

TITLE: Odontogenic Cysts and Tumors

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Introduction

There are a variety of cysts and tumors that affect the osseous marrow and cortex of the jaw bones, which may be uniquely derived from the tissues of developing teeth. It is important as an otolaryngologist to be aware of the variety of tumors and the presenting symptoms in these patients. A review of dental embryology is essential for further discussion of this topic.

Odontogenesis

In the earliest stage of tooth development, projections of dental lamina form invaginations into underlying ectomesenchyme. These cells differentiate into a layered cap with an inner and outer enamel epithelium, which contain inner stratum intermedium and stellate reticulum layers. Changes also occur in the underlying ectomesenchyme forming the dental follicle and dental papilla. Mesenchymally derived odontoblasts form along the dental papilla and secrete dentin, which induces the inner enamel epithelium to become ameloblasts. Ameloblasts are responsible for enamel production and eventual crown formation. Cementoblasts and fibroblasts from the dental follicle mesenchyme deposit cementum on the root surface and form the periodontal membrane, respectively. The penetration of these cells through Herwig's sheath at the edge of the enamel organ give rise to epithelial rests of Malassez within the periodontal ligament. The enamel organ then involutes to a monolayer, which becomes squamoid and ultimately fuses with the gingiva during eruption.

Diagnosis of Odontogenic Cysts and Tumors

The most important concept in the management of odontogenic pathology is obtaining a complete history and thorough physical examination. Questions about pain, loose teeth, recent occlusal problems, delayed tooth eruption, swellings, dysthesias or intraoral bleeding may be

associated with odontogenic tumors and/or cysts. In addition, parasthesias, trismus, and significant malocclusion may indicate a malignant process. The onset and course of the growth rate of a mass should be elicited.

The general head and neck examination should include careful inspection, palpation, percussion and auscultation of the affected part of the jaw and overlying dentition. Auscultation of the affected part of the jaw, as well as the common carotid and bifurcation may identify the bruit of a vascular malformation or tumor. Radiologic examination is usually the first procedure of choice in the evaluation of jaw related cyst and tumors. A panorex radiograph will often confirm clinical suspicions and have implications as to differential diagnoses. There are a variety of dental radiographic views that are routinely obtained during a dentist office visit that may incidentally discover occult cysts or tumors. In general, well-demarcated lesions outlined by sclerotic borders suggest benign growth, while aggressive lesions tend to be ill-defined lytic lesions with possible root resorption. With larger more aggressive lesions, computerized tomography may more clearly identify bony erosion and/or invasion into adjacent soft tissues.

A differential diagnosis is developed and tissue is then obtained for histologic identification of the lesion. Fine needle aspiration is excellent for ruling out vascular lesions prior to open biopsy and may be helpful to diagnose inflammatory or secondarily infected lesions. Open biopsy may be incisional (preferred especially for larger lesions prior to definitive therapy) or excisional (for smaller cysts and unilocular tumors).

Odontogenic Cysts

All true odontogenic cysts are characterized by epithelium lining a collagenous cyst wall. They are believed to arise from proliferation of normally quiescent epithelium in the jaw (i.e., gingival rests of Serres, rests of Malassez) Cysts can be divided into inflammatory and developmental categories.

Inflammatory Cysts

Radicular (periapical) Cyst – This is the most common odontogenic cyst (65%) and is thought to arise from the epithelial cell rests of Malassez in response to inflammation. In fact, practically all radicular cysts originate in preexisting periapical granulomas. Radiographic findings consist of a pulpless, nonvital tooth that has a small well-defined periapical radiolucency at its apex are diagnostic. Large cysts may involve a complete quadrant with some of the teeth occasionally mobile and some of the pulps nonvital. Root resorption may be seen. The cyst is painless when sterile and painful when infected. Microscopically, the cyst is described with a connective tissue wall that may vary in thickness, a stratified squamous epithelium lining, and foci of chronic inflammatory cells within the lumen. Treatment is extraction of the affected tooth and its periapical soft tissue or root canal if the tooth can be preserved.

Paradental Cyst – An inflammatory cyst forming most often along the distal or buccal root surface of partially impacted mandibular third molars, this cyst is thought to be the result of inflammation of the gingiva overlying a partly erupted third molar. Radiographically, it presents

as a radiolucency in the apical portion of the root and represents from 0.5% to 4% of all odontogenic cysts. Treatment is by enucleation.

