Multifocal lateral periodontal cysts: a report of 4 cases and review of the literature

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Lateral periodontal cyst (LPC) is a developmental jaw cyst of odontogenic origin. It has characteristic histopathologic features that are identical to those seen in the peripherally occurring gingival cyst of adults (GCA). The polycystic variant of LPC is termed the botryoid odontogenic cyst (BOC). The histogenetic origin of LPC is probably the rests of dental lamina in the alveolar bone. In the case of BOC, it might be that several adjacent epithelial rests simultaneously undergo cystic change and eventually form a polycystic lesion. Few previous examples of multifocal occurrence of LPC can be found in the literature. We report an additional 4 patients with this rare presentation of multiple, separate LPCs, and review the literature on this topic. (Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2011;111:225-233)

The lateral periodontal cyst (LPC) is a rather uncommon developmental odontogenic cyst, representing fewer than 1% of jaw cysts.1,2 It is typically located laterally to a root or roots of vital teeth, most often in the mandibular canine-premolar region.3,4 This particular type of cyst was first described by Standish and Shafer in 1958.5 The same year, Holder and Kunkel6 published a case with clinical, radiological, and histopathologic features consistent with LPC, but called it a periodontal cyst. Since then, more than 270 well-documented cases of LPCs (either uni- or polycystic) have been reported in the English language literature.7-23 The polycystic variant of LPC, termed botryoid (resembling a bunch of grapes) odontogenic cyst (BOC) was first described in 1973 by Weathers and Waldron.24 Interestingly, in their article they noted that one of the cysts presented by Standish and Shafer5 was consistent with a BOC.

Radiographically, LPCs usually present as unilocular, well-defined, oval or teardrop-shaped radiolucencies between the roots of vital teeth, and they are smaller than 1 cm in diameter.14,25 Most BOCs are also unilocular, but may sometimes present as a bilocular or multilocular radiolucency.8,13,20 Although these radiographic appearances could be attributable to a single cystic structure that grows in a multilocular pattern, the possibility that these lesions arise as a result of 2 or more cystic structures developing in the same area cannot be discounted.

The aims of this article were to present 4 unusual cases of multifocal LPCs, review the literature related to LPC and BOC, and discuss the possible pathogenetic mechanisms of the BOC.

REPORT OF CASES

Case 1
An asymptomatic 48-year-old male was referred for biopsy of 2 distinct, well-defined radiolucencies with sclerotic borders located between the mandibular left first premolar and canine (Fig. 1). The superior lesion was unilocular, whereas the inferior lesion had a bilocular radiographic appearance. Clinically, there was a small vesicle-like lesion visible on the gingiva overlying the superior lesion. On surgical exploration, the cystic cavities were found to be separated by alveolar bone, and 2 separate specimens...
were received for microscopic examination. The superior lesion showed a cystic cavity lined by thin, nonkeratinized stratified squamous epithelium with focal plaquelike thickenings (Fig. 2, A). The connective tissue wall was uninflamed. A few epithelial rests with clear cells and microcystic change were seen in the cyst wall (Fig. 2, B). The more apically located tissue specimen had a somewhat fragmented, folded appearance and it was difficult to determine if there was 1 large or 2 or more smaller, but folded, cystic cavities (Fig. 3, A). The cyst lining consisted of thin, nonkeratinized stratified squamous epithelium with focal epithelial plaques having a few clear cells (Fig. 3, B). The cystic cavity was supported by uninflamed fibrous connective tissue. The histopathologic features of both cases were consistent with LPC. Because this was a recent case, follow-up information was not thought to be pertinent.

Case 2
A 57-year-old female was discovered to have 2 well-delineated nonexpansile radiolucencies in the left mandible (Fig. 4, A and B). The lesions had thin sclerotic margins. The one located between the mandibular left second premolar and canine was 2.0 cm in diameter and had a “soap bubble”–like, multilocular appearance. A separate, 0.3-cm unilocular radiolucency was also noted distal to the mandibular left canine, but in a much more superior position, near the crest of the alveolar ridge. On surgical exploration, the lesions were found to be separate from each other. The associated teeth were vital. Both lesions were examined histopathologically and diagnosed as LPCs. Follow-up information was not available.

