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Case Challenge
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Recurrent Left Mandibular Enlargement

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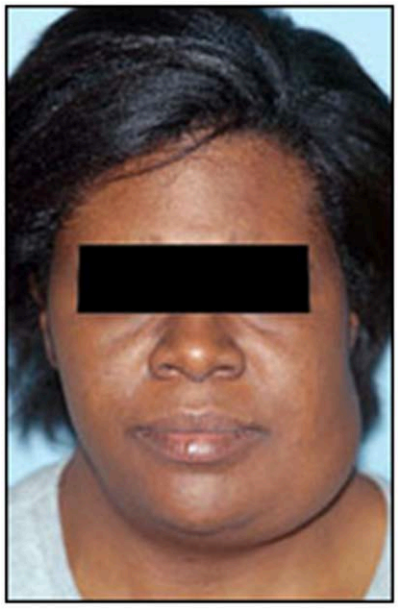


The following Case Challenge is provided in conjunction with the American Academy of Oral and Maxillofacial Pathology.

Case Summary

A 35-year old African-American female presented in February 2002 with enlargement of the left face in the area of the posterior mandible and ramus. The enlargement had extended to involve the submandibular area.

After you have finished reviewing the available diagnostic information, make the diagnosis.

Diagnostic Information

Chief Complaint

The patient's chief complaint was the facial disfigurement and pain produced by the enlargement in the left mandibular area. She also complained of some difficulty swallowing along with mobility and displacement (supereruption) of the mandibular left first molar tooth (#19). (Figures 1-3)

Past Medical History

Other than the facial deformity, the patient was in good general health with no significant medical problems. She had two normal full-term pregnancies, giving birth to a single child in 1999 and twins in 2000. She was pregnant, in the first trimester, with her fourth child at the time of her presentation in February 2002.

She denied any known allergies. She was taking no medication other than prenatal vitamins. A review of systems on physical examination was entirely negative.

History of Present Illness

The patient had been seen in early January 1994 for evaluation of intraoral enlargement of the left mandible in the same general location as the current lesion, although no extraoral involvement was noted as in the February 2002 presentation. Radiographic evaluation at that time (Figure 4) had revealed a "cystic" lesion measuring 3.5 by 3.0 cm associated with an impacted mandibular left third molar (#17).

Tooth #17 and the lesion were removed by another clinician and the defect packed with bovine hemostatic collagen. Following histopathologic

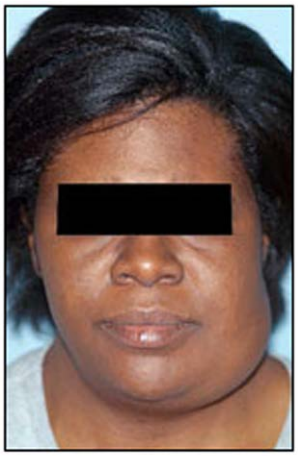


Figure 1. Facial view demonstrates enlargement of the left mandibular body and angle area of the mandible. The enlargement extends into the submandibular region as well.

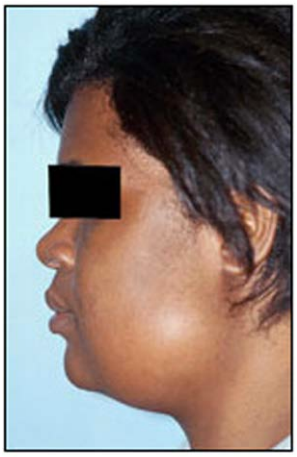


Figure 2. Profile view of the left face reveals involvement of the angle area by the lesion.

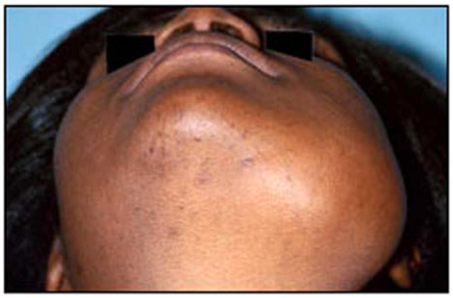


Figure 3. Viewing of the lesion from the submental region shows the involvement of the submandibular area as well as the extent of the buccal expansion.

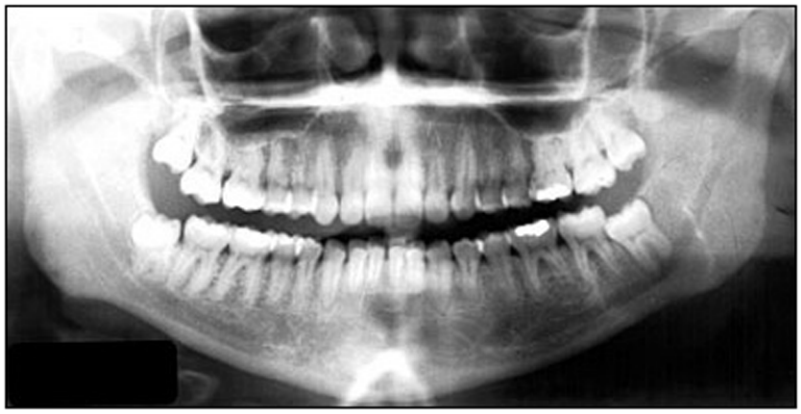


Figure 4. Panoramic radiograph from January 1994 showing impacted #17 and associated radiolucent lesion with a somewhat scalloped, corticated border.

diagnosis, it was decided to follow the lesion closely. The patient returned for follow-up in March 1994, two months after the surgery, at which time a panoramic radiograph "looked good." The next recall was scheduled for June 1994, but the patient failed to return at that time and was lost to follow-up.

The patient first presented to us for evaluation in early February 2002, nearly 8 years following her last visit with the previous clinician. She reported that she had been unaware of any problems in this area until approximately 2 years previously when some extraoral swelling first became evident. At about this same time, however, her husband lost his job due to a disabling injury and she delayed seeking treatment due to financial concerns.

For the last two years she had been having steadily increasing pain in the area of the mandibular enlargement. She had managed this pain by compressing the lateral portion of the mandible until it "burst." She had been doing this with increasing frequency, and she now had to perform this decompression twice a week.

Clinical Examination

Clinical examination revealed diffuse enlargement of the left body of the mandible, extending into the retromolar region and involving the entire alveolar ridge area. While there was some mild expansion lingually, most of the expansion was toward the buccal aspect, partially obliterating the mucobuccal vestibule. (Figure 5) The mucosa overlying the alveolar ridge was intact. The maxillary molar teeth were occluding on the elevated and expanded mandibular alveolar ridge mucosa, producing some visible indentation of the mucosa corresponding to the maxillary molar cusp tips. (Figure 6) Palpation of the mass revealed crepitus along the alveolus around teeth #19 and #20. Distant to these teeth, the mass was "woody" on palpation.

Of note, the mandibular left second molar (#18) was found to be missing on presentation to our service. This tooth had been present at the time of the initial surgery in 1994. When questioned about tooth #18, the patient reported it was extracted at about the time the swelling reappeared in 2000. Mobility of the tooth was cited as the reason for the extraction. The

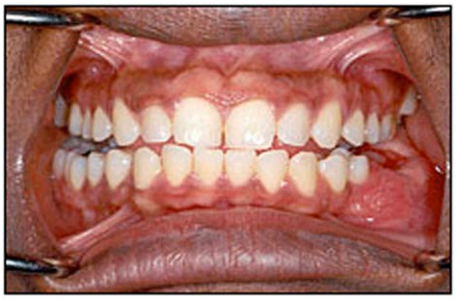


Figure 5. Intraoral view shows expansion of the left mandibular alveolar process in April 2002. Note the buccal expansion obliterating the vestibule in this area. Slight superior displacement of the mandibular left second premolar can also be seen. Tooth #19 has already been extracted and a biopsy sample obtained at the time of this photograph.