Developmental Cysts

Dentigerous (follicular) Cyst – This is the most common developmental cyst (24%) and is thought to originate via the accumulation of fluid between reduced enamel epithelium and a completed tooth crown. It is usually found in the mandibular third molars, maxillary canines, and maxillary third molars. These cysts are most prevalent in the second to fourth decades. Radiographically, a unilocular radiolucency with well defined sclerotic margins encircling the crown of an unerupted tooth is seen. Most cysts are asymptomatic, but large lesions can cause displacement or resorption of adjacent teeth and pain. Histologically, a cyst composed of thin connective tissue walls lined by stratified non-keratinizing squamous epithelium over a fibrocollagenous cyst wall. Treatment is with enucleation or decompression followed by enucleation if large.

Developmental Lateral Periodontal Cyst - This cyst may arise from epithelial rests in the periodontal ligament or may represent a primordial cyst originating from a supernumerary tooth bud. It is most frequently encountered in the mandibular premolar region in adult men over 40 years. On radiographs, this cyst is an interradicular radiolucency with well-defined or corticated margins. The adjacent teeth usually show some degree of root divergence and are vital. Microscopically, the cyst lining is either nonkeratinizing stratified squamous or stratified cuboidal epithelium with a minimally inflamed fibrous wall. The treatment is surgical enucleation or curettage with preservation of adjoining teeth.

Odontogenic Keratocyst (OKC) – This is a specific and microscopically distinct form of odontogenic cyst that may assume the character of any of the odontogenic cysts. OKC comprises approximately 11% of all cysts of the jaws and are most often seen in the mandibular ramus and angle. It may be associated with the crown of a tooth appearing as a dentigerous cyst or may represent a keratinizing variant of the lateral periodontal cyst. Radiographically, it can mimic any of the jaw cysts and may appear as a well-margined inter-radicular radiolucency, a pericoronal radiolucency or a multilocular radiolucency. When multiple keratocysts of the jaws are observed, the nevoid basal cell carcinoma syndrome should be investigated. The histologic features of OKCs include a thin epithelial lining with underlying connective tissue composed of a thin collagen layer with islands of epithelium that may represent other early cysts. Secondary inflammation may mask these characteristic features of OKC, resulting in misdiagnosis of a dentigerous, lateral periodontal, paradental or other more benignly behaving cyst. The most problematic clinical aspect of the OKC is the high frequency of recurrence, up to 62% in some studies, most recurring within the first 5 years of treatment. The thin and friable lining of the cyst wall often makes complete removal with enucleation difficult. Also, satellite cysts within the fibrous cyst wall may lead to recurrence if incompletely removed. Treatment often depends on the extent of the initial lesion. Small OKCs may be treated with simple enucleation if the entire cyst lining can be removed. Association with an impacted tooth requires removal of the cyst and tooth. A number of authors advocate removal of overlying soft tissues, which may contain remnant epithelial elements, in an attempt to decrease recurrences. The most common current method is total enucleation with or without a “peripheral ostectomy” to carefully excise the entire specimen. A recent study by Bataineh, et al., promotes complete resection without

continuity defects through an intraoral approach. They advocate resection of cortex bone approximately 1 cm around the lesion with sacrifice of any teeth in continuity with the lesion. When perforation of the cortex occurred, the overlying mucosa/soft tissues were also excised. The osseous walls of the defect were abraded with coarse surgical burs and the defect was packed with Whitehead's varnish on Iodoform gauze for 5 to 8 days. The inferior alveolar nerve was free of pathologic tissue and spared in all cases. No reported recurrences with a follow up from 2 to 8 years were found with this method. Long term follow-up with periodic x-ray is recommended, as OKCs have been known to recur 20 to 40 years after initial treatment.

