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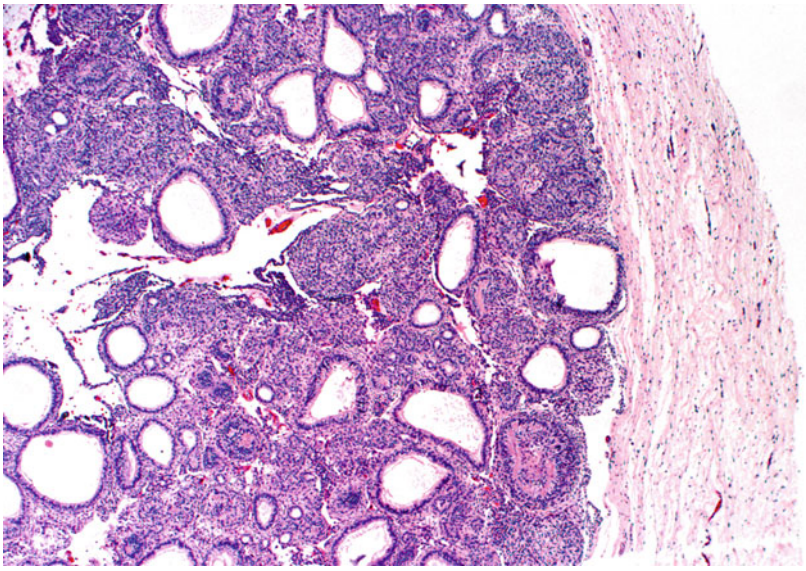
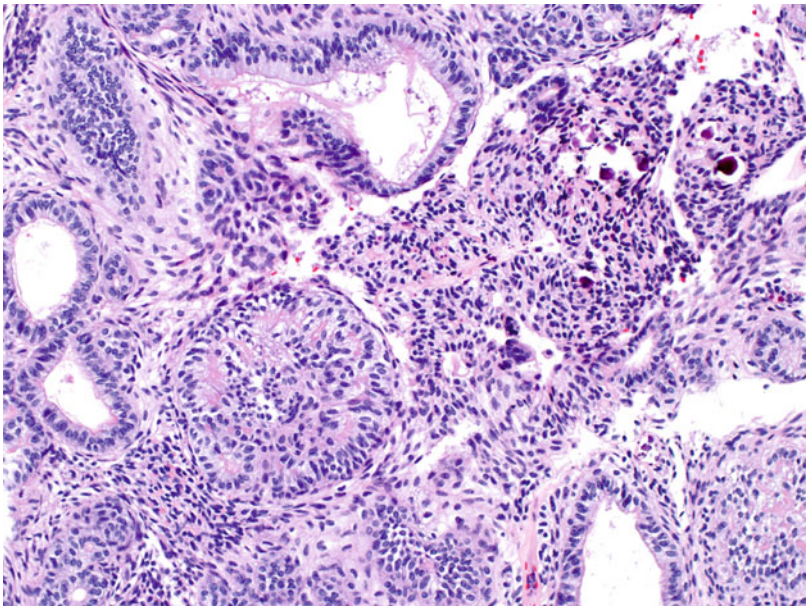


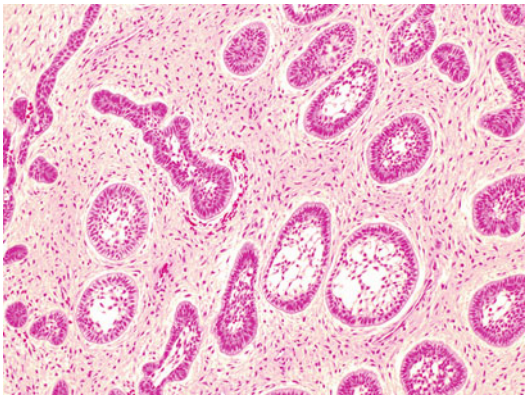
Adenomatoid Odontogenic Tumor, Fig. 1 Low-power examination shows a well-circumscribed mass surrounded by a thick fibrous capsule. The tumor cells are arranged in a whorled, nodular growth pattern with variably sized duct-like structures