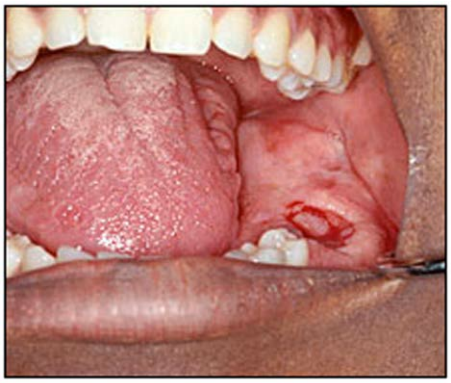


Figure 6. Intraoral view of the left mandibular alveolar ridge in April 2002, following biopsy and extraction of #19. Marked buccal expansion but only minimal lingual enlargement is evident. Soft tissue indentations on the crest of the ridge from occlusion of the maxillary second molar can be seen posteriorly.

recurrent swelling was noted by that practitioner but she reported being told, "it was a benign lesion and not to worry about it."

Radiographic Findings

A panoramic radiograph revealed a markedly expansile, multilocular radiolucent lesion of the left mandible. The borders of the lesion were well defined and, despite the multilocular appearance, it maintained a roughly symmetrical growth pattern. The lesion extended anteriorly to the mandibular left first premolar. Posteriorly, it appeared to extend upward into the ramus slightly and obliterated the normal architecture of the angle. Significant buccal expansion was present, but there appeared to be an intact rim of cortical

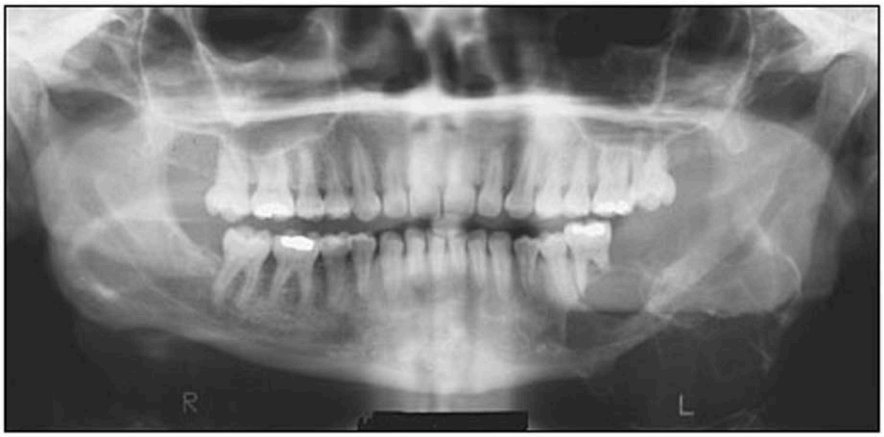


Figure 7. Panoramic radiograph of January 2002 reveals a markedly expansile, multilocular radiolucent lesion of the left mandible and distal root resorption of the first molar.

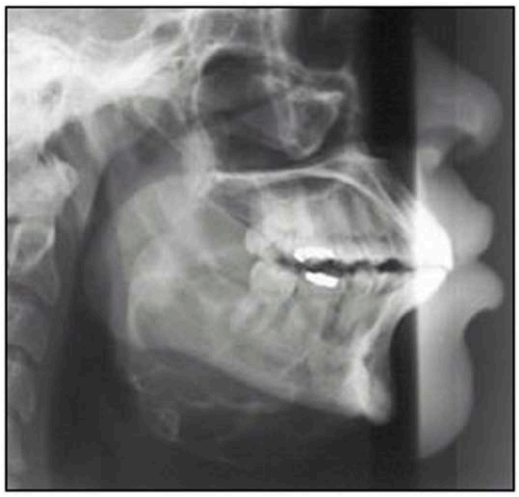


Figure 8. Lateral cephalometric radiograph demonstrates the inferior expansion of the mass in the left mandible, producing the submandibular extension seen clinically. The radiolucent destruction of the left mandible allows clear visualization of the right mandible through the lesion.

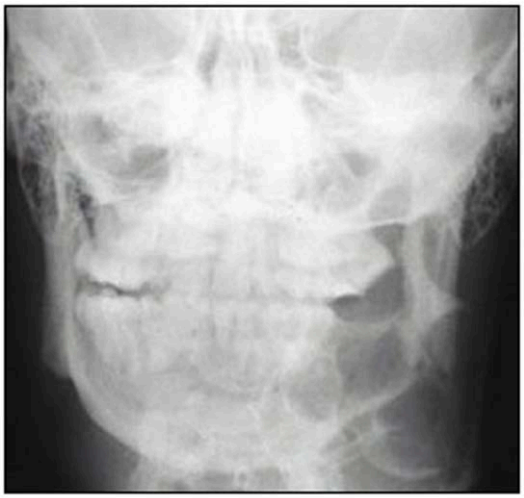


Figure 9. Posterior-anterior cephalometric radiograph of the mandible documents the extent of the buccal expansion.

bone covering the expanded buccal cortex. Superior expansion of the alveolar ridge was also noted. Slight superior displacement of the first molar and second premolar was observed. Distal root resorption of the first molar was also present. Internally, the radiolucent lesion showed numerous bony septations, compartmentalizing the lesion into varying sized locules. (Figure 7)

A lateral cephalometric radiograph (Figure 8) showed essentially the same features. The uninvolved right inferior border of the mandible could be easily visualized through the destructive radiolucent lesion in the left mandible. The lower border of the left mandible appeared to be bowed inferiorly by the expanding mass, a feature that was not as clearly appreciated in the panoramic film. A very thin but intact layer of cortical bone appeared to be present covering this expansion of the inferior border.

A posterior-anterior exposure of the mandible revealed the extent of the buccal expansion, but added little additional information. (Figure 9)

Treatment Plan

Due to the extent of the surgery anticipated to adequately treat the clinical lesion and the

possible untoward effects of such surgery on a developing fetus, the treatment plan called for delaying definitive therapy until the post-partum period. Tooth #19 was extracted in April 2002, due to its mobility and superior displacement. At the time of extraction, portions of the lesion were curetted in order to harvest tissue for microscopic examination and verify the provisional diagnosis. Where possible, disruption of the multiple cystic spaces was attempted during the curettage to facilitate decompression of the lesion. The lesion was packed open in an attempt to control re-accumulation of fluid that was deemed responsible for the patient's pain and increasing lesional size.

The patient returned for follow-up approximately one month later. An estimated 20% reduction in tumor size was noted clinically with less subjective complaints of compressive pressure, pain, and dysphagia. The lesion was re-packed in an attempt to buy time until delivery of the child. By the time of delivery, however, the attempt at decompression of the lesion was failing and most of the earlier reduction in tumor size had recurred. Two months following delivery, allowing sufficient time for the patient to wean the newborn, a hemimandibulectomy was performed.