Glandular Odontogenic Cyst (GOC)– This is one of the more recently described odontogenic cysts. It is uncommon, originally described in 1988 by Gardner, et al.. Most have been reported to occur in the mandible (87%), particularly the anterior region (90%). The age range is from 14 to 90 years, with a mean of 49.5 years. Swelling is the most common complaint with pain about 40% of the time. These cysts tend to have a very slow progressive growth. Radiographically, they can present as either unilocular or multilocular radiolucencies. Its histology shows a stratified epithelium with cuboidal, sometimes ciliated, surface lining cells. There is a polycystic nature to the lesion with both secretory elements and stratified squamous epithelium, often with epithelial spheres, plaques, or plaque-like thickenings. There is considerable overlap between the histologic features of the GOC and central low-grade mucoepidermoid carcinoma. This cyst has a considerable recurrence potential, about 25% after either enucleation or curettage, so some have suggested marginal resection. Curettage or enucleation can still be effective, provided the clinician follows the patient closely for several years, and the lesion does not involve the posterior maxilla.

Nonodontogenic cysts

Incisive Canal Cyst – This is a developmental nonodontogenic cyst derived from embryonic epithelial remnants of the nasopalatine duct or incisive canal. It typically occurs in adults (4th to 6th decades) with no sex predilection. It is a well-delineated oval or heart-shaped radiolucency located between and apical to the two maxillary central incisors in the midline. Palatal swelling is common, and occasionally, the incisors will show evidence of root resorption. The cyst is asymptomatic and is usually an incidental finding on routine dental radiographs. Histologically, the cyst may be lined by stratified squamous epithelium, respiratory epithelium, or both. Treatment may consist of surgical enucleation or periodic radiographic follow-up. Progressive enlargement warrants surgical intervention.

Stafne Bone Cyst – The Stafne (static) bone cyst or submandibular salivary gland depression is usually discovered incidentally on dental radiographs. It is asymptomatic and is not a true cyst, rather an anatomic depression in the lingual aspect of the body of the mandible where normal salivary gland tissue rests. The radiographs show a small, circular, corticated radiolucency below the level of the mandibular canal. Histologically, normal salivary tissue is found and no treatment is required except routine radiographic follow-up.

Traumatic Bone Cyst – The traumatic cyst is not a true epithelial cyst, but represents an empty or fluid-filled cavity of bone lined with a fibrous or granulation tissue membrane. The term traumatic was used to implicate trauma as the cause. However, less than half of the instances are associated with any significant trauma to the jaw with an unknown etiology. The

lesion is located most often in the body or anterior portion of the mandible, and radiographically it is radiolucent. A classic feature is its tendency to scallop between the tooth roots. The overlying teeth are vital. Microscopically, a thin membrane of fibrous granulation tissue may line the cavity. Treatment with exploratory surgery following aspiration causes hemorrhage which may expedite healing.

Surgical Ciliated Cyst (of Maxilla) – Following a Caldwell-Luc operation, fragments of sinus epithelial lining may become entrapped in the surgical site. If this epithelium undergoes benign cystic proliferation, a unilocular well-delineated radiolucency will become evident in the maxilla. The lesion lies within the alveolar bone subjacent to the antral floor and is generally confined to an edentulous or inter-radicular area in the posterior maxilla. Pain or discomfort may be present. Histologically, the cyst is lined by pseudostratified columnar ciliated epithelium with an inflammatory connective tissue wall. Treatment is with surgical enucleation.

Odontogenic Tumors

Epithelial Odontogenic Tumors

Ameloblastoma – The ameloblastoma is the most common odontogenic tumor. It is a benign but locally invasive neoplasm derived from odontogenic epithelium. It has three different clinicopathologic subtypes: multicystic (86%), unicystic (13%) and peripheral (extraosseous – 1%). It usually occurs in the 4th and 5th decades without a gender predilection. In the clinical sense, the ameloblastoma can be considered a basal-cell carcinoma, to which it may be related histologically. Classically, it presents as a multilocular radiolucency with a predilection for the posterior mandible. It may arise from the lining of a dentigerous cyst but more often arises independently of impacted teeth. It is characterized by a progressive growth rate and, when untreated, may reach enormous proportions. Early symptoms are often absent, but late symptoms may include a painless swelling, loose teeth, malocclusion, or nasal obstruction. Maxillary tumors frequently perforate into the antrum and may grow freely, with extension into the nasal cavity, ethmoid sinuses, and skull base. A small number of microscopically benign ameloblastomas have been reported to undergo distant metastases. Radiographs classically show a well-circumscribed, expansile soap-bubble radiolucency with clearly demarcated borders. However, the unilocular lesion is indistinguishable from an odontogenic cyst. The extent of root resorption may indicate a neoplastic process. Microscopic features shows two patterns of arrangement, plexiform and follicular, with no bearing on growth potential, metastatic potential or prognosis. Classic features are sheets and islands of tumor cells showing an outer rim of columnar ameloblasts with nuclei polarized away from the basement membrane. The center of these nests is composed of stellate-shaped epithelial cells that mimic the stellate reticulum. Rarely, they can exhibit cytologic features of malignancy with squamous differentiation (less than 1%). These tumors are diagnosed as ameloblastic carcinoma and carry a poor prognosis.

