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Case Challenge
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The Case of the Post-Extraction Bone Lesion

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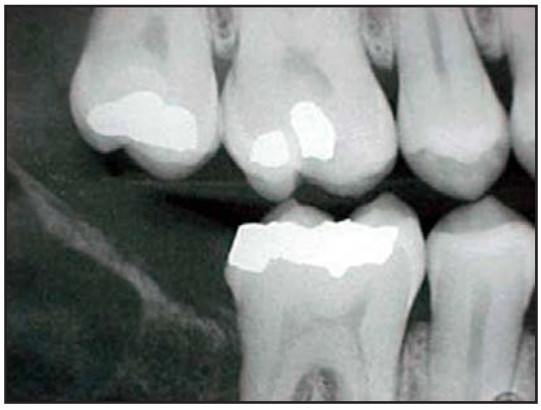


The following Case Challenge is provided in conjunction with the American Academy of Oral and Maxillofacial Pathology.

Case Summary

This case challenge presents a patient with a bone lesion that appeared following the extraction of a mandibular molar.

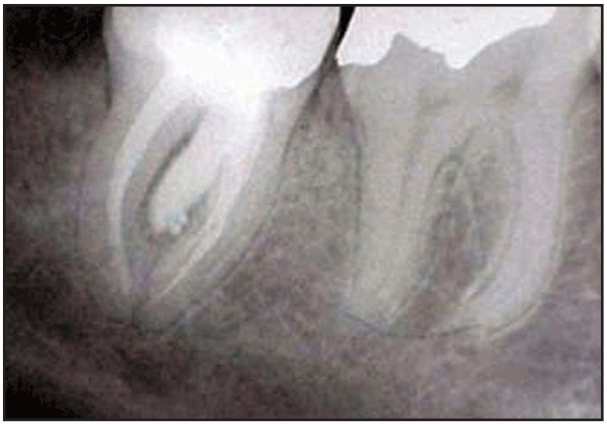
A 28-year old male patient presented for his routine dental health visit which included the bitewing radiograph shown. The radiograph was taken as a follow-up nine months after the extraction of the mandibular second molar by the oral surgeon. The patient had no discomfort and was unaware of any dental problem.

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

Diagnostic Information

Case History

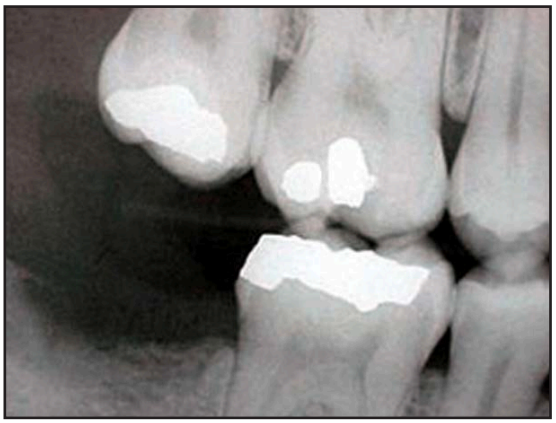
This 28-year old Caucasian male was referred to a general dental office for diagnosis and emergency treatment for pain in the mandibular right second molar area. The mandibular right third molar had recently been extracted and the patient was experiencing continued pain in this area. The patient's chief complaint was "it hurts when I chew something hard or tough like steak." All soft and hard tissue conditions were within normal limits with the exception of slight sensitivity to percussion of the mandibular right second molar. This tooth was non-vital to pulp testing with cold and electricity, and all other teeth tested with normal vitality. A periapical radiograph was taken and appeared as follows:

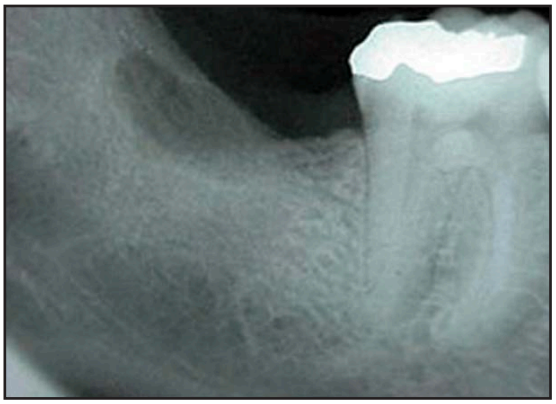


The furcation area of the second molar clearly shows a fracture/perforation with massive obturation material (gutta percha) and sealer exuded more than half way to the apex.

The patient was referred to an oral surgeon's office for extraction of the second molar.