Histopathologic Findings

Histologic examination revealed curetted fragments of a hard and soft tissue specimen with the architecture of a cyst. The lumen of the cyst was lined by epithelium and was supported by an underlying connective tissue wall of fairly uniform thickness. In many areas, a rim of trabecular bone encased the cystic lesion. (Figure 10)

The epithelial lining showed a prominent, hyperchromatic basal cell layer composed of tall columnar cells with palisaded nuclei. The underlying connective tissue of the cyst wall was well vascularized. (Figure 11)

On higher magnification, the epithelial lining exhibited reverse polarity of the nuclei in the basal cell layer with subnuclear vacuole formation. An irregular, thin layer of parakeratin was present on the luminal surface. A narrow band of acellular, hyalinized collagen was present immediately beneath the epithelium in the underlying connective tissue wall, suggesting an inductive effect by the odontogenic epithelium. (Figure 12)

In one area, the lining epithelium became proliferative, producing an intraluminal nodule with a plexiform growth pattern. However, no intramural growth of the epithelium was noted in this area. (Figure 13)

In other areas of the specimen, proliferating epithelium was seen within the connective tissue of the cyst wall, beneath the lining epithelium intramurally. This epithelium was growing in

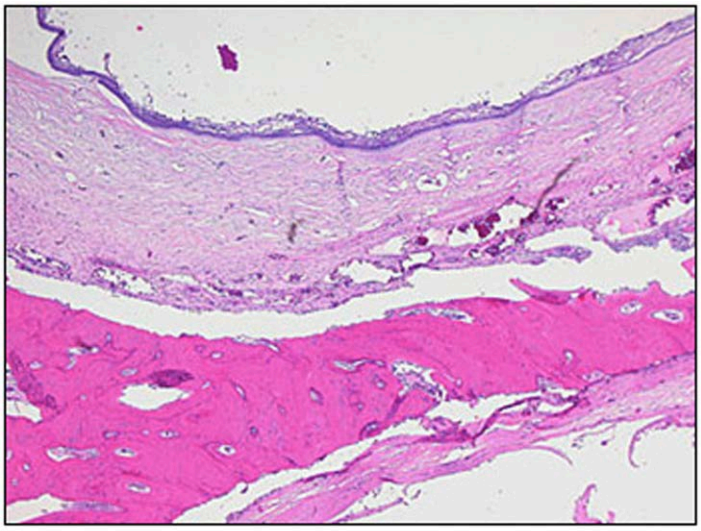


Figure 10. The lumen of the cyst was lined by epithelium and was supported by an underlying connective tissue wall of fairly uniform thickness. In many areas, a rim of trabecular bone encased the cystic lesion.

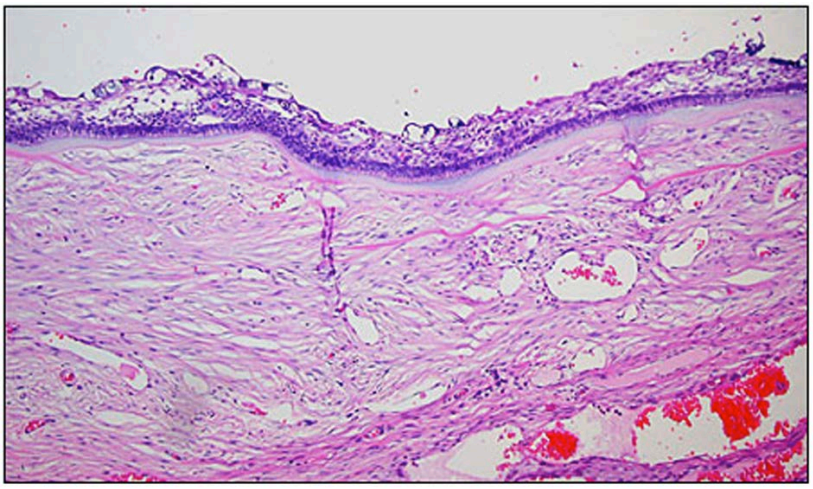


Figure 11. The epithelial lining showed a prominent, hyperchromatic basal cell layer composed of tall columnar cells with palisaded nuclei.

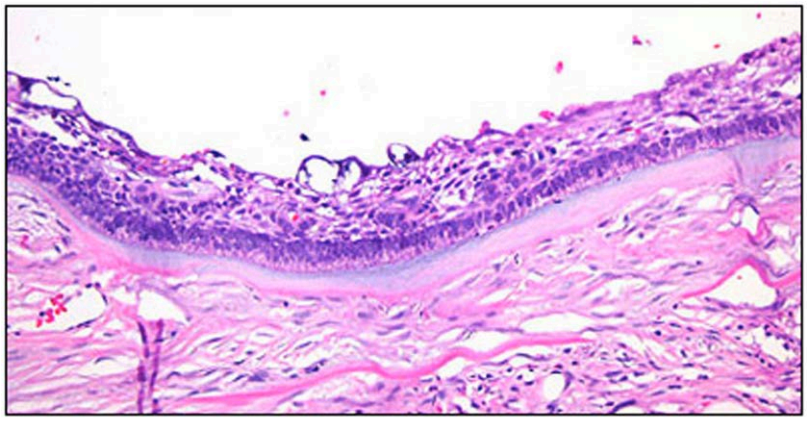


Figure 12. On higher magnification the epithelial lining exhibited reverse polarity of the nuclei in the basal cell layer with subnuclear vacuole formation.

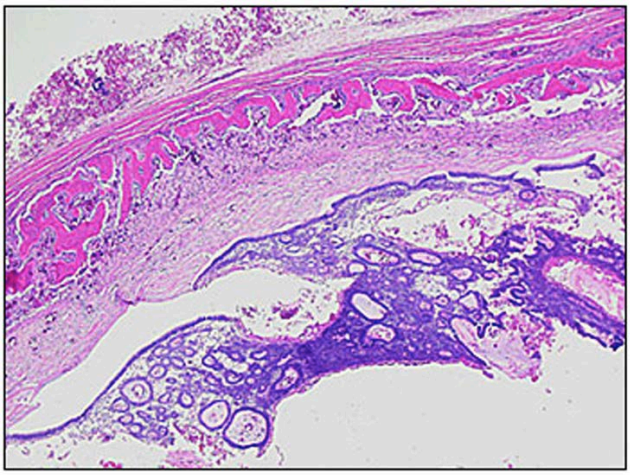


Figure 13. The lining epithelium became proliferative, producing an intraluminal nodule with a plexiform growth pattern. It was noted that there was no intramural growth of the epithelium in this area.

irregularly-shaped islands and elongated cords with the same notable peripheral layer of darkly staining columnar cells. (Figure 14) While some of the islands showed cystic areas in the center, most were solid and the central cells showed features of stellate reticulum. (Figure 15)

On high power magnification, reverse polarity of the nuclei with subnuclear vacuole formation could be seen in these infiltrating epithelial islands. (Figures 16 and 17)

Still other areas of the specimen showed obvious extension of the proliferating epithelium into the surrounding bone. (Figure 18) In addition, the tumor had apparently broken through the bony cortex and was expanding into the soft tissues of the alveolar ridge. (Figure 19)

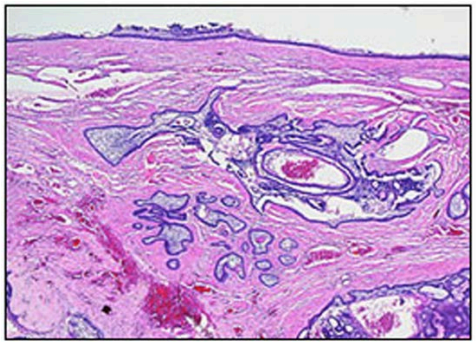


Figure 14. In other areas of the specimen, proliferating epithelium was seen within the connective tissue of the cyst wall, beneath the lining epithelium intramurally.

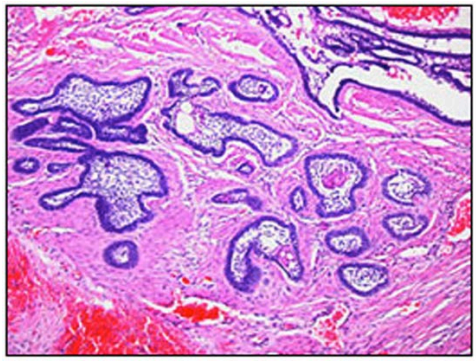


Figure 15. While some of the islands showed cystic areas in the center, most were solid and the central cells showed features of stellate reticulum.