Treatment varies according to type and the growth characteristics of each neoplastic entity. The peripheral subtype occurs as a soft-tissue mass, which can be treated successfully with complete excision, including a small rim of clinically uninvolved tissue. The unicystic subtype may be treated with complete removal provided that no satellite lesions at the periphery or extension of tumor cells through the fibrous cyst wall is seen on histopathologic examination. If this occurs after initial enucleation, peripheral ostectomy or marginal resection should be

performed. The treatment of the classic infiltrative, more aggressive ameloblastoma should not be taken lightly. Mandibular resection must include an adequate zone of normal-appearing bone around the main tumor mass. Extension of tumor into surrounding soft tissues is an ominous sign and demands surgery in these areas as vigorous as within the confines of the bone. Maxillary ameloblastomas require more aggressive initial management with at least a 1.5 cm margin of radiographically normal bone. Postoperative follow-up is critical for a minimum of 5, and preferably 10, years. Ameloblastic carcinoma should be treated with radical surgical resection as for squamous cell carcinoma, with neck dissection reserved for apparent lymphadenopathy.

Calcifying Epithelial Odontogenic Tumor – Also known as the Pindborg tumor, this is an aggressive odontogenic neoplasm of epithelial derivation. Most cases are associated with an impacted tooth, and the mandibular body or ramus is by far the most common site. The chief sign is cortical expansion. Pain is usually not a complaint. On x-ray, expanded cortices can be visualized in buccal, lingual, and vertical dimensions. It is usually radiolucent with poorly defined, noncorticated borders. It may be unilocular, multilocular or moth-eaten. Multiple radiopaque foci within the radiolucent zone may give it a “driven-snow” appearance. Root divergence and resorption are common findings and the impacted tooth is often significantly displaced with arrested root development. Histologically, sheets, nests and cords of eosinophilic epithelial cells prevail, which do not resemble tooth germ primordia. These islands of cells infiltrate bony trabeculae and often show degenerative nuclear hyperchromatism and pleomorphism, which may be misdiagnosed as squamous cell carcinoma. Small psammoma-like concentric calcifications called Liesegang rings are seen within the epithelial islands and aid the diagnosis. Their behavior is not unlike that of ameloblastoma, although recurrence rates are less. En bloc resection, hemimandibulectomy, or partial maxillectomy, are the treatment methods required to eradicate the disease.

Adenomatoid Odontogenic Tumor – While usually associated with the crown of an impacted anterior tooth, this tumor may arise between tooth roots as well. Painless expansion is often the chief complaint. The maxillary incisor-cuspids are common sites. Radiographically, the tumor is well defined, expansile with root divergence, and radiolucent with calcified flecks (target appearance). Microscopic features include a thick fibrous capsule with an inner epithelial neoplastic component composed of organoid clusters of spindle cells. Columnar cells are arranged in rosettes or ductal patterns dispersed throughout the organoid clusters. Treatment is with simple surgical enucleation and recurrence is extremely rare.

Squamous Odontogenic Tumor – This is a hamartomatous proliferation of odontogenic epithelium, probably arising from the rests of Malassez. The maxillary incisor-canine area and mandibular molar area are most commonly involved. Most cases are unifocal and tooth mobility is the usual chief complaint. On x-ray, a localized radiolucent area between contiguous teeth is well-circumscribed. Most cases are either triangular or semicircular in configuration. Histologic features include oval, round and curvilinear nests of squamous epithelium throughout a mature collagenous stroma. Cystic degeneration is commonly seen, and some of the nests exhibit ovoid crystalloid structures. Treatment is with extraction of the involved tooth and thorough curettage of the lesional tissue. Maxillary lesions may warrant resection to prevent recurrence if more extensive. Recurrences require more aggressive surgical treatment.