Case 3
Four asymptomatic radiolucencies were identified in the anterior mandible of a 51-year-old male (Fig. 5). In 1993, tissue from 2 of these lesions, from between the mandibular left canine and lateral incisor and from between the mandibular right central and lateral incisors, was submitted for microscopic examination. These 2 lesions showed histopathologic
features consistent with LPC. In 1994, another specimen described as a 3-mm cyst between the mandibular left lateral and central incisors was received, and the histopathologic findings were also consistent with LPC. In the periapical radiographs of this case (Fig. 5), there is also a cystic radiolucent lesion between the mandibular right lateral incisor and canine; however, tissue from this lesion was not submitted for microscopic study. Follow-up information was not available.

Case 4
A 42-year-old female presented with sensitivity of her mandibular left canine region. A periapical radiograph (Fig. 6) showed 3 round, well-defined radiolucencies of the left mandible, each of which was curetted and submitted for microscopic examination. The tissue obtained from the apex of the canine histopathologically was a periapical granuloma. The samples from between the mandibular left first premolar and canine and distal to the mandibular left second premolar were histopathologically consistent with LPC. Follow-up information was not available.

DISCUSSION
Multifocal LPCs
Our 4 cases showed radiographic and histopathologic evidence of multiple, distinct LPCs clearly separated by alveolar bone, and some of these were in close proximity to each other. Based on this finding, we believe it is possible that some BOCs may arise from fusion of multiple, separate LPCs. On the other hand, the polycystic presentation of BOC may result from cystic expansion of 1 cyst, creating locules with connective tissue septa that can be seen upon gross or microscopic examination.

The definition of BOC probably varies among oral pathologists. In the original report,24 the lesion grossly resembled a bunch of grapes and was therefore named botryoid. There have also been cases that were radiographically unilocular and grossly showed one single round “grape,” but on sectioning and microscopic examination multiple separate cystic compartments were evident.26 Thus, because of the multiple cystic compartments, these lesions were called BOCs. Conversely, other cases are radiographically multilocular but microscopically do not show a polycystic configuration, ei-
ther because they are truly not polycystic or because of artifacts occurring during surgery or handling thereafter. The authors prefer using the diagnosis of BOC when the lesion shows polycystic gross or microscopic features. The multilocular radiographic presentation alone should probably not be used as a criterion for the diagnosis of BOC.

We could find few radiographically documented examples of multifocal LPCs or BOCs in the literature. In A Textbook of Oral Pathology, a radiograph of a BOC showed 2 separate radiolucencies lateral to a mandibular premolar tooth. Moskow et al. presented radiographs of their cases that showed 2 to 3 distinct unilocular radiolucencies in the mandibular premolar-canine area. Bilateral occurrence of LPC was reported by Legunn, and Redman et al. published an interesting case of multiple LPCs. In the latter case, 3 separate unilocular radiolucencies were seen located adjacent to mandibular first premolar and canine teeth. Histopathologic evidence of actual separate LPCs with alveolar bone between 2 of the cysts was provided following resection of the lesion area of the mandible. The lesional tissue of the third radiolucency was lost during decalcification. Redman and colleagues rendered a diagnosis of multiple lateral periodontal cysts (botryoid variant) or botryoid odontogenic cyst, and speculated that the BOC may thus have a multicentric origin. They further stated that other BOCs may arise differently. We agree with their hypothesis, and would favor using the term “multiple (or multifocal) lateral periodontal cysts” rather than “LPC, botryoid variant” or “botryoid odontogenic cyst” in cases where no gross or microscopic evidence of a polycystic growth pattern can be seen in any of the separate LPCs.

Similarly, multifocal presentation of the gingival cyst of adult (GCA), thought to represent the soft tissue counterpart to LPC, seems to be as rare as multifocal LPCs. A patient with multiple GCAs was presented by Giunta, whereas Tolson et al. reported a patient who had 2 lesions in the mandible simultaneously: an LPC between the right first and
second premolars, and a GCA on the facial aspect of left lateral incisor.

Wysocki et al. proposed a hypothesis and provided histopathologic evidence for the formation of unicystic and polycystic types of LPC and GCA. Cystic change in a single odontogenic epithelial rest, or in multiple adjacent rests concomitantly, would result in a unicystic or polycystic lesion, respectively. However, in their series of cases, no radiographic features were presented, and no evidence of multifocality in the alveolar bone was presented, as in our 4 cases.

