36. Wang H, Su Z, Hu Z, Wen J, Liu B. Follicular dendritic cell sarcoma: a report of six cases and a review of the Chinese literature. *Diagn Pathol*. 2010;5:67.
37. Chen T, Gopal P. Follicular dendritic cell sarcoma. *Arch Pathol Lab Med*. 2017;141:596-599.
38. Vermi W, Giurisato E, Lonardi S, et al. Ligand-dependent activation of EGFR in follicular dendritic cells sarcoma is sustained by local production of cognate ligands. *Clin Cancer Res*. 2013;19:5027-5038.
39. Grogg KL, Lae ME, Kurtin PJ, Macon WR. Clusterin expression distinguishes follicular dendritic cell tumors from other dendritic cell neoplasms: report of a novel follicular dendritic cell marker and clinicopathologic data on 12 additional follicular dendritic cell tumors and 6 additional interdigitating dendritic cell tumors. *Am J Surg Pathol*. 2004;28:988-998.
40. Youens KE, Waugh MS. Extranodal follicular dendritic cell sarcoma. *Arch Pathol Lab Med*. 2008;132:1683-1687.
41. Shia J, Chen W, Tang LH, et al. Extranodal follicular dendritic cell sarcoma: clinical, pathologic, and histogenetic characteristics of an underrecognized disease entity. *Virchows Arch*. 2006;449:148-158.
42. Flood K, Stroud C, Lazarova Z, Vigneswaran N, Hsu S. Paraneoplastic pemphigus without antibodies to desmoglein 1 and 3. *Dermatol Online J*. 2018;24:4.

CLINICAL PATHOLOGIC CONFERENCE CASE 6: A MIXED RADIOLUCENT/RADIOPAQUE LESION OF THE POSTERIOR MANDIBLE: AN UNANTICIPATED FINDING

Angela C. Ritchie,[a] and Duane R. Schafer[b], [a]Indiana University School of Dentistry, Indianapolis, IN, USA, and [b]University of Tennessee Health Sciences Center (UTHSC) College of Dentistry, Memphis, TN, USA

Case Presentation: A 35-year old African American woman presented to an outpatient dental office for a routine dental appointment. The dental examination included panoramic radiographic study, which revealed an intact, well-maintained adult dentition, notable for missing maxillary third molars and mesioangular impaction of teeth #17 and #32 (Figure 1). Distal and immediately superior to the impacted tooth #17 was a well-demarcated, homogeneous, mixed radiolucent/radiopaque lesion, measuring 2×1.8 cm and causing slight compression and inferior displacement of the inferior alveolar nerve canal (Figure 2). The intraoral clinical examination of the left posterior mandible revealed no appreciable swelling in the area, and the patient reported no associated pain or discomfort. Review of the patient's medical history was significant for the diagnosis of invasive ductal carcinoma in her breast 3 years earlier. At the time of diagnosis, the tumor had been staged as IIIA, which encompasses both T(0-2)N2 M0 and T3 N(0-2)M0, according to the TNM (tumor–node–metastasis) classification; the significance of this is the recognition of abundant local disease with axillary lymph node involvement but, importantly, lack of the presence of distant metastasis at time of diagnosis. The patient reported that she subsequently underwent adjuvant therapies appropriate for the type and staging of the disease.

Differential Diagnosis: A preliminary differential diagnosis was established, and it included both reactive and neoplastic benign fibro-osseous lesions, several odontogenic tumors that contain or produce calcified matrix material, and the possibility of mandibular bone involvement by metastatic disease.

Benign fibro-osseous lesions are a sundry group of pathologic entities defined by replacement of normal bone by fibrous tissue intermixed with new mineralized product. Lesions in this category include fibrous dysplasia, focal cemento-osseous dysplasia and ossifying fibroma, all of which are significant lesions that had to be included in the differential diagnosis of our patient's lesion.

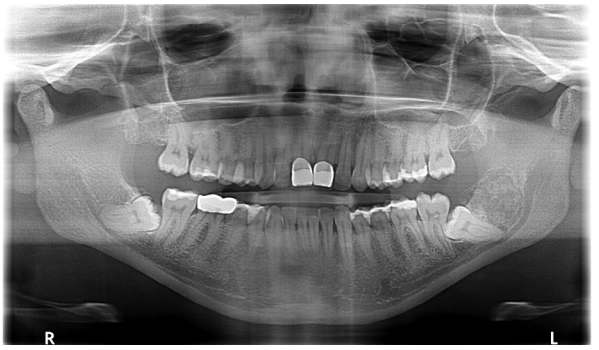

Fig. 1. Panoramic radiograph demonstrating a 2×1.8 cm, well-demarcated, mixed-density lesion in the left posterior mandible.