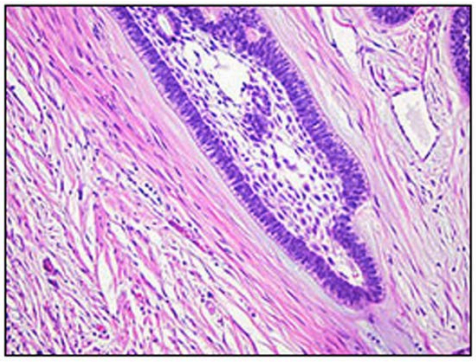


Figure 16. On high power magnification, reverse polarity of the nuclei with subnuclear vacuole formation could be seen in these infiltrating epithelial islands.

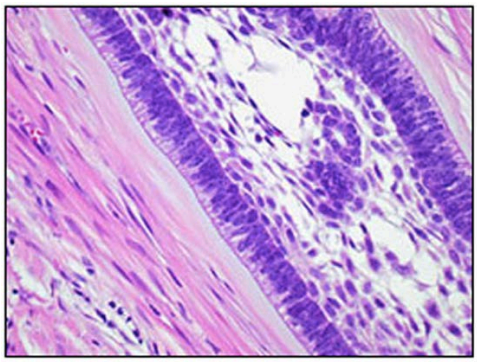


Figure 17. Higher magnification of Figure 16 allows clear visualization of reverse polarity and subnuclear vacuole formation.

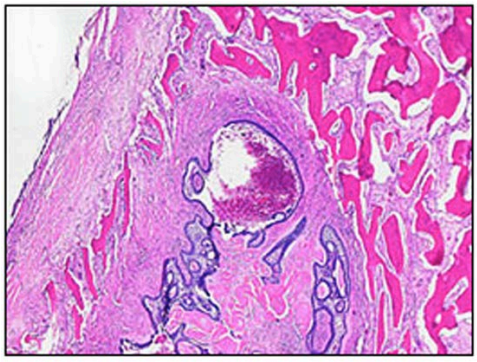


Figure 18. Additional areas of the specimen showed obvious extension of the proliferating epithelium into the surrounding bone.

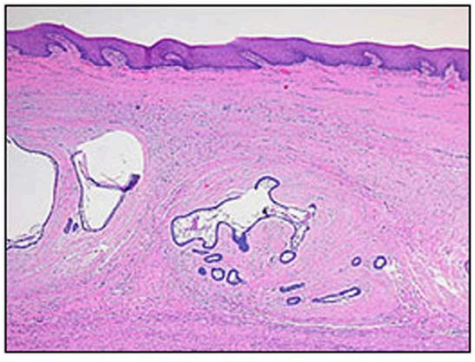
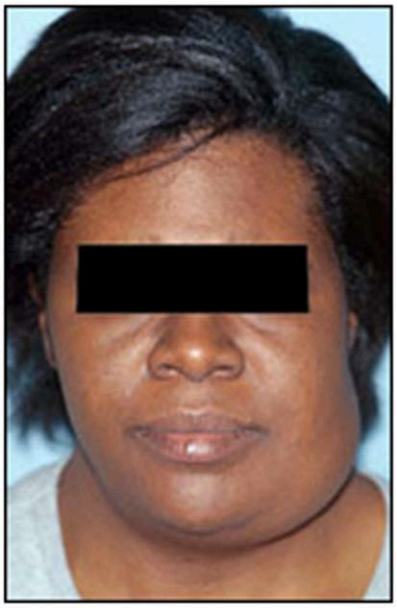


Figure 19. Tumor had apparently broken through the bony cortex and was expanding into the soft tissues of the alveolar ridge.

Can you make the diagnosis?

A 35-year old African-American female presented in February 2002 with enlargement of the left face in the area of the posterior mandible and ramus. The enlargement had extended to involve the submandibular area.



Select the Correct Diagnosis

A. Calcifying Odontogenic Cyst
B. Osteosarcoma
C. Aneurysmal Bone Cyst
D. Ameloblastoma
E. Odontogenic Keratocyst

Calcifying Odontogenic Cyst

Choice A. Sorry, this is not the correct diagnosis.

The calcifying odontogenic cyst, also known as the Gorlin cyst, typically presents as an intraosseous lesion and is found more often in the anterior regions of the jaws than in the posterior areas. Most cases occur in the second and third decades of life. It is most often found to be a unilocular, well-defined radiolucency, although it will occasionally present with a multilocular appearance. In some cases, it can present a mixed radiolucent-radiopaque appearance on radiographs. It usually has a cystic appearance surgically and on histologic examination, although solid variants can also occur ("dentinogenic ghost cell tumor" or "epithelial odontogenic ghost cell tumor"). The hallmark of the calcifying odontogenic cyst is the presence of ghost cell keratinization on microscopic examination, a feature that is not present in this case.

Please re-evaluate the information about this case.

Osteosarcoma

Choice B. Sorry, this is not the correct diagnosis.

Osteosarcoma is a malignant neoplasm of bone. While it often affects young adults, it typically shows a very aggressive clinical growth pattern. The long clinical history in this case would argue strongly against osteosarcoma. Osteosarcoma typically produces a poorly demarcated lesion on radiographic survey, and a multilocular radiographic appearance would argue strongly against osteosarcoma. On microscopic study, osteosarcoma shows malignant mesenchymal cells that produce bone matrix material. These microscopic features were not seen in this case.

Please re-evaluate the information about this case.

Aneurysmal Bone Cyst

Choice C. Sorry, this is not the correct diagnosis.

The aneurysmal bone cyst is an intraosseous lesion that does typically produce a multilocular appearance, as was seen in this case. It is a relatively rare lesion in the jaws, with most cases being seen in the long bones. It most often affects a younger population, with the mean age of jaw lesions being approximately 20 years. Swelling is a common clinical presentation, and a cystic lesion is often encountered at the time of surgery. However, on microscopic examination, the aneurysmal bone cyst shows numerous blood filled spaces of varying size which are surrounded by fibrous tissue containing multinucleated giant cells. These “aneurysmal” spaces do not appear to be blood vessels because they are not surrounded by endothelial cells. These histopathologic features were not present in this case.

Please re-evaluate the information about this case.

Ameloblastoma

Choice D. Congratulations! You are correct.

Treatment and Reconstruction

The patient was taken to the operating room for surgical excision of this mass. Standard operating protocol was followed. She was placed on the operating table in a supine position, general anesthesia was induced, and she was nasally intubated. A posterior throat pack was placed, intraoral and facial areas were prepped with povidone iodine solution, and the patient was surgically draped. Surgeons scrubbed, gowned, and gloved in sterile fashion. Lidocaine 2% with 1:100,000 epinephrine was infiltrated in the maxillary, mandible, and the neck skin incision. The surgical specimen, native mandible, and skin incision site were then marked in surgical ink. (Figure 20)

Arch bars were adapted to the maxilla and mandible. The incision was made extending from the skin in the subcutaneous fascia up to the midline of the mandibular symphysis. The platysma was identified and dissection continued through the superficial cervical fascia. A nerve tester showed the surgical site did not encroach upon the marginal mandibular branch of the facial nerve. The facial vein and artery were identified in the vicinity of the submandibular gland, dissected free, divided, and ligated. The submandibular gland was left intact. The tumor and periosteum were approached. A supra-periosteal dissection was done with continued monitoring of the facial nerve. Many small feeder vessels were dissected free and ligated or cauterized as appropriate. Hemostasis was meticulously kept through the exposure of the mass. Dissection continued until 1.5 cm of uninvolved proximal and distal mandible was noted. Then the dissection was taken into a sub-periosteal plane. Laterally, the dissection was continued up towards the alveolus, without entry into the oral cavity. Medially dissection was difficult due to access around the tumor, so at this time only the proximal site was exposed fully. (Figure 21)

Attention was then directed into the mouth. A bite block was placed on the right and tooth #21 was extracted simply. An intraoral incision was made from this extraction socket around all affected intraoral mucosa. This incision was then connected in appropriate planes to the distal, lateral, and proximal planes created from the extraoral entry. A reciprocating saw was used to make the proximal and distal osteotomies, which allowed the mobilization of the mass to allow access to the medial aspect. Meticulous supra-periosteal dissection continued and the tumor was delivered intact. (Figure 22) Neither the lingual nor hypoglossal nerve was transected. Hemostasis was excellent.