Clinical features

The LPC is typically an incidental radiographic finding, and more than a third of the patients may be totally asymptomatic. Expansion of the overlying bone can occur, resulting in a clinically evident dome-shaped swelling, typically on the facial aspect of the alveolar process. Sometimes the swelling may have a bluish color. The cystic expansion can cause erosion of the cortical plate, and therefore involve both bony and gingival soft tissues. Some patients experience symptoms associated with LPC, including tenderness on palpation, pain, periodic swelling, and drainage have been reported also. The adjacent teeth are characteristically vital, unless nonvital for other reasons.

Age and gender

The age range of patients with LPC, pooled from several studies, appears to be 14 to 85 years, with approximately 80% of patients being between 40 and 69 years. Carter et al. found that the mean age for men with LPC was 58.2 years versus 40.5 years for women. There is a peak in the prevalence of LPC in the sixth decade.

The gender distribution of LPCs has been almost equal in some studies, whereas others have shown a slight or clear male preponderance, with more than two thirds of the cases occurring in males in the latter 2 studies. Wysocki et al. patient population, however, included cases from the Armed Forces Institutes of Pathology, therefore a male predominance would not be surprising.

Location

Most case series have shown that the overwhelming majority of LPCs are located in the mandibular canine-premolar area. In a few studies, this site predilection has not been found, although this may be a reflection of the small numbers of cases. In one study of 20 LPCs, 52% (n = 11) were found in the maxilla, anterior to the first premolar, and in another series of 11 LPCs, 73% (n = 8) were in the anterior maxilla, between the lateral incisor and the canine. Other less common sites of occurrence are the mandibular incisor area and the maxilla anterior to the first molar. Few LPCs/BOCs have been reported in edentulous areas.

Radiographic features

The LPC presents radiographically as a well-defined, rather small, round, ovoid or teardrop-shaped, unicocular radiolucenty with sclerotic borders in an interradicular location between the cervical and apical part of the tooth root. Sometimes the LPC appears superimposed on the tooth root, and loss of lamina dura and periodontal ligament space may be noted. Divergence of the roots might occur, especially with larger LPCs, but root resorption is not seen. The polycystic variant of LPC (BOC) presents typically as a unicocular radiolucenty as well, so the botryoid nature is most often discovered on histopathologic examination. Occasionally, BOCs are radiographically bilocular or multilocular.

Size and growth rate

The size of LPCs ranges from 1 to larger than 10 mm, most lesions being 3 to 7 mm in size. The botryoid variant is generally larger, and may reach a size of several centimeters. Altini and Shear described a BOC that measured 5 cm in diameter. The LPC is generally considered a slowly growing lesion; however, considerable variation in the growth rate has been observed. Rasmusson et al. in their series of 32 LPCs, had radiographic follow-up ranging from 5 to 14 years in 4 of their cases, and found that the mean growth rate of the lesions was 0.7 mm per year. A considerably higher growth rate (approximately 2.5 mm per year) was observed by Suljak et al. in their case of an LPC that initially was a unicocular radiolucenty measuring 5 × 7 mm, and over a period of 25 months grew to an 11 × 12-mm multilocular lesion that showed histopathologic features of BOC.

Histopathologic features

The histopathologic features of LPC are characteristic, showing a cystic cavity (or in the case of BOC, multiple cystic cavities) lined by a nonkeratinizing squamous or cuboidal epithelium that is typically 1 to 5 cell layers thick and may resemble the reduced enamel epithelium. In most cases, epithelial thickenings referred to as plaques can be found and these are the most distinctive aspect of this type of cyst. The plaques, as well as the thin epithelial lining, may contain cells with clear cytoplasm. Glycogen has been shown to be present in the clear cells as well as the
squamous and cuboidal cells of the plaques and the lining epithelium. The plaques sometimes have a whorled appearance with fusiform or spindled cells. The epithelium may exhibit separation from the cyst wall. A subepithelial hyalinized zone can be seen in some LPCs. The cyst wall consists of fibrous connective tissue with no or minimal inflammation. Epithelial rests in the cyst wall are sometimes present, and they may contain clear cells and undergo cystic change, often referred to as microcysts. Wysocki et al. found that the epithelial cell rests were more common in the wall of BOCs than in unicystic LPCs. The LPC may lie in close association to, and be continuous with, the periodontal membrane, as demonstrated surgically or microscopically by some reports. Altimi and Shear proposed 3 different histomorphologic subtypes of LPCs: the unicystic, the multicystic encapsulated (2 or more cysts contained within a single round or oval fibrous capsule), and the botryoid (a multilobular lesion, consisting of several variably sized cystic cavities separated by fibrous tissue) forms.