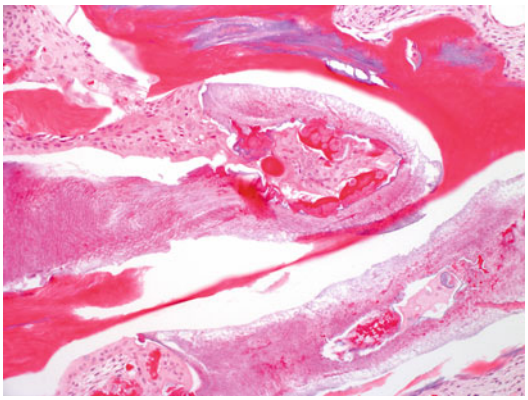
Adenomatoid Odontogenic Tumor, Fig. 2 High-power examination shows duct-like structures lined by cuboidal to columnar epithelial cells. Within the background, there are spindle-shaped epithelial cells. Focal rosette-like structures and calcifications also are present

Calcifications are a common finding as well. The amount of calcified material is highly variable. There may be small basophilic calcifications (consistent with dystrophic enamel) or larger masses of calcified matrix (consistent with dentinoid, osteodentin, or cementum). Small calcifications with a lamellar or ring-like pattern also may be seen. The diagnosis may be difficult in unusual cases of AOT with extensive calcified matrix formation. However, recognition of at least a focal epithelial component with characteristic microscopic findings should aid in diagnosis.

Occasionally, an AOT may exhibit focal calcifying epithelial odontogenic tumor-like areas (also known as a "combined epithelial odontogenic tumor"). Most authorities regard



Ameloblastic Fibro-Odontoma, Fig. 2 Medium-power photomicrograph of the ameloblastic fibroma-like component, characterized by small islands and cords of ameloblastic epithelium within a primitive, loosely arranged stroma



Ameloblastic Fibro-Odontoma, Fig. 3 Disorganized masses of enamel matrix and poorly formed dentin. Focal odontogenic epithelium also is present

rudimentary tooth structures. In unusual cases, melanin deposition may be evident within the tumor epithelium and/or ectomesenchyme.

The term *ameloblastic fibrodentinoma* may be used for cases in which the hard tissue component is restricted to dentinoid or tubular dentin in the absence of enamel. Although some authors regard the ameloblastic fibrodentinoma as a distinct entity, others regard it as a variant of ameloblastic fibro-odontoma or ameloblastic fibroma.

Immunophenotype

The epithelial component of ameloblastic fibro-odontoma expresses various cytokeratins. A small number of cases have been reported to exhibit positive reactivity with KL-1 antibody (which detects CK1, CK2, CK5, CK6, CK7, CK9, CK11, CK14, CK16, CK17, and CK18), PKK-1 antibody (which detects CK8, CK18, and CK19), and monoclonal antibodies for CK4, CK7, CK8, CK13, CK14, CK18, and CK19 (Miyauchi et al. 1996; Yamamoto et al. 1995). The ectomesenchymal component expresses vimentin (Miyauchi et al. 1996; Yamamoto et al. 1995). There is no reactivity for S-100 protein (Yamamoto et al. 1995).

Molecular Features

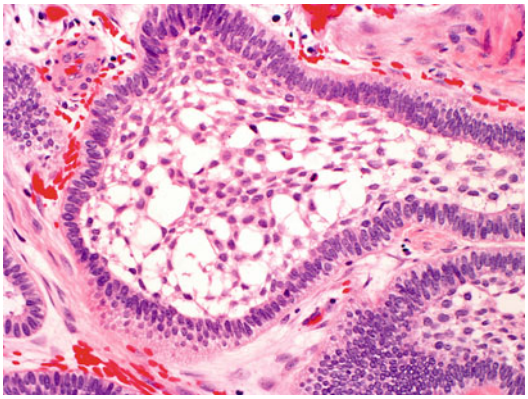
Papagerakis et al. used in situ hybridization to demonstrate osteocalcin and collagen type III mRNA in ameloblastic fibro-odontomas and other mixed odontogenic tumors (Papagerakis et al. 1999). These authors observed osteocalcin transcripts in the high columnar epithelial cells and collagen type III transcripts in the ectomesenchymal cells. Corresponding protein expression was confirmed by immunohistochemistry.