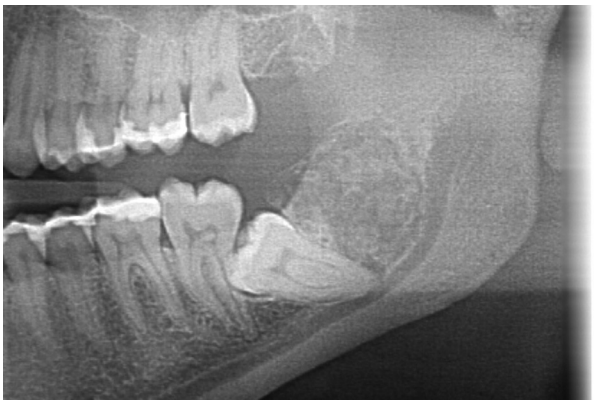

Fig. 2. A portion of the panoramic radiograph demonstrating mild bony expansion of the intrabony lesion with slight decompression and inferior displacement of the inferior alveolar nerve canal.

Fibrous dysplasia is a bone disorder wherein during skeletal growth normal bone is replaced by a dysplastic proliferation of fibrous tissue and woven bone.[1] This condition results from a mutation in the *GNAS* gene and can present as a unifocal lesion confined to one bone (monostotic) or multifocally (polyostotic) anywhere in the skeleton. The majority of patients with fibrous dysplasia have disease limited to a single bone with the initial clinical signs and radiographic changes arising during the first 2 decades of life. When fibrous dysplasia affects the gnathic bones, the maxilla being more frequently affected than the mandible. Regardless of jaw partiality, there is a demonstrative predilection for the posterior region.[2] Unlike the findings in our patient, fibrous dysplasia typically presents as a slow-growing swelling. However, when affecting the craniofacial region, the radiographic appearance of fibrous dysplasia can be quite variable to include well-defined or ill-defined borders and only minimal bone enlargement, and the changes may be confined to the normal anatomic contour, similar to what was seen in the remodeled alveolar crest of the retromolar region of our patient.

Cemento-osseous dysplasia is a benign reactive condition confined to the tooth bearing areas of the jaws, with proposed origin from the periodontal ligament.[2] Three types of cemento-osseous dysplasia are recognized: periapical cemental dysplasia, focal cemento-osseous dysplasia, and florid cemento-osseous dysplasia.

Focal cemento-osseous dysplasia (fCOD), as the term implies, is localized to a single site of involvement with a peak incidence during the fourth and fifth decades of life.[3] It is most common in African American females. The mandible is affected with greater frequency than the maxilla, and distribution between the anterior and posterior sextants is relatively even. In general, fCOD seems to have a limited growth capacity, with most lesions being smaller than 1 cm. Clinical expansion is not a commonly encountered feature, with the majority of patients being asymptomatic and unaware of the lesion. An important diagnostic feature of fCOD, not present in our case, is the ubiquitous intimate association with the root apices of a carious/restored tooth or in a site of tooth extraction. Radiographically, the majority of fCOD presents as a predominantly opaque or a mixed radiolucent/radiopaque lesion with an ill-defined border. Progressive mineralization of the lesion has been documented in numerous radiographic series, and if accurately recognized as fCOD, no treatment is necessary for the asymptomatic patient.

Ossifying fibroma is a benign neoplasm composed of fibrous stroma and bone elements showing various degrees of maturation.[4] Clinically, ossifying fibroma occurs over a wide age range, with a noted predilection for females. The most frequently encountered locations are the mandibular premolar and molar areas. Smaller ossifying fibromas are usually asymptomatic and detected on screening examinations, as in our case. Larger tumors can produce significant swelling and facial deformity, with downward bowing of the inferior border of the mandible considered a "characteristic" radiographic finding.[2] However, the comprehensive radiographic presentation can be quite variable, with the amount of calcification present being dependent on the maturity of the lesion. Early lesion may appear entirely radiolucent and only demonstrate increased production of calcified matrix and subsequent radiopacity with time. A thin radiolucent periphery is a consistent finding and correlates with the relative ease of enucleation reported with the smaller tumors. Larger lesions causing significant deformation, belying their benign categorization, often require radical surgical resection.