After several months of healing time, the patient was appointed for an initial examination and treatment plan that included the following radiographs in the full mouth series:





The patient returned for a routine six-month dental health visit (which was approximately 9 months after the extraction of the mandibular right second molar) without any complaints and presented with the elements of this case challenge. He was immediately referred to an oral surgeon for an excisional biopsy.

Soft Tissue Examination

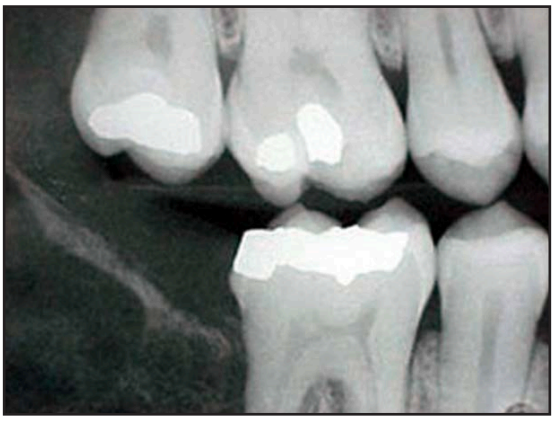
The alveolar ridge in the area of the extracted second molar was slightly bluish with a translucent appearance. The soft tissue had slight expansion bucco-lingually as did the bony cortical plates. There was an absence of fluctuance and no evidence of any exudate. The image below was taken of the alveolar ridge in the area of the extracted second molar.

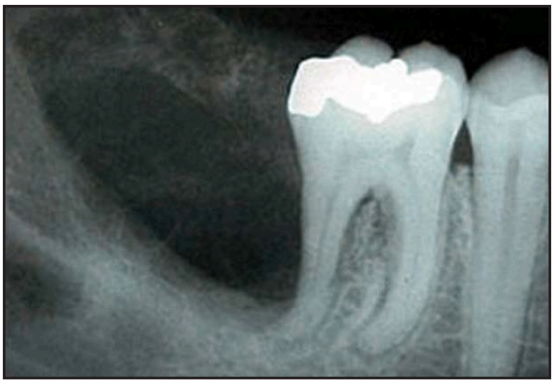
Pulp Vitality Tests

All teeth tested normal to electric pulp testing and cold tests using “Endo-Ice” on a cotton applicator.

Supplemental Periapical Radiograph

The periapical radiograph below was ordered after the bitewing radiograph on the left was examined and a clinical examination was performed. The large radiolucent lesion distal to the first molar appears to have wispy internal septa and osseous expansion.





Excerpts from the Pathology Report

Clinical Surgical Findings: A 6.0 X 3.0 X 2.0 CM radiolucent, multilocular lesion of the right mandible.

The submitted specimen is in two containers labeled A and B. Specimen A comprises multiple, irregular, tan, soft tissue fragments 3.0 X 2.0 X 1.0 cm in aggregation. One of the fragments is cross sectioned revealing solid, brown, gray cut surfaces. Specimen B comprises multiple, irregular, brownish gray soft tissue fragments 3.0 X 2.0 X 0.8 cm in aggregation.

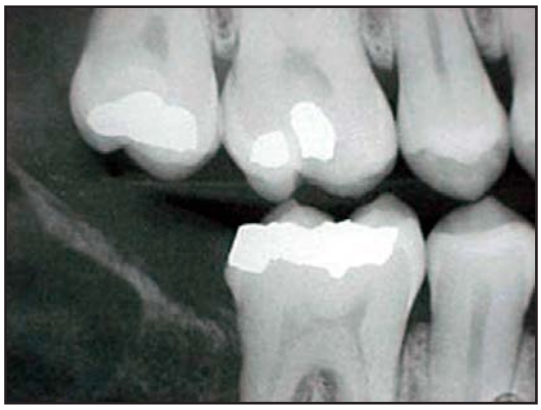
Microscopic Evaluation: Both specimens evaluated in this accession comprises similar morphologic variations. All portions of this specimen are essentially identical.

They reveal a cellular reactive-type response featuring fibroblastic, fibrous histiocytic, and benign giant cells. The giant cells are frequently multinucleated and occasionally smaller epitheliod or binucleated transition forms are observed. The fibroblastic type stroma features tightly-packed, plump, spindle-shaped, or rounded nuclei. These are frequently vesicular and associated with scattered mitotic activity. Hyperchomatism or atypia of stromal nuclei is not observed. The stroma contains large numbers of capillaries and extravasated red blood cells. Fragments of the specimen reveal a peripheral margin of cancellous bone suggesting specimen displacement or replacement of medullary connective tissues by this reactive-type proliferation.

Evaluation of the mitotic activity of the specimen reveal as many as 10 MF per 10 HPF of stromal cells. Additional preparations of this accession are ordered to date to further evaluate cytological details and especially the apparently increased rate of mitotic activity. Mitotic activity is not greater in multiple, additional preparations of the specimens.