Differential Diagnosis

Microscopic distinction between an ameloblastic fibro-odontoma and a developing odontoma is virtually impossible. In practice, lesions exhibiting progressive growth consistent with true neoplasms are best classified as ameloblastic fibro-odontomas, whereas lesions with more limited growth consistent with hamartomas are best classified as developing odontomas.

The epithelium within an ameloblastic fibro-odontoma resembles that of ▶ ameloblastoma. However, the presence of enamel, dentin, and primitive mesenchymal stroma readily distinguishes the former from the latter.

Differentiation between an ameloblastic fibro-odontoma and an *ameloblastic fibro-*



Ameloblastoma, Fig. 2 Follicular type. High-power photomicrograph of a tumor island. The cells at the periphery of the tumor island are columnar, with nuclei that are hyperchromatic and polarized away from the basement membrane (reverse polarization). The cells within the center of the tumor island are loosely arranged with stellate reticulum-like differentiation

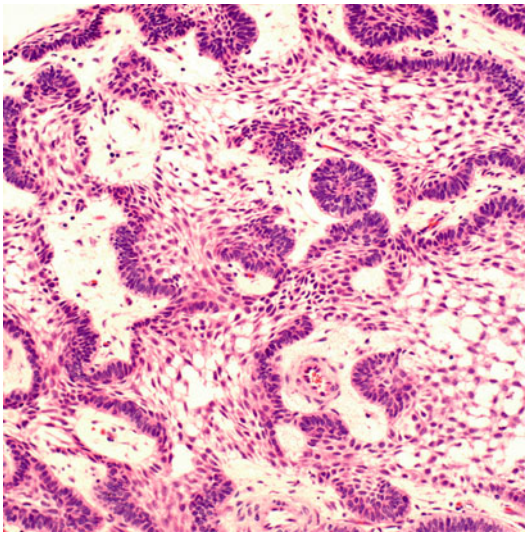
formation is commonly found within the center of the epithelial islands.

The *plexiform type* is comprised of long, anastamosing cords and sheets of odontogenic epithelium (Fig. 3). These cords and sheets exhibit a peripheral layer of columnar to cuboidal cells with reverse polarization. The background stroma is often loosely arranged and vascular. Cyst formation is less common in the plexiform type compared to the follicular type.

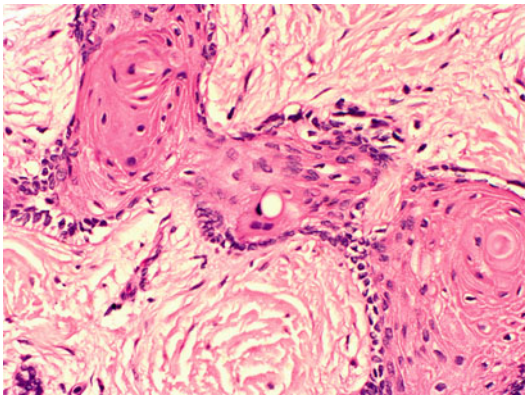
The *acanthomatous type* exhibits squamous differentiation within the central portions of the tumor islands (Fig. 4). Keratin formation, including keratin pearls or individual cell keratinization, may be evident.

In rare cases, extensive keratin-filled cyst formation within epithelial islands has been referred to as ▶ keratoameloblastoma. The keratoameloblastoma is discussed further under a separate heading.

The *granular cell type* is characterized by cells with abundant eosinophilic, granular cytoplasm occupying central portions of the tumor islands (Fig. 5). Ultrastructural studies have shown the granular cells to possess high lysosome content. Increased apoptosis of tumor cells and phagocytosis of these apoptotic cells may be the underlying mechanism.