Calcifying Odontogenic Cyst (Gorlin cyst) – This is a tumor-like cyst found predominantly in the mandibular premolar region. Nearly one quarter of such cysts are peripheral, producing radiographically evident calcification above the underlying cortex and manifesting a gingival swelling. Intrabony lesions may cause expansion, and teeth remain vital. Radiographically, the lesion starts as a radiolucency and progressively calcifies, yielding a target lesion (opaque, with a circumferential lucent halo). Root divergence is common. Histologically, the cyst lining is composed of stratified squamous epithelium with a polarized basal layer. The lumen contains eosinophilic keratinized cells devoid of nuclei (ghost cells). Enucleation with curettage is the treatment of choice with rare recurrences.

Mesenchymal Odontogenic Tumors

Odontogenic Myxoma – This tumor is believed to originate from the dental papilla or follicular mesenchyme. It is usually multilocular and expansile, sometimes associated with impacted teeth. On x-ray, the radiolucency has coursing septae which look like a finely reticulated spider web. These are slow growing tumors but are aggressively invasive and may become quite large. The body of the mandible is the favored site. Microscopically, spindle and stellate fibroblasts are associated with basophilic ground substance and myxomatous tissue. Treatment should be with en bloc resection to prevent recurrence, although curettage may be attempted for more fibrotic lesions.

Central Odontogenic Fibroma - This tumor shows more collagen and less ground substance than the myxoma. Clinical findings, when present, include swelling or depression of the palate mucosa with tooth mobility. X-ray shows a uni- or multilocular radiolucency involving periodontal and crestal bone adjacent to dental roots. Recurrence is unlikely following complete removal.

Cementoblastoma – This is a true neoplasm of cementoblasts, which arises most often on the first mandibular molars. The cortex is slightly expanded both buccally and lingually without pain. The involved tooth is ankylosed to the tumor mass and vital. Percussion reveals an audible difference between affected and unaffected teeth. On x-ray, the apical mass may be lucent with either central opacities or a solid opacity. A thin radiolucent halo can be seen around densely calcified lesions. Microscopic appearance of radially oriented trabeculae from the attached root cementum with a rim of osteoblasts and fibrous marrow is apparent. Treatment is with complete excision with sacrifice of the involved tooth.

Mixed Odontogenic Tumors

The mixed odontogenic tumors include ameloblastic fibroma, ameloblastic fibrodentinoma, ameloblastic fibro-odontoma, and odontoma. Only ameloblastic fibroma is entirely radiolucent. While all of the mixed odontogenic tumors may begin as radiolucent lesions, the remainder will eventually develop radiopaque foci. The mixed odontogenic tumors possess both epithelial and mesenchymal tumor elements, and mimic the differentiation of the developing tooth germ. The least differentiated is the ameloblastic fibroma, which is composed of a diffuse mass of embryonic mesenchyme traversed by columnar or cuboidal odontogenic epithelium resembling the dental lamina. Ameloblastic fibrodentinomas are similar, yet a dense eosinophilic dentinoid material lies next to the epithelial element. Ameloblastic fibro-odontomas

are further differentiated in that both dentin and enamel matrix are formed and mixed with ameloblastic fibroma zones. The odontoma contains all elements of the mature tooth germ yet does not have a significant soft tissue cellular overgrowth. Enucleation or thorough curettage with extraction of the impacted tooth is recommended for these tumors. The ameloblastic fibroma has a limited tendency to recur. There has been a microscopically malignant and aggressive mixed odontogenic tumor described as ameloblastic fibrosarcoma. The ameloblastic fibrosarcomas are aggressive and commonly recur after curettage, therefore en bloc resection is recommended for these tumors.

