely present in any histologic subtype of ameloblastoma, and any increase in either parameter should raise the suspicion for a malignant process such as ameloblastic carcinoma or odontogenic sarcoma. The clinical and radiographic findings in most cases of Unicystic ameloblastoma suggest that the lesion is an odontogenic cyst. These lesions are usually treated by enucleation. The diagnosis of ameloblastoma is made only after microscopic examination of presumed cyst. If the ameloblastic elements are confined to the lumen of the cyst, with or without intraluminal tumor extension, then cyst enucleation is the treatment. The patient however should be kept under long-term follow-up. If specimens show extension of tumor into fibrous cyst wall for any appreciable distance, subsequent management is more controversial. Some surgeons believe that local resection of area is indicated as a prophylactic measure, while others prefer to keep the patient under radiographic observation and delay further treatment until there is evidence of recurrence. Recurrence rate of 10-20% has been reported after enucleation and curettage of Unicystic ameloblastoma. This is considerably less than 50-90% recurrence rate noted after curettage of conventional solid and multicystic extra osseous ameloblastoma [24]. The probable reason for a bad prognosis is that the Unicystic ameloblastoma is generally cystic, well localized and surrounded by a fibrous capsule. However, once the tumor has broached the periphery of the capsule, it can infiltrate the surrounding cancellous bone and therefore may behave more aggressively.

Preoperative diagnosis of Unicystic ameloblastoma can be difficult or sometimes impossible. An incisional or excisional biopsy may be done depending on the size of the lesion and its clinical features. An incisional biopsy is advantageous if a representative specimen can be obtained. This will provide the clinician with a definitive diagnosis and allow for an appropriate workup before developing a therapeutic protocol. If subsequent microscopic examination confirms an ameloblastoma, the clinician must then decide on additional surgery and take the necessary measures. Recurrence rates also vary for the different procedures used to treat the primary lesion. Several authors have found a recurrence rate of 55 to 90% for all ameloblastomas treated conservatively (enucleation and curettage). However, the incidence of recurrence following radical resection is 5 to 15% [25]. Radical surgery, as defined by Muller and Slootweg [26], is a procedure in which the ameloblastoma is removed with a margin of 'normal bone'. Most investigators believe in resecting at least 1 cm of normal bone beyond the tumor margin. When the tumor has perforated bone, removal of adjacent soft tissue extending to the next adjacent anatomic boundary must be performed to ensure complete tumor-free soft tissue margins. Preservation of the inferior alveolar nerve is not prudent when it is involved by the tumor, and it should be resected en bloc with the specimen in such cases. Immediate nerve reconstruction after extirpation of the tumor restores lower lip sensation for the patient. Reconstruction of the defects with bone graft material allows good functional and esthetic outcome and decreases the number of surgeries. For reconstructing the mandible bone grafts from the iliac crest is preferred. The natural curvature and variable bone height offers the possibility of exact reconstruction of the defect. It is most important to emphasize, to both the clinician and the patient, the need for a definitive treatment protocol and lifetime periodic follow-up for detection of recurrence as even a 5 year tumor- free period does not necessarily mean a cure.

An ameloblastoma is an epithelial tumor similar to a basal cell carcinoma histologically. Therefore, some investigators contend that their radio sensitivities must also be similar. However, radiation therapy is rarely used as a primary treatment. Gardner believes that radiotherapy should only be used for inoperable cases. Other investigators advocate that radiotherapy in conjunction with surgery may have a place in the management of selected patients with recurrence. Pinsolle *et al* [27] believe that surgery and radiotherapy (50 Gy postoperatively) should be used for (1) mandibular recurrences when the first surgical treatment was adequate, (2) for all recurrences and (3) when soft tissue involvement or positive surgical margins are present after a wide resection.

**7. Resemblance with Dentigerous cyst:** This variant of ameloblastoma shows considerable similarities with dentigerous cysts, both clinically and radiographically and some authors have raised the possibility of its origin from a preexisting dentigerous cyst. Furthermore, the epithelial lining of a Unicystic ameloblastoma is not always uniformly characteristic and is often lined partly by a nonspecific thin epithelium that mimics the dentigerous cyst lining. The true nature of the lesion may only become evident when the entire specimen is available for histologic examination [28].

## 8. Conclusion

Ameloblastoma has a high rate of local recurrence if it is not adequately removed. Radical surgical resection of ameloblastoma is the treatment of choice. Especially in cases of large, expansive tumors a radical surgical protocol is a very good option to prevent relapse of the tumor on a long-term basis. Careful clinical examination combined with thorough imaging investigation to evaluate the general aspects of the lesions and the margins, as well as its internal architecture and its relationship to adjacent anatomical structures can be assisted in treatment planning.

