Clinico-Pathologic Conference: Case 6

David Booth · Jerry Bouquot

Received: 30 September 2010 / Accepted: 25 October 2010 / Published online: 24 November 2010
© Humana 2010

Clinical Presentation

A 36 year old Caucasian male visited his family dentist for a routine annual examination. Periapical radiographs of long-impacted mandibular third molars showed radiolucencies associated with the crowns of each. An orthopantomograph taken at the time confirmed bilateral pericoronal radiolucencies, with the right lesion larger than the left (Fig. 1). There was no obvious cortical expansion, no overlying mucosal changes and no symptoms or history of posterior mandibular pain. The patient was not aware of any systemic diseases, nor was he aware of any other family members with similar jaw radiolucencies.

Differential Diagnosis

Very few radiographic disorders can be definitively diagnosed without microscopic evaluation; nevertheless, a great deal of information can be gleaned from a thorough review of the radiographic features of a particular case. In truth, the more changes one can describe, the better the differential diagnosis becomes and, of course, the more logical the management plan. The present case is especially interesting because of the wealth of features visible within one cone beam CT scan (CBCT). It also points out a

growing problem with CBCT images, namely, that we lack the extensive experience needed to properly interpret them [1]. With routine dental radiographs, despite the tremendous imaging artifacts associated with them, health professionals long ago developed confidence in their interpretation of images. Someday, undoubtedly, we will have the same confidence in our interpretation of CBCT—but we are not there yet.

At first glance (Fig. 1), this case is a simple one of bilateral, pericoronal, unilocular radiolucencies without calcifications and with well demarcated borders. The sharp borders and mild sclerotic rimming around the lesions provide strong assurance that their biological behavior is that of benign, slowly enlarging entities. These signs also point out a lack of salient infection or inflammation in the area, as does the asymptomatic nature of the lesion and the fact that overlying soft tissues show no clinical signs of inflammation. Moreover, in the pantographic view (Fig. 1) there is no evidence of cortical or inferior border expansion, cortical perforation or root resorption, although the right lesion seems to demonstrate destruction of at least a portion of the lamina dura on the adjacent erupted molar.

The left side lesion is small enough to *strongly* suggest either a hyperplastic follicle or early dentigerous cyst [1–3]. Much less likely, and based primarily on the pericoronal location and unilocular appearance, would be odontogenic fibroma, odontogenic keratocyst (keratinizing odontogenic tumor), orthokeratinized odontogenic cyst, unicystic ameloblastoma or adenomatoid odontogenic tumor (AOT) [2]. Age, alone, would tend to rule out unicystic ameloblastoma, and the posterior mandibular location speaks against the AOT. Of course, the dentigerous cyst is the most common bilateral pericoronal lesion and it must be kept in mind that all bilateral cystic odontogenic lesions suggest involvement with the nevoid basal cell carcinoma

J. Bouquot (✉)
Department of Diagnostic Sciences, University of Texas Dental
Branch at Houston, 6516 M.D. Anderson Blvd., Suite 3.094b,
Houston, TX 77030, USA
e-mail: Jerry.Bouquot@uth.tmc.edu

D. Booth
School of Dentistry, University of Western Australia, 17 Monash
Avenue, Nedlands 6009, Australia

Fig. 1 Orthopantomogram shows bilateral, well-demarcated, unilocular radiolucencies around the crowns of both mandibular third molars

Fig. 2 **a** Right lesion appears unilocular and well demarcated, and shows pressure resorption of the lamina dura of the second molar root, as well as saucerization of the inferior alveolar canal, with resorption of its superior wall; **b** shows saucerization of inferior border of the mandible and “extension” of the lesion into a multilocular-type of bone change anteriorly (arrows)

syndrome (Gorlin syndrome) [2–4]. The keratocysts in the latter disease, however, usually manifest much earlier and there is nothing in the medical history of our patient to point to such a syndrome.

The right side lesion is similar to the left side one but it is much, much more problematic. In the first place, Fig. 2 demonstrates obvious destruction and saucerization of the inferior mandibular border, with apparent pressure erosion through the superior aspect of the inferior alveolar wall. This is a sign of a much more aggressive lesion than a

dental follicle or a moderate-sized dentigerous cyst. While still in keeping with a benign behavior, this sign, in addition to the posterior mandibular location, suggests odontogenic keratocyst, ameloblastoma, odontogenic myxoma, calcifying epithelial odontogenic (Pindborg) tumor without radiographically visible calcifications, glandular odontogenic cyst or, even, ameloblastic fibroma [1, 2]. The patient is too old for the latter lesion; the unilocular nature of the radiolucency speaks against the first two; and the well demarcated borders speak against the myxoma.