Intermaxillary fixation was secured with the use of the arch bars. A 2.4 locking reconstruction plate was adapted to the mandible to allow the use of 4 holes both proximally and distally. After adaptation, the plate was secured with 8-10 mm screws proximally and 12-14 mm screws distally. A 1.0 x 0.5 x 6.0 cm silicone block with 2 holes was placed and secured to the reconstruction

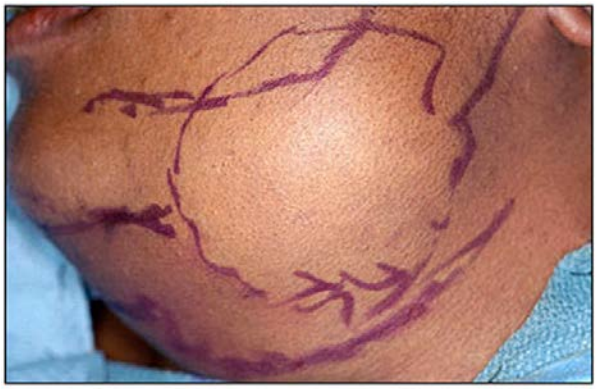


Figure 20. Surgical notation of intended specimen, native mandible, and 10.5 cm skin incision with a steeped anterior Z configuration.

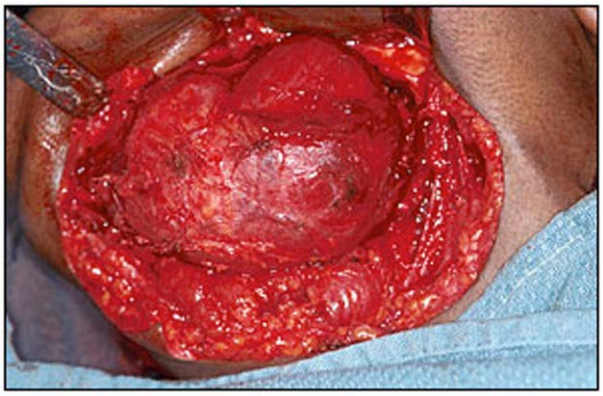


Figure 21. Surgical exposure of the mass in a supra-periosteal plane. Proximal and distal margins of 1.5 cm of uninvolved mandible are present but not clearly visible.

plate with 8 mm screws. This was used to maintain space in preparation for the second stage bone grafting procedure. (Figures 23-26)

The surgical site was irrigated thoroughly. The extraoral wound was closed in a layered fashion with #3.0 resorbable suture closure of the periosteum and platysma layer. A suction drain was placed prior to the closure of the platysma layer and secured with #2.0 non-resorbable suture. Subcutaneous tissues were closed with #4.0 resorbable suture and the skin closed with #6.0 non-resorbable suture. The intraoral cavity was again irrigated thoroughly and the mucosa closed without tension with #4.0 resorbable suture. A dressing was placed over the extraoral wound. The drain was removed on day 3.

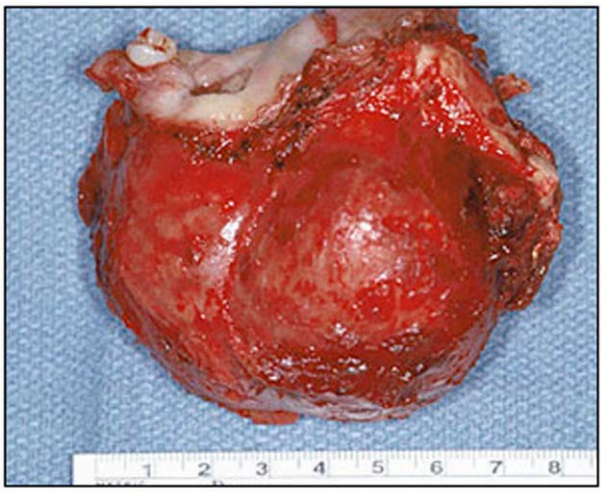


Figure 22. Surgical specimen showing the supra-periosteal dissection plane, intraoral mucosa, tooth #20 and 1.5 cm on proximal mandible. The distal mandible is unseen lying on the table.

Extraoral sutures were removed in phases, with half at 7 days. The remaining extraoral sutures were removed at 14 days and replaced with steristrips for another 2 weeks. The remaining intraoral sutures were also removed at one month. All incisions stayed closed during this time.

Discussion

The ameloblastoma is a true neoplasm of odontogenic epithelial origin. With the exception of the odontoma, which some actually consider a hamartoma rather than a neoplasm, it is the most common odontogenic neoplasm.[1,2] In sheer numbers, if odontoma is excluded, more ameloblastomas are diagnosed than all the other odontogenic tumors combined.[2]

Ameloblastoma affects an extremely broad age range. Cases have been reported affecting children in the first decade of life through elderly

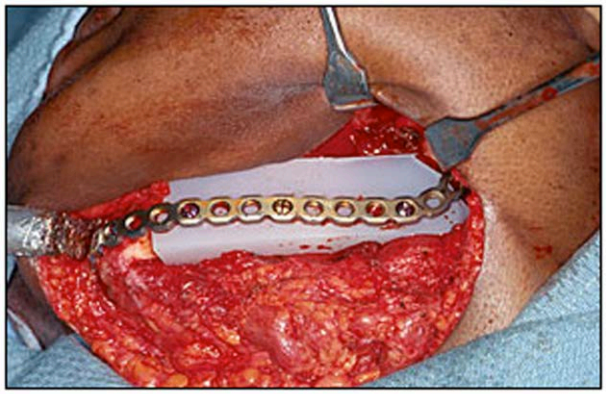


Figure 23. Surgical site after delivery of the mass and primary reconstruction with a 2.4 locking reconstruction plate and silicone block for space maintenance.

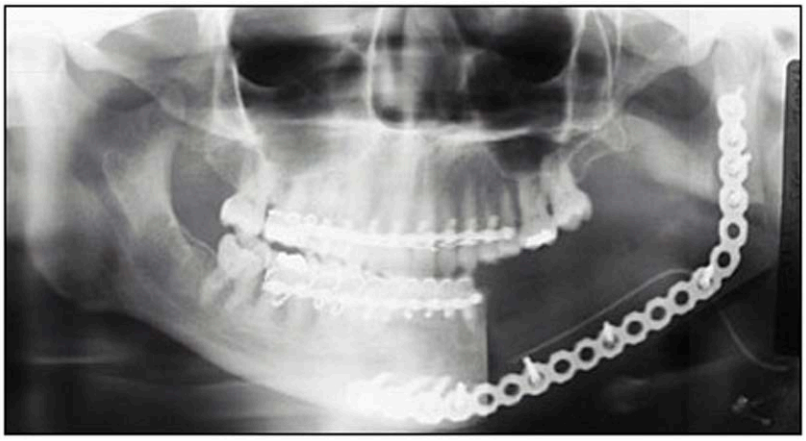


Figure 24. Panoramic radiograph of surgical reconstruction.