Can you make the diagnosis?

This case challenge presents a patient with a bone lesion that appeared following the extraction of a mandibular molar.



Select the Correct Diagnosis

A. Recurrent/Residual Radicular Cyst
B. Odontogenic Keratocyst (OKC)
C. Ameloblastoma
D. Adenomatoid Odontogenic Tumor
E. Central Giant Cell Granuloma

Recurrent/Residual Radicular Cyst

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

This is a good choice considering the dental history of the site, but it was not confirmed histologically.

Please re-evaluate the information about this case.

Odontogenic Keratocyst (OKC)

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

This is the incorrect diagnosis. Although this is a possible diagnosis and should be considered in the differential diagnosis, a keratocyst characteristically presents as a well-circumscribed radiolucency with smooth radiopaque margins.

Please re-evaluate the information about this case.

Ameloblastoma

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

This is a good choice and was the probable clinical diagnosis that was sent to the oral surgeon for referral. This must be included in the differential diagnosis but was ruled out by the histology.

Please re-evaluate the information about this case.

Adenomatoid Odontogenic Tumor

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

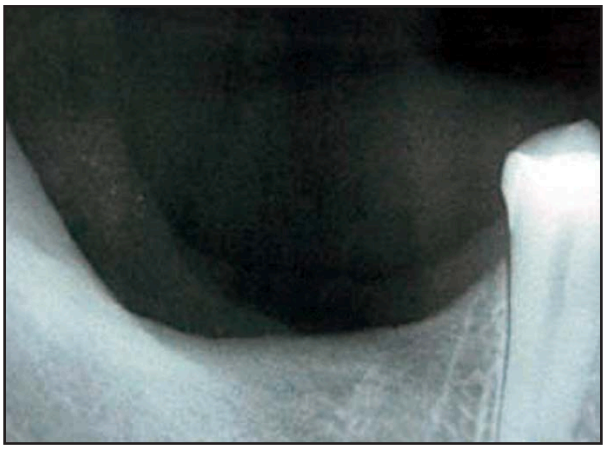
You are incorrect. This is a reasonable choice and should be included in the differential diagnosis. The diagnosis must be confirmed by histology.

Please re-evaluate the information about this case.

Central Giant Cell Granuloma (CGCG)

Choice E. Congratulations! You are correct.

Discussion
The oral pathologist provided the histological information to make the final diagnosis of CGCG described in the pathology report and was appointed for subsequent dental follow-up periods to follow this lesion area. A post-surgical radiograph of the site of the lesion is shown below:



Blood Chemistry
The patient was referred to his physician for evaluation for Hyperparathyroidism.

In a patient with Primary Hyperthyroidism (benign or malignant tumor of the parathyroid glands), the serum calcium levels would most likely be increased and the serum phosphorus levels, as well as serum alkaline phosphatase levels would most likely be elevated.

CGCG can also occur in a patient who has Secondary Hyperparathyroidism. This occurs when parathyroid glands are stimulated to produce excess amounts of parathormone to correct for decreased serum calcium such as in chronic renal disease and osteomalacia. Serum calcium levels in a patient with Secondary Hyperparathyroidism would most likely be increased. On the other hand, serum phosphorus levels would most likely be decreased. The serum alkaline phosphatase levels most likely would be elevated.

Post-surgical Dental Treatment
The patient was provided with a unilateral removable partial denture as an interim appliance to assess the possibilities of tooth replacement with implants for the first and second molars.

Expert System as an Aid for Differential Diagnosis
This case challenge of diagnosing CGCG helps review the thought processes and skills required for lesion evaluation. The case also affords an opportunity to examine the use of a web-based expert system as an aid in diagnosis. The ORAD II system should be used for the following exercise in this case challenge. Please connect to the ORAD II site written by Dr. Stuart C. White at UCLA and enter the patient data provided below for this particular case. Click on the blue highlighted links for descriptions of the data to be entered if you need help. You may use your own assessments of the radiographic appearance to explore various possibilities after applying the following information:

- Sex – Male
- Race – Non-black
- Age – 28
- No pain or paresthesia
- One lesion
- Mandibular site of lesion
- Occurance in molar region
- Radiolucent contents of lesion
- Lesion was 4.0 X 3.0 cm
- Boarders are defined but not corticated
- Multilocular
- Central origin
- Relationship to missing tooth
- Lesion caused expansion of bony cortex
- No root resorption
- No tooth displacement or impaction
- Consider prevalence