The list of odontogenic cysts and tumors that can present radiographically as a well-demarcated mixed radiolucent/radiopaque lesion is somewhat limited and includes ameloblastic fibro-odontoma, adenomatoid odontogenic tumor, calcifying epithelial odontogenic tumor (CEOT), and calcifying odontogenic cyst.[5] On the basis of the clinical and radiographic findings in our case, CEOT, or Pindborg tumor, was given strongest consideration. CEOT is a rare neoplasm of odontogenic epithelium accounting for 0.4% to 3% of all odontogenic tumors.[6] Similar to the presentation in our patient, CEOT is most often encountered in patients between ages 30 and 50 years and arise in the posterior portion of the mandible.[7] However, the most characteristic clinical presentation is that of an asymptomatic, slow-growing, expansile intraosseous mass, whereas there was no appreciable expansion in our patient. The CEOT has a variable radiographic pattern, depending on the size as well as the location of the tumor, with the most common radiographic presentation being that of a mixed radiolucent/radiopaque lesion associated with an unerupted tooth.

Metastatic disease is the most common form of cancer involving bone; however, it rarely involves the bone of the craniofacial region.[2] When metastatic dissemination of a disease does occur to the oral cavity, the molar region of the jaws is the most frequently involved site.[8] The most commonly encountered cancers that metastasize to the oral cavity in females include primary lesions from the breast, the female genital organs, kidneys, and the colorectal

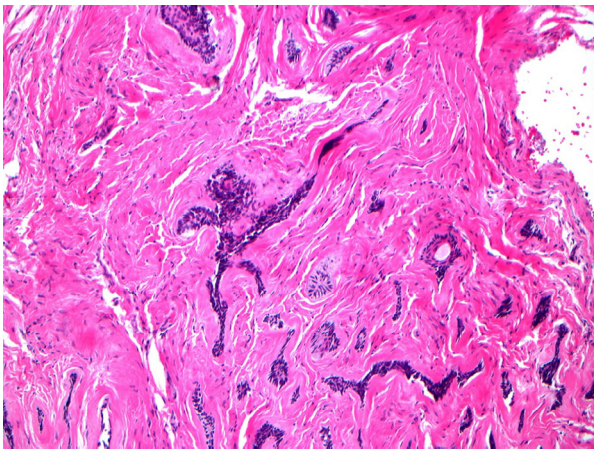

Fig. 3. Low-power photomicrograph highlighting the dense fibrous stroma containing numerous proliferative islands, strands, and cords of odontogenic epithelium.

tract. Most patients with mandibular metastases complain of pain, swelling, tooth mobility, trismus, and paresthesia. The radiographic appearance of metastatic breast carcinoma to the jaws is variable, ranging from a well-circumscribed radiolucency to a "moth eaten" appearance to a mixed radiolucent/radiopaque lesion.[9] This last presentation is similar to the radiographic appearance of the lesion in our patient and warranted inclusion in the differential diagnosis. In contrast, the clinical signs of metastatic breast cancer often differ from those in the present case, in that patients usually present with symptoms of pain or paresthesia and rapid soft tissue or bony expansion at the metastasis site.

Diagnosis and Management: After consideration of the potential differential diagnosis and consultation between the oral and maxillofacial pathology staff and oral and maxillofacial surgeons at the UTHSC, treatment options were discussed with the patient. Upon agreement, surgical exploration of the lesion and extraction of the adjacent impacted third molar was performed with the patient under local anesthesia, and lesional tissue was submitted for histologic examination. A diagnosis of desmoplastic ameloblastoma was rendered (Figures 3–5). On the basis of the unanticipated diagnosis, we determined that additional surgical intervention was warranted, and definitive treatment strategies were established.

Discussion: In most high-volume head and neck surgical biopsy practices, ameloblastoma is the second most common odontogenic tumor encountered, second only to odontoma in frequency of occurrence, while unquestionably representing the most clinically disconcerting tumor.[5] Conventional/solid, unicystic, and peripheral/extraosseous clinicoradiographic subtypes of ameloblastoma are recognized.[10] The tumor is characterized by its progressive and expansile growth, with clinical consequences that may include loosening of teeth, malocclusion, masticatory difficulties, facial deformity, and potential airway obstruction. An increased risk of tumor recurrence appears to be directly related to the more conservative the nature of the surgical treatment.

Several histologic patterns of ameloblastoma are recognized in the literature, with the follicular and plexiform patterns found in the overwhelming majority of cases. The desmoplastic variant is one of the more recently described patterns, having been introduced by Eversole et al. in 1984.[11] It reportedly accounts for 4% to 13% of ameloblastoma, according to the data from the larger