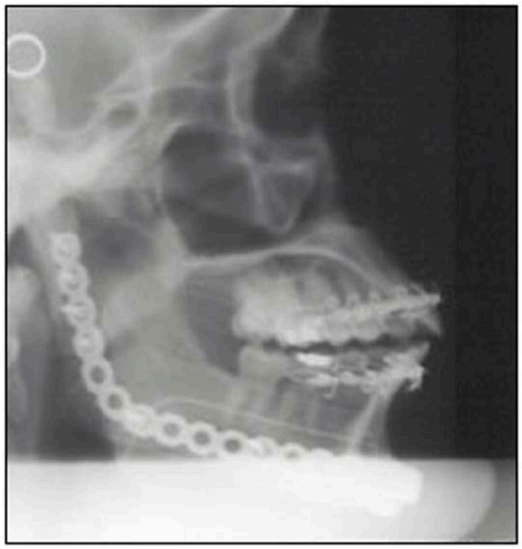


Figure 25. Lateral cephalometric radiograph of surgical reconstruction.

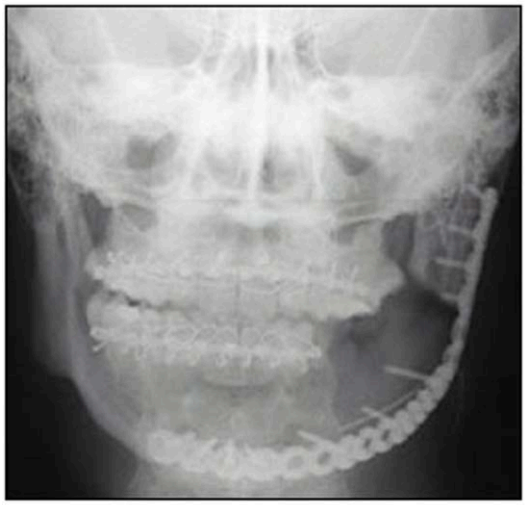


Figure 26. Posterior-anterior cephalometric radiograph of surgical reconstruction.

adults in their tenth decade.[1] The greatest number of cases occur in young to middle-aged adults between the ages of 20-60 years.[2] The average age of occurrence varies slightly when comparing multiple large studies, but it is consistently reported in the 33-39 year age range.[1-4] Only about 10% of all cases arise in children, with less than one-third of those occurring under age 10.[5] No significant sex predilection is noted.[1-4] While some studies report a greater incidence of ameloblastoma in black individuals,[2] sizeable numbers of cases are reported in every racial group. In fact, a biologic profile of 3,677 cases of ameloblastoma reported by Reichart et al[1] noted that Asian individuals made up the largest percentage of patients. Their data included cases culled from numerous individual case reports (693 total) as well as 248 review articles that reported multiple cases. While this demographic data is valuable in helping to characterize the disease in general, considerable variation is seen when individual subgroups are considered separately. For instance, the average age at diagnosis for black individuals (28.7 years) is significantly younger than for whites (39.9 years) or Asians (41.2 years).[1] However, this may be a reflection of the significantly younger age of occurrence of ameloblastoma reported in African patients. Interestingly, the average age of occurrence of ameloblastoma in black patients in the United States shows no statistical difference from white patients, suggesting other factors besides race may have a significant influence on the etiology of the disease. General health status and nutrition have been suggested as possible factors that modulate development of ameloblastoma.[1] This is supported by data that show the average age of occurrence of ameloblastoma in developing countries is 10-15 years younger than in industrialized countries.[1]

Ameloblastoma is found in all areas of the jaws. The mandible is the preferred site with more than 80% of all cases occurring there.[1-4] Whether the lesion occurs in the mandible or the maxilla, there is a predilection for ameloblastoma to occur in the posterior regions. The mandibular molar/angle/ramus area is the site of occurrence for 66% of all ameloblastomas and another 6% occur in the maxillary molar region.[2] Thus, only 28% of all ameloblastomas are seen anterior to the molars, with the mandibular symphysis and premolar regions accounting for three-fourths of those cases.[2] The anterior maxilla (incisor region) is a rare site of occurrence, with as few as 2% of all ameloblastomas reported there in some studies.[3,6] Because of the close association of the maxilla with the paranasal sinuses and nasal cavity, a goodly number of cases are reported involving these structures. One study reports 33% of all maxillary ameloblastomas involve the maxillary

sinus or floor of the nose.[3] The incidence of occurrence of the tumor in different sites within the jaws has been shown to vary among racial groups. Asians have a lower percentage of tumors affecting the ramus area than blacks or whites, while blacks have a higher incidence of involvement of the anterior mandible than other groups.[1] Several authors have reported maxillary tumors tend to occur, on average, at a slightly older age.[3]

The most common presenting complaint of patients with ameloblastoma is the clinical swelling produced by the neoplasm.[1,2,5] The enlargement is typically bony hard on palpation but not painful.[2] Pain may, however, be an accompanying symptom.[2] Lesions tend to already be large when the presenting complaint is the swelling. The average reported size of tumors detailed by Reichart et al[1] was 4.3 cm. When very large, ulceration of the mucosa overlying the involved area may be seen.[1] Small lesions are occasionally discovered, often as an incidental finding on routine radiographic examination or due to other local effects of the neoplasm.[1,2] These effects include delay in normal eruption time of teeth in the area and displacement or mobility of adjacent teeth.[1]

The intraosseous ameloblastoma may present with a variety of radiographic appearances. The most commonly cited appearance is that of a multilocular, soap-bubble radiolucency.[2,7] Debate remains as to whether or not these lesions are truly multilocular. Evidence is accumulating from the use of CT imaging of ameloblastomas that the multilocular appearance seen on plane films and panoramic radiographs may be a reflection of scalloping resorption of the cortical plate by the tumor rather than true septated loculation of the lesion within bone. Multilocular lesions tend to be large and can produce significant expansion of the cortical plates surrounding the lesion. They may be associated with impacted teeth in 15-40% of cases.[7]

Another common radiographic appearance of the ameloblastoma is that of a unilocular radiolucency. Unilocular lesions may or may not be associated with the crown of an impacted tooth. However, more than 50% of unilocular ameloblastomas are associated with an impacted tooth.[7] When an impacted tooth is present, the mandibular third molar is most commonly involved. Unilocular ameloblastomas associated with impacted teeth tend to occur in a significantly younger age group than the multilocular lesions,[1] with a large number of lesions with this radiographic appearance being seen in children.[5]

While for many years it was taught ameloblastoma never produces a mixed radiolucent-radiopaque lesion, Eversole et al[8] in 1984 described the desmoplastic variant of ameloblastoma that can produce a mixed lucent-opaque appearance in approximately 25% of cases.[9] When it presents in this manner, it is habitually misinterpreted as a benign fibro-osseous lesion.[10] The radiopaque component of the lesion is theorized to be unresorbed or newly formed bone trabeculae rather than a product of the tumor.[10] An important diagnostic feature, however, is this variant of ameloblastoma, in contradistinction to the other types of intraosseous ameloblastoma, regularly presents with an ill-defined border to a multilocular lesion.[1,10] Occasional cases of unilocular desmoplastic ameloblastoma have been documented as well.[9,10]