This case challenge of diagnosing CGCG helps review the thought processes and skills required for lesion evaluation. In particular, this lesion was a radiolucent type lesion with margins relatively well demarcated and a boarder somewhat characteristic of a CGCG. A CGCG can be either unilocular or multilocular and often has radiographic contents that are “wispy” with internal septa which are seen in this case.[1] The patient experienced no pain and had not even

noticed the cortical expansion or visible soft tissue changes. It has been reported that very aggressive types of CGCG can exhibit rapid growth and produce pain, root resorption, and perforate the cortical bone.[2] More commonly, as was the case here, no root resorption occurs and the lamina dura of adjacent teeth may be missing.[3]

The clinical description of CGCG indicates they occur predominantly in children and young adults usually occurring in the second and third decades and is more common in females.[4,5] CGCG has been reported in facial bones, small bones of the hands and feet, but is mostly found in the maxilla and mandible. Lesions are rarely found in the posterior of an arch as was the case in his report. Normally, the lesions occur in the premolar area forward and can commonly cross the midline.[6]

Considerable controversy exists in the literature regarding the etiology of central giant cell granulomas. As early as 1975, it was reported using a scanning electron microscope (SEM) that there were degenerative features in the endothelial cells within CGCG's.[6] Although the true nature of the origin of CGCG remains unknown at this time, three schools of thought regarding etiology exist. The first proposes the lesion occurs as a developmental anomaly closely related to the aneurismal bone cyst. The second considers CGCG to be a true neoplasm related to the giant cell tumor of long bones. Finally, the third approach proposes that the CGCG lesion is a reparative response to intraboney hemorrhage and inflammation. Normally a traumatic or inflammatory episode cannot be related to the lesion, but in this particular case challenge one could argue that the endodontic material could cause such a response.

Some investigators, on the basis of clinical and histomorphic comparisons, believe that CGCGs are to be part of a spectrum of a single disease process that includes the giant cell tumor.[7] This concept is supported by immunohistochemical studies of both the CGCG and CGT suggesting that p53 inactivation by MDM2 expression is involved in the pathogenesis of both types of lesions.[8]

The clinical and histological features of cherubism have also been compared to central giant cell granulomas (CGCG) and giant cell tumors (GCT).[9] Ruggieri et al[10] have recently reported on a case of an unusual recurrent form of CGCG in the mandible and lower extremeties in a patient with neurofibromatosis type 1. They note the problems of lack of reliable histologic criteria for distinguishing between CGCG, GCT, cherubism, brown tumors of hyperparathyroidism, Jaffe-Campanacci syndrome, McCune-Albright syndrome, Noonan-like/multiple giant cell lesion syndrome, and multiple nonossifying fibromas of bone. One case report of a pregnant 17-year old patient provides a possible relationship of the giant cell lesion to a pre-existing fibrous dysplasia.[11]

Fine needle aspiration biopsy (FNAB) has been used to evaluate histochemistry[12] and cytology[13] of the contents of CGCG prior to surgical treatment. This technique is not widely used since the surgeon must assume the multilocular lesion may be an ameloblastoma. Similarly, the possibility that a multilocular radiolucent lesion might be a vascular lesion must always be considered.[14]

Synopsis

This particular case challenge represents a rapidly developing lesion associated with recent extraction sites. The multilocular radiolucent appearance requires the clinician to consider a wide range of pathology in the initial differential diagnosis. The central origin and expansion of cortical bone helps narrow the differential diagnosis, as does the somewhat "soap-bubble" appearance, instead of a "honeycomb" or "tennis racket" character. The slight radiographic, "wispy," character of the lesion contents is characteristic of CGCG, but the diagnosis cannot be made without the histological examination as was done in this case.

This case challenge was meant to help the general dentist review the process involved in making a differential diagnosis of a clinical and radiographic lesion of which the patient had been unaware until the time of a routine oral examination at a normal dental health visit.

References

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About the Author

Note: Bio information was provided at the time the case challenge was developed.

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Dr. Jensen received his DDS from the University of Minnesota in 1976 and completed a general practice residency at the VA Hospital in Minneapolis, Minnesota in 1978. He then completed a 3-year Post-Doctoral Fellowship in Cariology and also a Ph.D. in oral biology from the University of Minnesota. Dr. Jensen established the Center for Clinical Studies at the University of Iowa and has published extensively and lectured internationally. He is a lifetime Diplomat of the American College of Forensic Examiners, a Fellow of the Academy of General Dentistry, board certified by the American Board of General Dentistry and a Fellow of the Academy of Dental Materials. Dr. Jensen was in private practice and conducted clinical research in Minnesota from 1990 until 2005. He is in private practice in Bay St. Louis, Mississippi and is an Adjunct faculty member of the Department of General Dentistry at Baylor College of Dentistry.

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