A closer look at Fig. 2b shows a region of low bone density just anterior to the lesion, with the appearance of multilocularity (arrows), similar to the poorly demarcated, usually multilocular radiolucency of the odontogenic myxoma [2, 5]. Figure 3b, moreover, seems to demonstrate an intimate connection between the well demarcated, more posterior part of the lesion with the anterior, more poorly demarcated part. The myxoma is almost alone among odontogenic lesions in presenting with this biphasic appearance. On the other hand, could the anterior cancellous bone change simply represent osteopenic bone in a thinly sliced CBCT image? In other words, is the multilocular, poorly demarcated appearance real or simply an undescribed feature of unassociated osteopenic bone in CBCT imaging [1, 6]?

Figure 3 demonstrates a few other signs of a locally aggressive but benign lesion. There is mild expansion of the facial cortex and there appears to be direct communication between the two phases of the lesion. Figure 4a and b also shows perforation of the lingual cortex. Part of the cortical erosion may be from the associated molar crown

Fig. 3 Demonstrated facial expansion and “extension” of the well demarcated lesion into the inferior cancellous bone or marrow spaces

Fig. 4 **a** Axial view shows the right lesion to be expansile to the facial, with perforation of the lingual cortex, partial extrusion of the third molar through the cortex and confirmation of lesional attachment to the cervical region of the impacted tooth; **b** sagittal view shows cortical perforation from the lesion rather than the tooth, and scalloping of the inside of the facial cortex; **c** pantographic view shows very wide mental foramen

being pushed through the cortex, but the radiolucent lesion itself is obviously responsible for most of the bone loss. Additionally, Fig. 4b shows a slight scalloping of the lesional border, indicating that it is not truly unilocular, as initially suspected, but is, in fact, multilocular.

The likely diagnoses now, again taking into account the patient's age and the lesion's location in the posterior mandible, are more limited. In the order of preference, they include: (1) glandular odontogenic cyst; (2) odontogenic keratocyst; (3) ameloblastoma. Nothing else would fit the total combination of these radiographic signs and, of course, only biopsy will determine which of these is correct.

It must be pointed out here that another lesion, the neurofibroma, can present within bone and can have both well demarcated and poorly demarcated regions [2]. The extremely wide inferior mandibular canal in Fig. 2 is suggestive of this entity, especially when it so nicely “breaks out” of the canal and fills the marrow spaces more anteriorly (presumably). Figure 4c demonstrates, moreover, that the very wide diameter of the inferior alveolar nerve remains wide through the mental foramen (arrow). This intra-canal presentation of a benign nerve tumor, however, is almost never seen outside of neurofibromatosis and the patient shows no apparent signs of that disorder. Moreover, the portion of the canal visible in the well demarcated region (not shown in this paper's figures) is only widened in a vertical direction, it has normal width, and the opposite alveolar canal is also widened (Fig. 1). Perhaps the two things that speak most strongly against a neural tumor, however, are: (1) the different densities between the inferior alveolar canal contents and the pericoronal radiolucency (Fig. 2); (2) the direction of the pressure erosion on the canal wall is from above the wall and pushing into the canal (Fig. 2b).

With all of the presenting signs in this case, then, it seems best to eliminate neurofibroma and keep with the three entities previously listed, i.e. glandular odontogenic cyst, odontogenic keratocyst, ameloblastoma. The odontogenic keratocyst is the *least* likely of the three to expand the cortex and, conversely, an ameloblastoma this size would surely have expanded the cortex *more* than is seen in the present case. With this in mind, the preferred working diagnosis for this case is glandular odontogenic cyst and biopsy is the next logical step.

Diagnosis and Discussion

At surgery both lesions proved to be fluid-filled cystic sacks attached to the associated molars in the cervical region. The histopathology of the left cyst showed a lining of atrophic, nonkeratinized, stratified squamous epithelium, with a general loss of rete processes (Fig. 5). This was overlying a moderately dense fibrovascular stroma without inflammatory cells. The microscopic diagnosis was dentigerous cyst.

The right lesion showed a different histopathology. It was comprised of a combination of squamoid and cuboidal epithelial cells with occasional focal proliferations extending slightly into the lumen (Fig. 6). There was a general loss of rete processes and occasional areas showed small accumulations of mucoid material, consistent with goblet or mucus cells. These were positive for mucus with periodic acid-Schiff diastase staining. Occasional very small duct-like structures were seen to be lined by cuboid or polygonal cells (arrow). Cilia were visible on the surface in some regions (Fig. 6b). The histopathologic diagnosis was glandular odontogenic cyst. An orthopantomograph taken 6 months after surgical removal of the cysts and

Fig. 5 **a** Epithelial cyst lining is thin, with loss of rete processes; **b** higher power view

Fig. 6 **a** Slightly nodular surface change in a lining epithelium with loss of rete processes; **b** small clear spaces with mucus and sometimes with duct-like surrounding cells (arrow)

impacted teeth showed a somewhat multilocular or lobular radiolucent lesion still present, but smaller, in the right mandibular third molar region, with a somewhat ground glass radiopaque change suggesting healing of the cystic lesion with woven bone formation. The left mandibular lesion was almost completely healed and no new or additional pathoses were in evidence.