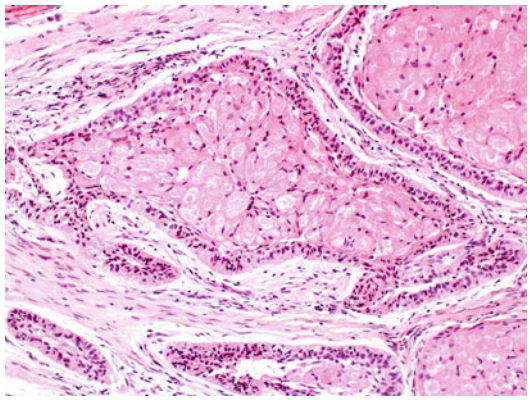
Ameloblastoma, Fig. 3 Plexiform type. Anastamosing cords and sheets of odontogenic epithelium. The peripheral cells are columnar to cuboidal and often exhibit reverse nuclear polarization



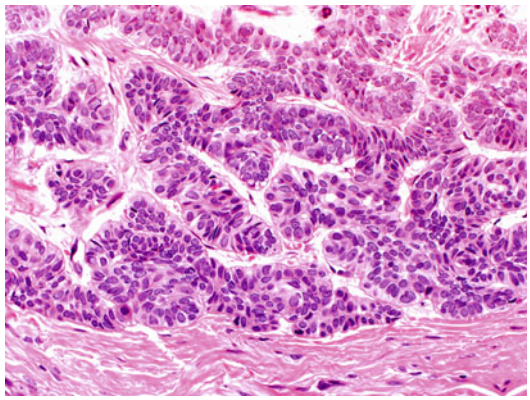
Ameloblastoma, Fig. 4 Acanthomatous type. The cells within the center of this tumor island exhibit squamous differentiation with associated keratinization

The *desmoplastic type* exhibits a densely collagenized background stroma, with a relatively sparse epithelial component that appears to be compressed into irregular tumor islands and strands. ▶ Desmoplastic ameloblastoma is discussed further under a separate heading.

The *basal cell type* is an uncommon variant, resembling basal cell carcinoma of the skin. There tumor is comprised of nests or islands of basaloid



Ameloblastoma, Fig. 5 Granular cell type. The center of this tumor island is filled with cells exhibiting abundant eosinophilic, granular cytoplasm



Ameloblastoma, Fig. 6 Basal cell type. There are nests and islands of basaloid epithelial cells. Peripheral nuclear reverse polarization and central stellate reticulum-like differentiation are not prominent features in this type

epithelial cells (i.e., cells with deeply basophilic nuclei and little cytoplasm) (Fig. 6). The cells at the periphery of the tumor nests and islands tend to be cuboidal, and nuclear reverse polarization may be less prominent compared to the follicular and plexiform variants. ▶ Stellate reticulum-like differentiation is not seen within the center of the tumor islands.

Note that the so-called clear cell ameloblastoma is now regarded as ▶ clear cell odontogenic carcinoma, rather than a variant of ameloblastoma.

Features of several of these microscopic variants may be seen within a given tumor, with the dominant growth pattern determining the overall microscopic diagnosis. However, neither the microscopic variant nor the relative amounts of cystic and solid areas within a conventional ameloblastoma have any bearing on treatment and prognosis.

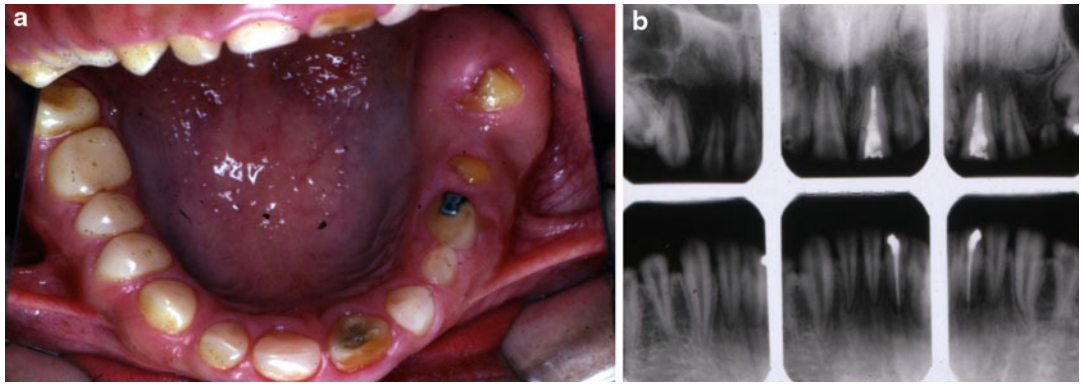
Immunophenotype

Ameloblastomas typically exhibit immunoreactivity for various cytokeratins, including AE1/AE3, CK8, CK14, and CK19. Reactivity is variable for CK6, CK7, CK15, CK16, and CK17. The tumor cells are usually negative for CK1, CK4, CK10, and CK20. The tumor cells also express amelogenins and epidermal growth factor receptor (EGFR).