On microscopic examination, six cytomorphologic subtypes of ameloblastoma are recognized: follicular, plexiform, acanthomatous, granular cell, basal cell, and desmoplastic.[2,9] Mixtures of these patterns within a single lesion, particularly when it is a large lesion, are commonly encountered.[2] While there is some minor correlation between histologic subtype and both the age of the patient and the location of the lesion in the jaws, no clinical significance is derived from these findings.[1] Previously, it was generally accepted the cytomorphologic subtype of the ameloblastoma had little or no impact on the expected biologic behavior of the lesion or the treatment.[2,11] However, the study by Reichart et al[1] raises the question of whether the histologic subtype might have an influence on the rate of recurrence. According to their study, the follicular type of ameloblastoma had the highest recurrence rate at 29.5%, while the acanthomatous type showed a recurrence rate of only 4.5%.[1] The other subtypes had recurrence rates that varied between 9.1% and 16.7%.[1] Lesions with a mixed histologic appearance had a recurrence rate of 14.3%.[1]

For many years there has been considerable debate concerning the appropriate treatment of ameloblastoma, and that debate continues even

now. It has been tempered, to some extent, by the recognition of distinct clinical presentations of ameloblastoma that have noteworthy prognostic implications and, therefore, do affect treatment decisions. Therefore, planning for treatment of ameloblastoma currently requires clinical-pathologic correlation. Factors that must be considered when deciding on a treatment approach include: (1) the clinical presentation, (2) the jaw in which the tumor is found, (3) the size of the lesion, (4) the radiographic appearance, and (5) the histopathologic findings.

In this clinical-pathologic correlation of ameloblastoma, three categories are recognized: (1) peripheral ameloblastoma, (2) unicystic ameloblastoma, and (3) conventional ameloblastoma. These three types have each been shown to have a distinctive clinical behavior and differing treatment responses.11 Peripheral ameloblastoma is the least common type encountered, making up 1%-10% of all ameloblastomas.[12,13] It tends to occur in an older population group, with an average age of 51 years.[1,13] It is found in the soft tissues of the gingiva and alveolar ridge without involvement of the bone. The incisor and premolar areas are most commonly affected.[1,12] Occasionally it is seen to produce superficial cupping erosion of the underlying cortical bone as it enlarges, but otherwise, radiographs show no abnormality. It is believed to arise from neoplastic transformation of epithelial remnants of the dental lamina that are commonly found in the gingiva.[1,13] Because it is limited to the soft tissues, complete assured surgical excision should be curative, but recurrence rates are surprisingly high, in the range of 15-19%.[12,13] This has been attributed to incomplete removal rather than aggressive growth characteristics.[13] However, one case of transformation to ameloblastic carcinoma has been documented,[13] and epithelial dysplasia of the overlying epithelium has been reported in another.[12] An additional confounding feature is the report of 5 cases of peripheral ameloblastoma that were not located in the gingiva. These cases were reported in the buccal mucosa and floor of the mouth, areas where remnants of dental lamina are not expected to be found.[13]

Unicystic ameloblastoma comprises approximately 6% of all ameloblastomas.[1] The average age of occurrence is much younger than for ameloblastomas as a whole.[1,7,11,14,15] The mean reported age for unicystic ameloblastoma is 22.1 in one large study.[1] A high percentage of unicystic ameloblastomas are associated with impacted teeth.[5,6,11] In fact, the provisional diagnosis for most unicystic ameloblastomas prior to microscopic confirmation is dentigerous cyst.[11]

Unicystic ameloblastoma presents an ongoing problem in diagnosis. This is primarily due to disagreement among pathologists as to what constitutes a unicystic ameloblastoma. Some investigators have defined unicystic ameloblastoma as “a cystic lesion that shows clinical and radiologic characteristics of an odontogenic cyst, but on histologic examination shows a typical ameloblastomatous epithelium lining as part of the cyst cavity, with or without luminal and/or mural tumor proliferation.”[14] The disagreement stems from use of the term “mural tumor proliferation” as part of this definition. If the ameloblastic epithelium is confined to the cyst lining epithelium or limited in its proliferation to the internal portion of the cystic cavity (i.e., luminal proliferation), conservative therapy, such as enucleation or thorough curettage, should allow for excellent long-term results and a recurrence rate that approaches zero. Nearly all oral and maxillofacial pathologists accept and agree with this concept. This belief is based on the perception that, in its cystic presentation, the ameloblastic epithelium is not yet growing in the invasive pattern (i.e., mural tumor proliferation) that seems to correlate with increased recurrence rates. The problem arises in those cases where there is an obvious cystic ameloblastoma, with or without luminal proliferation of tumor, but the ameloblastic epithelium also shows proliferation into the connective tissue wall of the cystic structure. The epithelium may remain in direct contact with the cystic ameloblastic epithelium or it may appear as separate islands of tumor. Here is where the opinions diverge. As long as the “invasive” epithelium is confined to the connective tissue of the cyst wall and has not penetrated into the surrounding bone, some pathologists will categorize the lesion as a unicystic ameloblastoma. Others reject this concept and believe any mural proliferation, however slight, warrants classification of the lesion as a conventional ameloblastoma. In the absence

of agreement on this critical feature, reporting of lesions as unicystic ameloblastoma is not uniform, and the reported incidence of recurrence of unicystic ameloblastoma reflects this. The recurrence rate for unicystic ameloblastomas is not zero, but is reported, in assorted studies, to range from 10.7% to almost 25%.[7,11] This is still much lower than the reported recurrence rate for conventional ameloblastoma.[1,7,14] This would seem to reflect classification of some conventional cases as unicystic ameloblastomas, inflating what would be an even lower recurrence rate. Some pathologists have further refined their definition of unicystic ameloblastoma and will accept only a unilocular lesion as a true unicystic subtype. Others will accept multilocular lesions as unicystic, if the histologic features are consistent. All tend to agree only by thorough sampling of the entire specimen can an accurate diagnosis of unicystic ameloblastoma be made.[7,11,14]

Conventional ameloblastoma is the best recognized and accepted of the three clinical-pathologic types of ameloblastoma, and it makes up the majority of cases. In Reichart et al's study,[1] 92% of all ameloblastomas were in this category. While some debate about treatment of this type of ameloblastoma remains, the concept it behaves as a locally aggressive neoplasm capable of infiltration of bone and having a high recurrence rate is broadly accepted. Recurrence rates for conventional ameloblastoma show a considerable range. This range is probably due to two factors: (1) the various modalities of treatment that have been used to manage this disease and (2) the inclusion of unicystic lesions with the conventional category in calculating the statistics in some studies.[16] Recurrence rates of as low as 20.6% are quoted,[1] but most studies cite a recurrence rate significantly higher.[6,14] Conservative treatment of conventional ameloblastoma by simple enucleation or curettage has the highest reported recurrence rate, ranging from 55-100%.[3,4,6,11,14] This is believed to be due primarily to the ability of this neoplasm to infiltrate into marrow spaces between small bone trabeculae. Once islands of tumor have infiltrated the bone, they may be protected by a nearly intact bone rim when curettage or enucleation is attempted. (See Figures 27 and 28). These small islands of tumor continue to grow and eventually produce a clinical recurrence.