Artifactual alteration during the surgical removal of the tissue sample may cause difficulties in the accurate interpretation of the cystic growth pattern in some instances. A unicystic lesion may collapse or be fragmented, and cause a false appearance of a polycystic lesion microscopically. Also, the orientation of a collapsed cystic specimen may contribute to a suboptimal plane of section, such that it may be difficult to determine whether the lesion contains 1 cystic cavity with locules or multiple cysts separated by connective tissue. This is mainly of academic interest because LPCs showing evidence of polycystic histopathologic or multilocular radiographic features should probably be followed more carefully than those that are clearly unicystic.

Differential diagnosis

The histopathologic features of LPC are usually distinct enough to allow differentiation from other cystic lesions (e.g., lateral radicular cyst, glandular odontogenic cyst (GOC)/sialo-odontogenic cyst, or odontogenic keratocyst/keratocystic odontogenic tumor) that might occur in the same location and have the same clinical and radiographic presentation.

Even though GCA originates in the gingival soft tissues, it may sometimes cause a cup-shaped erosion of the underlying bone, but this is normally not evident radiographically. In a case where distinction between GCA and LPC seems difficult based on radiographic and clinical findings, the decision could be made by evaluation of the borders of the bone cavity during surgery. The GCA may also rarely be polycystic histopathologically.

In 1990, Angelopoulou and Angelopoulos published an excellent review of the literature on LPC, and found that in the past, many cases reported as LPCs or BOCs could not unequivocally, on the basis of presented evidence, be diagnosed as such. Conversely, the case published by Holder and Kunkel in February 1958, obviously was an LPC, but was named periodontal cyst, before the establishment of LPC as a distinct pathologic entity. In the more recent literature, there has been some confusion about the diagnostic features of BOC, especially in relation to GOC. GOC was first presented by Gardner as a “mucus-producing odontogenic cyst/sialo-odontogenic cyst” at a meeting in 1984, followed by case reports in 1987 by Padayachee and van Wyk and in 1988 by Gardner et al. We believe that before and after these initial descriptions of this cyst, some cases that were reported as BOCs but showed atypical radiographic or histopathologic features, often combined with recurrences or aggressive behavior, were actually more consistent with the diagnosis of GOC. High et al. proposed the term “polymorphous odontogenic cyst” for a group of cystic lesions, some of which were GOCs. Kaplan et al. suggested diagnostic criteria for GOC, and remarked that a lesion should exhibit at least focally these specific epithelial characteristics to be diagnosed as GOC. Therefore, even a focal GOC-like epithelium in a cyst that otherwise exhibits LPC/BOC features should alert the pathologist to consider GOC in the differential diagnosis. The presence of mucous cells is generally not accepted as part of the histopathologic features of LPC. Some reports have claimed these to be a result of mucous metaplasia in an otherwise typical LPC. However, there seem to be cases that show features of both LPC and GOC, i.e., epithelial crypts and luminal low columnar (“hob-nail”) cells. The possibility that GOC might represent part of the clinicopathologic spectrum of LPC/BOC cannot be completely excluded at this time.