Scheper et al. performed an immunohistochemical study of various participants in the phosphatidylinositol-3-kinase (PI3K)/Akt/mammalian target of rapamycin (mTOR) pathway (Scheper et al. 2008). They found a majority of ameloblastomas expressed AKT, mTOR-activated pS6K(ser240/244), and ERK. They concluded that aberrant signaling in the PI3K/AKT/mTOR pathway in ameloblastomas may represent a valuable tool for elucidating pathogenesis, aggressiveness, and novel modes of therapy.

Molecular Features

Using microsatellite analysis, Borkosky et al. found a high frequency of loss of heterozygosity (LOH) in each member of the inhibitor of growth (*ING*) gene family in ameloblastoma (Borkosky et al. 2010). The ING proteins are tumor suppressors that interact with p53 during apoptosis, DNA repair, cell cycle regulation, and senescence. There was a high frequency of LOH in *ING5* and *ING3* loci in solid tumor types, and more frequent LOH was observed in recurrent cases. The authors concluded that LOH of *ING* family genes appears to be a common genetic alteration in solid ameloblastoma.



Amelogenesis Imperfecta, Fig. 1 (**a**) Clinical photograph showing relative lack of enamel and open contact points between teeth as well as the yellowish color of the teeth in a patient with sporadic amelogenesis imperfecta. Some of the teeth also show evidence of dental caries. (**b**) Periapical radiographs of the same patient shown in (**a**) show absent or very thin enamel with wide interdental spaces

Amelogenesis Imperfecta, Fig. 2 Clinical photograph of a patient with autosomal dominant amelogenesis imperfecta. The enamel is of full thickness, so there is no spacing between the teeth, but it has a matt/opaque appearance with varying degrees of discoloration

Amelogenesis Imperfecta, Fig. 3 Hypoplastic vertical grooves in a female with X-linked amelogenesis imperfecta

then a diagnosis of sporadic AI would be reasonable as a working diagnosis. If this represents a spontaneous mutation, then the possibility of this being passed onto future generations needs to be considered in the longer term management of that patient which should include a consideration of genetic counselling. Radiographs can provide invaluable further information in the assessment of patients with AI. A dental panoramic radiograph may identify unerupted teeth. The failure of eruption of some teeth in some individuals with AI presumably reflects a defect in the enamel organ caused by the mutant gene. Such teeth may undergo resorption, possibly because the integrity of the enamel is compromised. Where there is a mineralization defect, the distinction between enamel and dentin is less obvious – this may be seen in extraoral radiographs such as a dental panoramic radiograph; bitewing or periapical radiographs will best illustrate this phenomenon. In some families, taurodontism is also seen. This manifests in multirooted teeth as elongation of the coronal pulp chambers at the expense of the roots, with displacement of the furcation of the roots. In some such patients, the pulp chamber can also appear

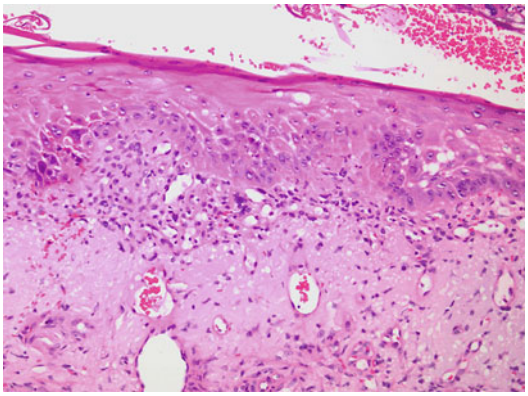
Macroscopy

The lesions of actinic cheilitis are dry whitish grey scaly plaques, although in the initial stages, the changes can be subtle (Fig. 1). Often there are associated areas of atrophy, erythema, erosion, or ulceration (Fig. 2). A loss of the distinction of the vermillion border is often reported. Some studies report a predominance of solitary lesions, while in others widespread abnormality of the lip is reported.