For this reason, more aggressive treatment of conventional ameloblastoma is generally accepted.[1,2,6,11] Enucleation or curettage following by some type of fulguration of the bony margin is advocated by some.[11] Various chemical agents have been used to attempt to cauterize the edge of the bone, but specific recurrence rates with these type agents are not known.[11] In some cases, peripheral ostectomy using a bone bur has shown good results, with no recurrences being reported with follow-up periods of 2-15 years.[11] Cryotherapy has also been used, with one case free of recurrence at 5 years post treatment.6 Cryotherapy is believed to decrease the chance of recurrence due to devitalization of bone to a depth of 1-3 cm.[6] Bony resection (marginal or en bloc) has also been extensively used to attempt

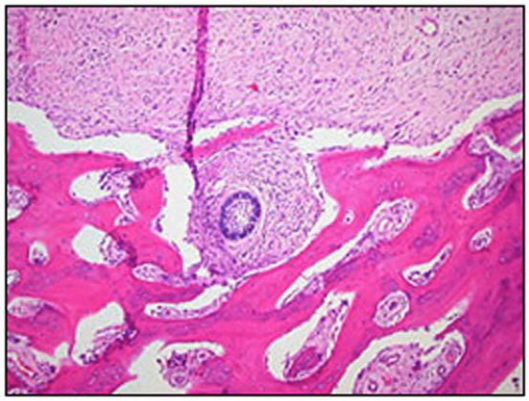


Figure 27. Small island of tumor infiltrating bone within a "protected" area. The connective tissue of the cyst wall is seen at the top of the photomicrograph.

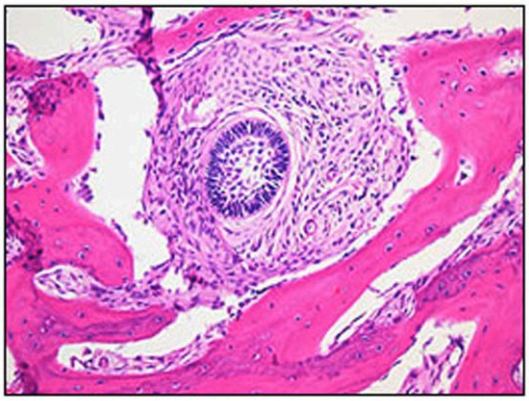


Figure 28. Higher power of the ameloblastic island of epithelium.

to eradicate the lesions. Typically 1-2 cm margins past any radiographic evidence of disease is advised in order to account for the infiltration of intact cancellous bone trabeculae.[2,6] It has been shown tumor islands are invariably present beyond the radiologic border, and recurrence should be expected unless this 1-2 cm "margin for error" is incorporated.[11] While recurrences following resection are somewhat less frequent, a significant recurrence rate is still seen even with this radical approach. The recurrence rate for radical treatment in one study was 17.7%, compared to 22.6%-34.7% for more conservative treatment.[1] In general, the larger the lesion, the more likely small foci of infiltrative growth by the tumor will have occurred, increasing the likelihood of recurrence. Multilocular lesions also tend to show a much higher incidence of recurrence when compared with unilocular lesions.[6]

The insidious nature of the conventional ameloblastoma is manifested by the time of recurrence, even following aggressive resection. While most recurrences occur within the first 2 years, the average time to recurrence was 7.2 years.[1] Late recurrences, 13 years or more following initial treatment, have been reported.[14] For this reason, patients diagnosed with ameloblastoma are typically followed for life. Radiation treatment and chemotherapy have been attempted in the treatment of ameloblastoma, but results are poor compared to the surgical options.[4,6,11] In fact, one study reports the use of radiation treatment or chemotherapy may increase the potential for metastatic spread of the ameloblastoma.[4] The use of radiation treatment or chemotherapy should be reserved for palliative measures in advanced cases where the patient is expected to die of the disease.[4,6,11]

Selection of the treatment approach for conventional ameloblastoma is, of course, based on the best judgment of the surgeon for the individual case but should be highly influenced by the specific location of the lesion in the jaws. Maxillary lesions behave distinctly differently than mandibular lesions. This is attributed to the difference in cancellous bone percentages between the maxilla and the mandible. The spongy osteoarchitecture of the maxilla tends to facilitate the spread of tumor, while the dense cortical plates of the mandible limit, to some extent, the ability of ameloblastoma to spread in that jaw.[1,11] The close association of the maxilla to adjacent vital structures, sinuses, orbit, and the base of the skull, increases morbidity and mortality associated with maxillary ameloblastomas. Whether it occurs in the mandible or the maxilla, once an ameloblastoma has recurred, re-treatment becomes more difficult.[6] Treatment of mandibular recurrences are approximately 80% successful with radical re-treatment. However, re-treatment of maxillary recurrences are far more problematical, and multiple recurrences, even following radical re-treatment, are commonly seen.[6] Several reports of extension of maxillary ameloblastoma to the brain, resulting in the death of the patient, have been noted.[3,6] For these reasons, aggressive treatment of maxillary ameloblastoma is strongly advocated, even for the unicystic ameloblastoma.[3,6] Once there is a recurrence of a maxillary ameloblastoma, treatment is far more difficult and the lesion is often found to invade adjacent critical areas. One study[17] reports a 5 year survival rate of only 16% when initial treatment for maxillary ameloblastoma was limited resection. Maxillectomy is usually the recommended treatment of choice.[6,17]

Approximately 2% of ameloblastomas display malignant behavior by metastasizing.[3] In 75-80% of these cases, the metastatic lesions are found in the lung.[4] Most cases of lung metastasis by ameloblastoma appear to be hematogenous in origin. This belief is supported by tumor foci in the lungs being found diffusely scattered bilaterally, with clusters of tumor cells often found in or surrounding blood vessels.[4] Other sites reported include cervical nodes, bone outside the jaws, soft tissue, and brain,[4] although the brain lesions reported seem more likely due to local disease spread from a maxillary primary. Most metastatic lesions are reported after a delay of more than 10 years from initial treatment. The reported range for metastasis is 3 months to 31 years, with a median disease free interval of 9-12 years.[3,4] Factors that have been implicated in increasing the potential for metastatic spread of ameloblastoma include a long duration of the tumor, large size of the initial presentation, multiple surgeries, multiple recurrences, and the use of radiation or chemotherapy as a treatment modality.[4]

In this case presentation, the patient initially presented with a unilocular radiographic lesion that demonstrated a scalloped margin and was associated with an impacted third molar. The initial biopsy done in 1994 revealed a primarily cystic ameloblastoma but with definite intramural islands of ameloblastoma in the cyst wall. The patient did well for 6 years following the initial surgery, only to develop recurrence in the same site 6 years later. This highlights the danger of recurrence in unicystic appearing lesions that have intramural tumor proliferation, and it emphasizes the persistent slow growth of the ameloblastoma, with the potential for late recurrence many years following initial surgery. Once the lesion recurred, progressive and more rapid growth appeared to be present, eventually producing significant facial disfigurement. A biopsy of the recurrent lesion in 2002 showed a cystic component was maintained in the recurrence and areas of intraluminal proliferation were seen. However, intramural tumor proliferation was also present with extension through the cyst wall and into the underlying bone. The lesion had also perforated the cortical bone of the mandible to extend into the soft tissues of the alveolar process. This necessitated an aggressive surgical resection.

Odontogenic Keratocyst

Choice E. Sorry, this is not the correct diagnosis.

The odontogenic keratocyst is one of the most common of the developmental odontogenic cysts. While it is the lesion that is most likely to produce a multilocular appearance on radiographs, the majority of odontogenic keratocysts present as unilocular radiolucencies. It typically affects patients between 10 and 40 years of age, but has a very broad age range, with elderly adults not uncommonly affected. It has a relatively high recurrence rate. The posterior mandible is the most common location. The histologic appearance of odontogenic keratocyst, however, is quite characteristic. It presents as a cystic lesion lined by epithelium of uniform thickness showing a prominent palisaded basal layer of columnar cells, but without subnuclear vacuole formation. The epithelium is classically 6-10 cell layers thick and has a luminal surface of parakeratin, often with a corrugated appearance. These histopathologic features were not present in this case.

Please re-evaluate the information about this case.

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