We certainly encourage all lesions suspected to be LPC but exhibiting atypical clinical, radiographic or histopathologic features to be serially sectioned and thoroughly examined microscopically. These atypical features would include, in our opinion, unusual signs or symptoms, such as paresthesia, large size, rapid growth, atypical location, multilocular radiographic pattern, root resorption or displacement, mucous cells, columnar or cuboidal (“hob-nail”) luminal epithelial cells, ciliated cells, glandular or pseudoglandular structures, microcysts or mucous pools in the epithelium, atypical epithelial proliferation, or aggressive behavior (recurrence).
Histogenetic origin

The histogenetic origin of LPC is undoubtedly odontogenic epithelial rests in the periodontium; however, the exact source of these epithelial rests is still a matter of controversy. Altini and Shear favor origin from reduced enamel epithelium, as the lining epithelium of LPC closely resembles it histologically. Furthermore, they believe it is possible that the LPC is a secondary presentation of a dentigerous cyst (DC) after the associated tooth has normally erupted and left behind residual dental follicle in a lateral position. This theory about the histogenesis of LPC was speculated by Standish and Shafer in 1958, based on the discussion of development of lateral follicular cyst by Bernier in 1955. According to Altini and Shear, further support for the origin of LPC from DC comes from the fact that the LPCs tend to occur where DCs are often associated with vertically positioned unerupted teeth, such as mandibular premolars, maxillary incisors, or canines. However, DCs commonly arise in association with mandibular third molars, and LPCs are exceedingly rare at this anatomic site. Altini and Shear also remarked that the epithelial plaques often seen in LPCs may occasionally be found in the lining of DCs.

A more widely supported view of the histogenesis of LPC suggests that the rests of dental lamina are the cells of origin of LPC. The clear cells often seen in LPCs are reminiscent of the rests of Serres, consistent with a dental lamina origin. Moreover, the rests of dental lamina are found mostly on the facial aspect of the alveolus, the location where most LPCs occur. Shear points out, however, that the epithelial plaques do not consist of clear cells de novo, but rather begin as fusiform cells with scanty cytoplasm that appear to develop from local proliferation of the basal cells. Weathers and Waldron, in their report presenting 2 BOCs, speculate that the epithelial islands in the connective tissue wall of a BOC may actually arise by extending and separating from the proliferating epithelial plaques into the connective tissue wall of the cyst. These “pinched off” epithelial nests could then undergo cystic change and add a new, separate cystic locule to the lesion, a theory supported by Shear.

Other suggested, but less likely, possibilities for the source of epithelium in LPC include stratum intermedium, the rests of Malassez, and cystic degeneration of a supernumerary tooth germ. Regardless of the origin of the lesional epithelium, the stimulus for the cystic change in the epithelial rests is unknown.

Treatment

Treatment of LPC and BOC normally entails complete enucleation/curettage of the lesion. A careful approach is needed to avoid damaging the adjacent root during the surgery. Unnecessary procedures, such as endodontic or periodontal treatment, should be avoided by proper diagnostic workup, including vitality testing of the associated teeth.

Recurrence

In general, LPCs have a low rate of recurrence, estimated to be 3% to 4%, but recurrences have been described after several years. However, the risk of recurrence of BOCs has been reported to be considerable. In a series of 33 patients, where follow-up was available from 16 patients, the recurrence rate of BOCs was 17%. BOCs can recur after several years, even a decade after initial treatment. The fact that polycystic lesions (BOCs) are more difficult to excise completely could contribute to higher risk of recurrence. New cyst development in the area could also explain recurrence, and some individuals may be more prone to develop cystic change of epithelial rests.

It should be noted that in many of the case series, information about follow-up was not available or the follow-up was relatively short. Also, the BOC recurrence rates of more than 30%, found in some reviews, could be questioned on the basis of inclusion of cases that do not represent classic BOC, but show features of GOC, which is known to have a relatively high (up to 30%) rate of recurrence. Therefore, the true recurrence rate of LPCs and BOCs may well be unclear, and case series with strict diagnostic criteria and long follow-up would probably give more accurate information about the recurrence rate.

CONCLUSIONS

In this article, we have presented 4 cases of unusual multifocal LPCs. Some of the lesions occurred in close proximity to each other, and it is reasonable to believe that if left untreated, they could have continued to enlarge and eventually fuse to form 1 polycystic lesion (BOC). Documentation of a multifocal presentation of LPCs is uncommon, although it is impossible to determine what percentage of reported cases of BOCs were, in fact, examples of confluent growth of multiple synchronous LPCs. So-called recurrence of some examples of BOC may also represent development of new LPCs. Long-term follow-up of patients with multifocal LPCs would be prudent.
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