Microscopy

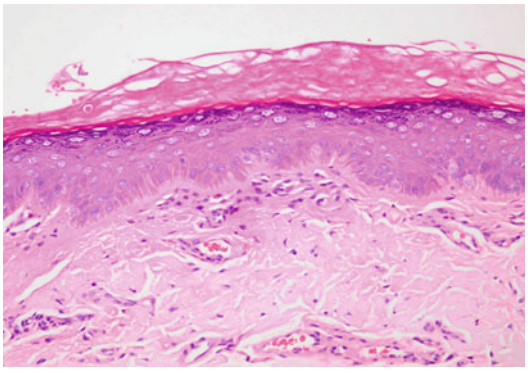
The most consistent histological feature is epithelial dysplasia, although the grade or severity varies between studies (Kaugars et al. 1999; Cavalcante et al. 2008; Markopoulos et al. 2004). Other commonly reported features include hyperkeratosis, with ortho- and parakeratin forms often occurring within the same specimen (Figs. 3 and 4). The thickness of the keratin layer varies and this is correlated with the level of dysplasia. The epithelium is often acanthotic, which is also correlated with the extent of dysplasia. Prominent changes in the underlying connective tissues include the basophilic change associated with elastosis, vasodilatation/telangiectasia, and variable chronic inflammation, particularly associated with areas of ulceration. The inflammatory infiltrate is present in a perivascular location in approximately 50 % of

Cheilitis Actinica, Fig. 1 Mild clinical changes on a sun exposed lower lip. The lesion is *red* with a *yellow-grey* crust



Cheilitis Actinica, Fig. 3 Moderately dysplastic atrophic epithelium adjacent to an area of ulceration. There is pronounced telangiectasia and solar elastosis of the underlying connective tissues

Cheilitis Actinica, Fig. 2 A more extensive clinical lesion with areas of erosion and ulceration superimposed on a *white* hyperkeratotic background



Cheilitis Actinica, Fig. 4 Mildly dysplastic atrophic epithelium which is markedly hyperkeratotic. There is marked solar elastosis of the underling tissues

The lesion frequently is discovered as an incidental finding on dental radiographs as a well-circumscribed radiolucency between the roots of two teeth (Fig. 1). Most examples measure less than 1 cm in diameter and the radiographic border often appears corticated.

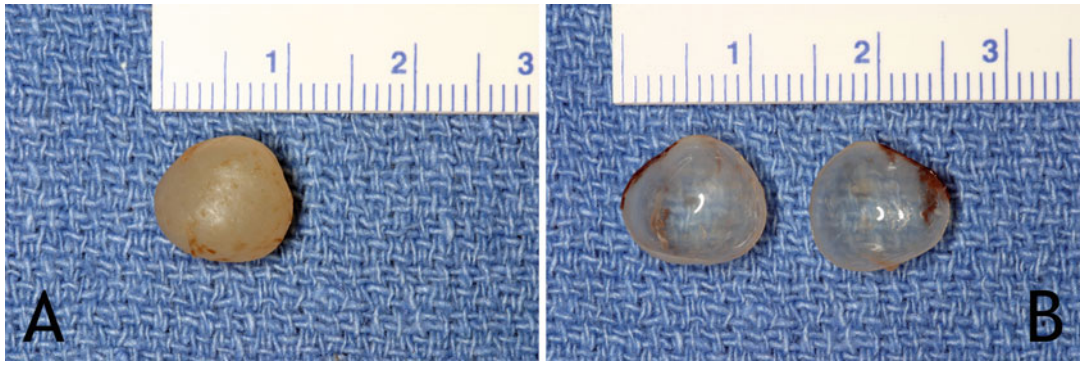
Cyst, Lateral Periodontal, Fig. 1 Well-circumscribed ovoid radiolucency located between the roots of the mandibular canine and first bicuspid (Courtesy of Dr. Lee Ayers)

Some lateral periodontal cysts will produce buccal cortical expansion, presenting as a gingival swelling that might resemble its soft tissue counterpart, the gingival cyst of the adult. Occasional lateral periodontal cysts will exhibit a multilocular radiographic appearance; such cases often correspond to the clinicopathologic variant known as the **botryoid odontogenic cyst**. Rare examples have been reported that occurred in a periapical location, thereby mimicking a radicular cyst radiographically. A few patients with multiple separate cysts have been documented.