Related Jaw Lesions

Giant Cell Lesions

Central Giant Cell Granuloma (CGCG)– This is a neoplastic-like reactive proliferation of the jaws that accounts for less than 7% of all benign lesions of the jaws in tooth-bearing areas. It commonly occurs in children and young adults with a slight female predilection. The lesion is more common in the mandible than maxilla underlying anterior or premolar teeth. Expansile lesions can cause root divergence or resorption. The clinical features vary according to the type of development the lesion assumes. Lesions may be slow-growing and asymptomatic or rapidly expanding with pain, facial swelling and root resorption. The fast growing variants have a high rate of recurrence. Because of the higher incidence of these lesions among girls and women of child-bearing years, hormonal influences have been suggested as influential in their development. The radiographic appearance ranges from unilocular to multilocular radiolucencies with either well-defined or irregular borders. Multinucleated giant cells, dispersed throughout a hypercellular fibrovascular stroma often with bony trabeculae are present on histology. Treatment regimens for CGCG have historically included curettage, segmental resection, and radiation therapy. Radiation therapy has been discouraged recently, due to the small risk of malignant transformation to osteogenic sarcoma. Intralesional steroids have also been advocated for managing CGCG in younger patients as a nonsurgical alternative. Individualized treatment depending on the aggressiveness of the lesion is the rule. Small, nonaggressive lesions will usually respond to through excision with careful curettage with a recurrence rate of less than 15%. Larger, more aggressive lesions, which have higher recurrence rates, require more extensive surgery, which may include en bloc resection.

Brown Tumor of Hyperparathyroidism – This represents a local manifestation of a systemic metabolic disease that is histologically identical to central giant cell granuloma. When this histology is present, serum calcium and phosphorus should be obtained, especially in older patients (unlikely to have central giant cell granulomas), to rule out Brown tumor.

Aneurysmal Bone Cyst – This is not a true cyst, and is closely related to the giant cell granuloma with its aggressive reactive process. The lesion is composed of large vascular sinusoids, and blood can be aspirated with a syringe. A bruit, however, cannot be auscultated due to the low pressures. It has a great potential for growth and can result in marked expansion and deformity. A multilocular radiolucency traversed by thin septae with cortical expansion is present on x-ray. The mandible body is the most frequent site. Histologically, large blood-filled sinusoids lined by an endothelial layer with surrounding fibroblastic, hypercellular tissue is present. Simple enucleation is the preferred treatment. Recurrence is rare.

Fibroosseous Lesions

Fibrous Dysplasia – Fibrous dysplasia is the most common disease of the jaws to manifest a ground-glass radiographic pattern. There are two forms, monostotic form, which is more common in the jaws and cranium, and polyostotic, which is often associated with McCune-Albright's syndrome (cutaneous pigmentation, autonomic hyper-functioning endocrine glands, and precocious puberty). The monostotic variant is by far the most common type seen when the jaw is involved and presents as a painless expansile dysplastic process of osteoprogenitor connective tissue. The maxilla is the most common site of involvement. The lesion does not cross the midline and tends to be limited to one bone. The antrum is often obliterated, and the orbital floor (with globe displacement) may be involved. The histology is characterized by irregular osseous trabeculae in a hypercellular fibrous stroma. Treatment should be deferred, if possible until skeletal maturity. Children with fibrous dysplasia should be followed quarterly with clinical and radiographic evaluation. Quiescent and non-aggressive lesions that have been observed to exhibit no growth are treated by contour excision for esthetic and/or functional reasons. When disabling functional impairment or paresthesia occurs, contour or en bloc excision may be performed. Accelerated growth or aggressive lesions require early surgical intervention with en bloc resection and bone graft reconstruction. Malignant transformation has been reported after radiation therapy, which is contraindicated.

Ossifying Fibroma – Similar to fibrous dysplasia histologically, this is a true neoplasm of the medullary portion of the jaws. These lesions arise from elements of the periodontal ligament, and tend to occur in younger patients, most often in the premolar-molar region of the mandible. These tumors when small are asymptomatic but frequently grow to expand the jaw bone. On x-ray, a well-demarcated radiolucent lesion is seen in the early stages which becomes increasingly calcified with maturation. The progression from the radiolucent to the radiopaque stage takes at least 6 years. After surgical excision of the lesion which tends to shell out, recurrence is uncommon.

Condensing Osteitis

Focal areas of radiodense sclerotic bone are found in about 4% to 8% of the population. These are usually in the mandible around the apices of the first molar and are thought to be reactive bony sclerosis to low-grade pulpal inflammation. They are irregular in shape, radiopaque with superimposed periapical inflammation. Once formed, these lesions are stable. No treatment is necessary.

Conclusion

In summary, there are a multitude of odontogenic cysts and tumors that may present in head and neck patients. The key to diagnosis is a careful history and physical examination accompanied by radiographic evidence and pathologic confirmation. Many of these entities represent benign cysts and tumors, however significant pathologic disease may be lurking which necessitates prompt treatment and immediate consultation as necessary.

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