This information coupled with clinicopathological confirmation of the diagnosis will allow for the selection of the best individual therapeutic approaches, increasing the treatment efficacy in patients diagnosed with this tumor. The diagnosis of Unicystic ameloblastoma was based on clinical, clinicopathologic and radiographic features. Unicystic ameloblastoma is a tumor with a strong propensity for recurrence, especially when the ameloblastic focus penetrates the adjacent tissue from the wall of the cyst. The ability to predict this potential occurrence prior to surgery would greatly enhance therapeutic strategies for reducing the incidence. Hence, the Pathologist should examine the tissue sections carefully in an attempt to determine whether ameloblastoma has penetrated the wall of the cyst or not so that the complications can be minimized.

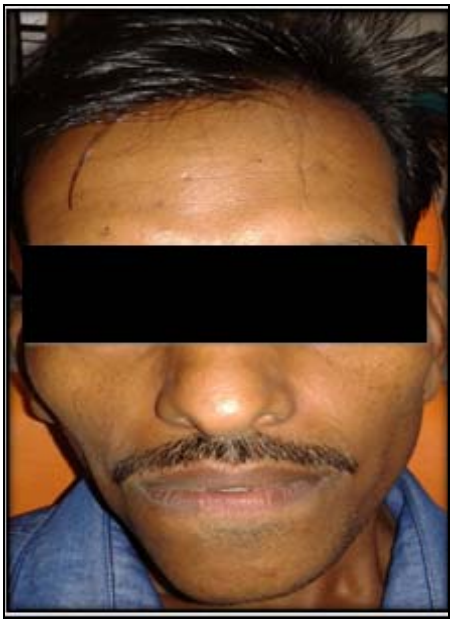

**Fig 1:** A frontal view of the patient demonstrates facial asymmetry with firm swelling in chin region

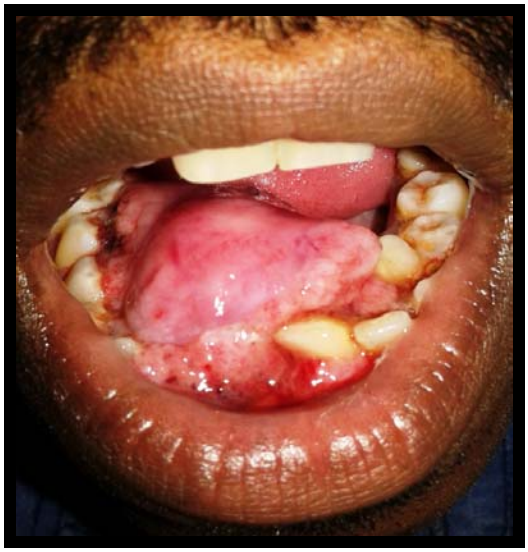

**Fig 2:** Intraoral examination of the patient demonstrates a large mandibular mass.

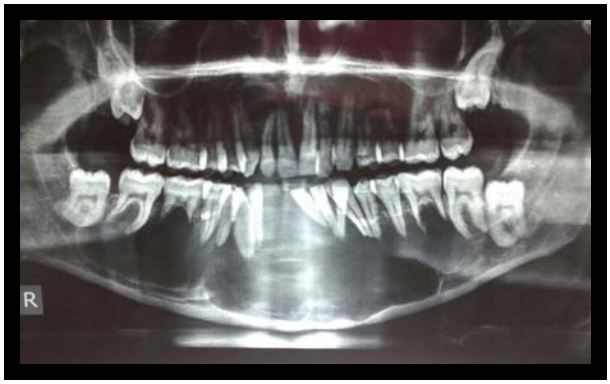

**Fig 3:** Digital panoramic radiograph showing a loculated lesion in the mandible with an expansile lesion with erosive changes, cortical destruction and thinning & displacement of mandibular anterior teeth.

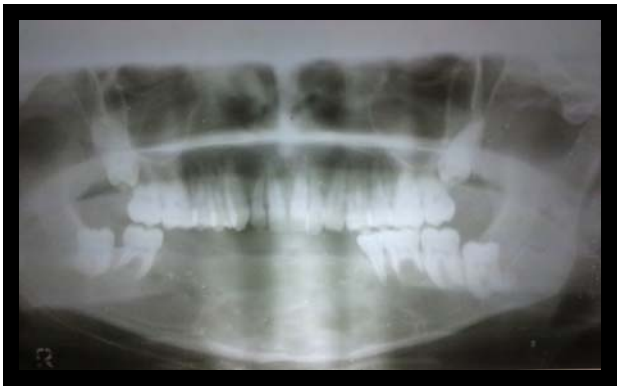

**Fig 4:** Post-operative panoramic radiograph after excision of tumor and extraction of 31 32 33 34 41 42 43 44 45 46

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