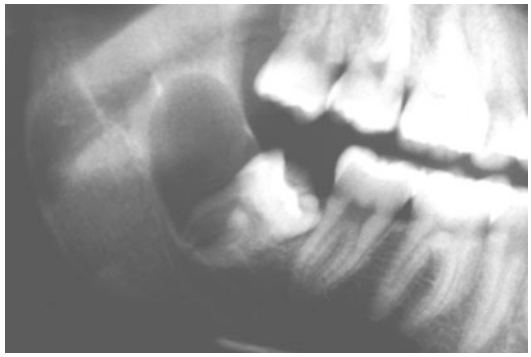
Some lateral periodontal cysts will be associated with local pain or tenderness to palpation. However, the teeth in the area should have vital pulps, unless they happen to be nonvital for unrelated reasons. Also, if the teeth have already been extracted, it is still possible for a lateral periodontal cyst to develop in an edentulous site, presumably arising from epithelial rests of the dental lamina that are still present within the alveolar bone.

- **Treatment**

The lateral periodontal cyst is usually treated by conservative surgical enucleation from its bony crypt. The adjacent teeth typically are still vital, so neither extraction nor root canal therapy is mandated. Because the botryoid variant has a greater chance for recurrence, more aggressive curettage for multilocular examples is advisable.

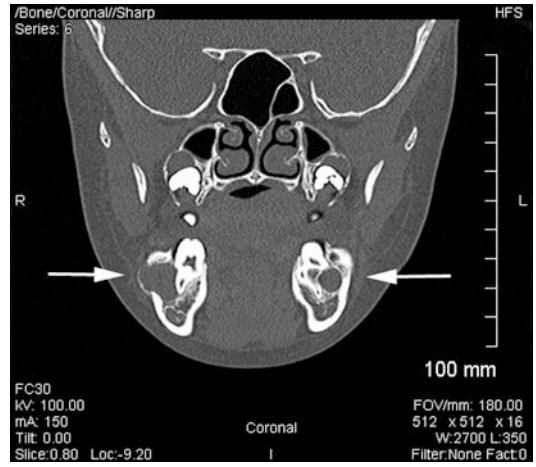


Cyst, Lateral Periodontal, Fig. 2 Gross specimen of a lateral periodontal cyst. Image A shows an intact cyst that resembles a small yellowish pearl. Upon bisection (Image B), clear fluid was released, revealing a markedly thin, translucent wall



Cyst, Paradental, Fig. 1 A well-circumscribed unilocular radiolucency is found distal to an unerupted mandibular right third molar. The gross specimen from this case is shown in Fig. 4 (Courtesy of Dr. Derek Dunlap)

Cyst, Paradental, Fig. 2 This juvenile paradental cyst shows a characteristic cup-shaped radiolucent defect associated with the mandibular first molar, with extension forward to the area of the second premolar. At surgery, the lesion was located on the buccal aspect of these teeth (Courtesy of Dr. James Lemon)



Cyst, Paradental, Fig. 3 This coronal CT image shows bilateral juvenile paradental cysts associated with the mandibular first molars (*arrows*). The lesions are characteristically located on the buccal aspect of the teeth (Courtesy of Dr. Amir Marashi)

mandibular third molar accounts for 61 % of cases, which are often associated with a history of pericoronitis of this tooth. Juvenile paradental cysts of the mandibular first and second molars comprise 36 % of all cases. Approximately 24 % of juvenile paradental cysts occur bilaterally, compared to only 4 % of third molar cases.