Dentigerous cysts are, of course, not an uncommon experience in the practice of dentistry, especially for the oral and maxillofacial surgeon and the oral and

maxillofacial pathologist. Bilateral examples, however, are either decidedly rare or considered to be not interesting enough to submit to journals for publication [3]. In a child or teenager one should be at least suspicious of a developmental syndrome or systemic disease, such as mucopolysaccharidosis, cleidocranial dysostosis or Gorlin's syndrome [2, 4]. In fact, in the current literature, only 17 cases of bilateral dentigerous cysts have been described in the absence of a syndrome [2]. Our case is an additional case without a syndrome or systemic association.

Moreover, we are here reporting not two dentigerous cysts, but a dentigerous cyst and a look-alike pericoronal lesion, the glandular odontogenic cyst.

The glandular odontogenic cyst, sometimes referred to as the sialo-odontogenic cyst, is a relatively rare form of developmental odontogenic cyst. Like the odontogenic keratocyst (keratocystic odontogenic tumor), it can be quite aggressive locally but it does not metastasize and thus far there have been no reports of malignant transformation in such a cyst. The cyst is well accepted as being of odontogenic origin, but also shows distinctly glandular or salivary features, such as mucus cells and ductal structures; presumably demonstrating the pluripotentiality of odontogenic epithelium.

The glandular odontogenic cyst occurs most frequently in middle-aged adults (mean age = 48 years) and almost never is seen in persons younger than 20 years of age. Three-fourths of reported cases have occurred in the mandible, as in the present case, but there is a rather strong predilection for the anterior region, with a frequent presentation of crossing the mandibular midline [2]. Perhaps some of the previously diagnosed median mandibular cysts, a diagnosis seldom used today, were actually glandular odontogenic cysts?

The cyst may remain less than 1 cm in diameter but a certain proportion, perhaps the majority according to the literature, slowly enlarge to become as much as 5–6 cm in diameter. It seems to have a greater propensity to expand the facial (sometimes lingual) cortices than does the odontogenic keratocyst, although it seldom perforates the cortex. Radiographically, the glandular odontogenic cyst is either a unilocular or multilocular radiolucency with equal frequency. The margins of the radiolucency are usually well defined, typically with a thin, uniform sclerotic rim.

The glandular odontogenic cyst is lined by squamoid epithelium with cuboidal or columnar cells superficially, sometimes imparting a hobnail or even papillary surface change. Other features are as previously described for the

present example, including occasional spherical nodules within the epithelium or protruding above it.

Early examples of glandular odontogenic cyst demonstrated microscopic features similar to the intraosseous, low-grade mucoepidermoid carcinoma, which can be predominantly cystic. The pathologist is, therefore, cautioned to take this into account when diagnosing either entity. Examination of multiple levels might be required for appropriate diagnosis.

The glandular odontogenic cyst is typically treated by enucleation or curettage. However, it shows a rather strong propensity for recurrence, approximately 30%. Recurrence appears to be more likely when the cyst is multilocular. Because of its potentially aggressive nature and tendency for recurrence, some authors have advocated *en bloc* resection, particularly for multilocular lesions.

Acknowledgments We thank Clinical Professor Andy Whyte, Radiologist, University of Western Australia and Perth Radiological Clinic, and Mr. Clive Purcell, Oral & Maxillofacial Surgeon, South Perth, for permission to report this mutual case.

References

1. Bouquot JE. Diagnostic oral pathology with computed tomography. In: Kau CH, Richmond S, editors. Three-dimensional imaging for orthodontics and maxillofacial surgery. Oxford: Blackwell; 2010. p. 73–88.
2. Neville B, Damm D, Allen C, Bouquot J. Oral and maxillofacial pathology. 3rd ed. Philadelphia: W. B. Saunders; 2008.
3. Freitas DQ, Tempest LM, Sicoli E, Lopes-Neto FC. Bilateral dentigerous cysts: review of the literature and report of an unusual case. Dentomaxillofac Radiol. 2006;35:464–8.
4. Manfredi M, Vescovi P, Bonanini M, et al. Nevroid basal cell carcinoma syndrome: a review of the literature. Int J Oral Maxillofac Surg. 2004;33:117–24.
5. Li T-J, Sun L-S, Luo H-Y. Odontogenic myxomas: a clinicopathologic study of 25 cases. Arch Pathol Lab Med. 2006;130: 1799–806.
6. Shankland WE II, Bouquot JE. Focal osteoporotic marrow defect: report of 100 new cases with ultrasonography scans. J Craniomand Pract. 2004;22:314–9.