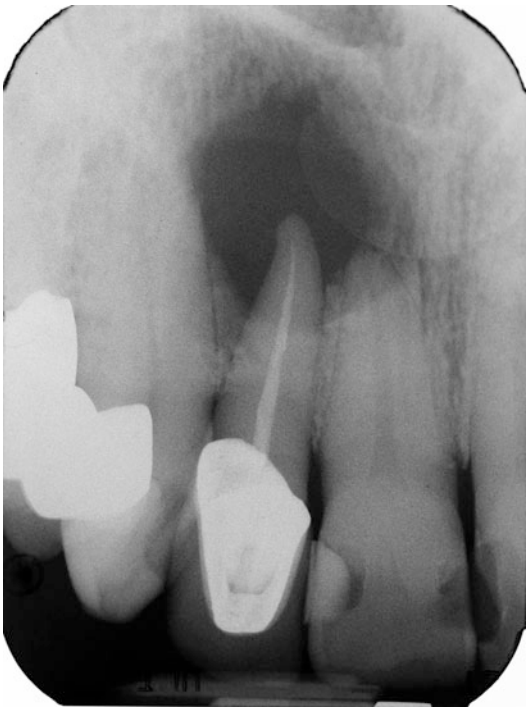
Examples associated with third molars occur as circumscribed radiolucencies, which usually are located distal or distobuccal to the roots of the tooth (Fig. 1). Rare examples on the mesial aspect of the tooth have also been described. Some cases will be discovered as incidental findings, whereas others may be associated with pain and swelling. Most paradental cysts are relatively small lesions measuring between 1.0 and 1.5 cm in diameter. The cyst may communicate to the mucosal surface through a periodontal pocket.

The juvenile paradental cyst develops on the buccal aspect of the roots of the mandibular first or second molar – hence, the alternate term *buccal bifurcation cyst*. The most common presenting sign/symptom is buccal swelling, although many cases will be asymptomatic. Some examples will result in pain, tenderness, and purulent drainage. Panoramic or periapical radiographs will demonstrate a circumscribed, cup-shaped radiolucency surrounding the roots of an erupting or newly erupted tooth (Fig. 2). Occlusal radiographs or CT imaging will reveal the characteristic buccal location of the cyst, which results in tilting of the tooth roots toward the lingual cortical plate (Fig. 3). Many cases are also associated with proliferative periostitis of the overlying buccal cortex.

- **Treatment**
  Paradental cysts in the third molar area are treated by extraction of the tooth with

- **Sex**
  The radicular cyst may not have a significant sex predilection. Although some series have suggested that these cysts occur slightly more frequently in men, other studies have shown a similar slight predominance in women.
- **Site**
  Approximately 60 % of radicular cysts occur in the maxilla, and 40 % occur in the mandible. Maxillary examples show a marked predilection for the incisor/canine region, whereas mandibular cysts are more equally distributed throughout the jaw.

  Radicular cysts usually appear on dental radiographs as a circumscribed radiolucent defect located at the root apex (Fig. 1). However, if the tooth has a pulp canal that exits the tooth along the lateral root surface, then the cyst may develop along the side of the root (Fig. 2). Such a lesion, known as a *lateral radicular cyst*, should be distinguished from the *lateral periodontal cyst*, which is developmental in origin. Many radicular cysts are asymptomatic, although spontaneous pain or sensitivity to biting pressure may be reported, especially if significant infection is present. If the cyst becomes large enough, expansion of the overlying cortical plate can be observed.
- **Treatment**
  If the associated tooth is being extracted, then the radicular cyst should be enucleated/curetted from the tooth socket and submitted for microscopic examination. Many times, the cyst will come out attached to the root apex. If the tooth can be restored, it may be possible to perform root canal therapy and save the tooth. Once the necrotic pulp has been removed, it is theorized that the body may then be able to eliminate the cyst because the source of the irritation has been eliminated. Of course, in such instances, one would never know if the periapical lesion had been a true epithelium-lined radicular cyst or simply the inflammation of a periapical granuloma. In cases where root canal therapy has already been performed but the cyst does not resolve, then surgical endodontic treatment may be



Cyst, Radicular, Fig. 1 Periapical radiograph showing a radiolucent zone of bone destruction at the apex of the right maxillary lateral incisor, which already has had root canal therapy (Courtesy of Dr. Michael Piepenbring)

Cyst, Radicular, Fig. 2 Periapical radiograph showing an ovoid radiolucent defect between the roots of the left mandibular canine and first bicuspid, which was nonvital. Such a lesion is often designated as a *lateral radicular cyst* and should be distinguished from a developmental lateral periodontal cyst (Courtesy of Dr. Philip Prickett)