Facial Bone Tumors

Diagnosis of Odontogenic 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. 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. Jaw lesions are difficult to distinguish from each other on radiography. The patient's history and an analytical approach to radiographs help in narrowing down the differential diagnosis. Any jaw lesion should be evaluated taking into consideration the following radiological features:

Density of lesion, margin, locularity Jaw lesions can be described as having either a radiolucent, radiopaque, or mixed appearance, relative to density of the adjacent bone. The majority of jaw lesions are radiolucent (> 80%). Unilocular radiolucent lesions with well-defined borders usually indicate a slow proliferating benign process (Dentigerous cyst, Odontogenic keratocyst, Ameloblastoma). Multilocular lesions with well-defined borders indicate a benign yet aggressive process. Radiopaque lesions which are welldefined, usually represent a benign or inflammatory aetiology. In general, lesions with well-defined borders are usually benign, whereas lesions with ill-defined borders invariably represent aggressive, inflammatory or neoplastic processes (acute osteomyelitis, primary bone neoplasm). Mixed radiolucent-radiopaque lesions can be due to inflammatory, metabolic conditions, fibro-osseous lesions, or less commonly, malignant processes (Fibrous dysplasia, Chronic osteomyelitis, Osteosarcoma).

Anatomical location, relation to dentition. Certain lesions have a predilection for a particular site, whereas others can occur anywhere in the jaw). Non-odontogenic lesions usually have no specific relationship to the dentition or can involve the bone around two or more teeth, whereas odontogenic lesions typically involve only one tooth or a specific part of the tooth. Relationship of the lesion with respect to the inferior alveolar canal indicates tissue types that

compose the lesion. Lesions above the canal are likely to be odontogenic, whereas lesions below it are usually non-odontogenic in nature. If the abnormal appearance affects all the structure of maxillofacial region, systemic disorders such as metabolic or endocrine abnormality should be considered.

Cortical integrity, periosteal reaction and soft tissue Slow-growing lesions often cause expansion with cortical bowing, while cortical destruction denotes aggressive inflammatory or neoplastic lesions. Presence of periosteal reaction and soft tissue is also suggestive of an inflammatory or malignant aetiology. Some types of periosteal reactions are quite specific, like the sunburst type in osteosarcoma.

Effect on surrounding structures Evaluating the effect of a lesion on the surrounding structure helps in inferring behaviour of the lesion. Displacement of teeth is seen more commonly with slow-growing, space-occupying lesions. Lesions with an epicentre above the crown of the tooth (i.e., dentigerous cyst and occasionally odontomas) displace the tooth apically. esions that start in the ramus, such as cherubism, may push teeth in the anterior direction. Resorption of the tooth usually occurs in more chronic and slow-growing processes; however, malignant lesions also occasionally resorb teeth. If a lesion involves only one tooth, it is important to note the degree of tooth development, relationship of the lesion with portion of tooth (crown vs.root vs. entire tooth) and any signs of tooth resorption. Malignant lesions can quickly grow down the ligament space, resulting in irregular widening and destruction of lamina dura. Widening of inferior alveolar canal with maintenance of a cortical boundary may indicate presence of benign lesion of vascular or neural origin.

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). *Peculiar*

The key to diagnosis is a careful history and physical examination accompanied by radiographic evidence and pathologic confirmation.

Classification of bone maxillofacial tumors. I. Odontogenic Tumors a) Epithelial Odontogenic Tumors, b) Mesenchymal Odontogenic Tumors, c) Mixed Odontogenic Tumors. II. Non odontogenic benign jaw tumors: 1. Tumors of osteoblastic derivation (ostema, osteoid-osteoma); 2. Tumors of cartilage (chondroma); III. Non odontogenic, non osteoblastic benign jaw tumors - Related Jaw Lesions - (desmoplastic fibroma, giant cell granuloa, neurofibroma, hemangiomas, lipoma).

Odontogenc 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 (extraosseus – 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 then 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 Pindorg 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 no 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 includes 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 fibrodentinomas, ameloblastic fibro-odontoma, and odontoma (compound composite odontoma, complex composite 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.

Odontoma: compond and complex. The odontoma is a binign tumor containing all the various component tissue of teeth. It is the ost common odontoenic tumor represening 67% of all odontogenic tumors. Odontoma is a term applied to odontogenic proliferations in which enamel, dentin, and pulp are present within the lesion, this represents terminally differentiated odontogenic tissue. Although toothy tissues are present, the structure formed are arranged either as collections of small, morphologically atypical teeth (compund odontoma), or as a disorderly mass of dental tissues that lack recognizable tooth form altogether (complex odontoma).

In the compound odontoma, multiple small and malformed tooth-like structures are formed creating a “bag of marbles” radiographic appearance. In the complex odontoma, there is little or no tendency to form tooth-like structures. The dentin and enamel are entwined in a mass that bears no resemblance to teeth. Both types of odontoma are found in the early years, usually in the teens or early twenties. Compound odontoma is more common in the anterior jaw segment whereas the complex type is found more commonly in the posterior jaws. Many are associated with an unerupted tooth. Odontomas behave more like developmental abnormalities (hamartomas) than true neoplasms. Although they may reach a large size, they do eventually cease growing in contrast to true neoplasms which show continuous growth. Treatment is elective surgery. They have a limited growth potential and cause no pain or cosmetic deformity

Non odontogenic bone tumors. *Osteoid osteoma* is a distinct benign entity. It has a nidus less than 2 cm in diameter composed either of immature osteoid, woven bone or a mixture of both. The nidus causes considerable pain and can often provoke reactive sclerosis in contagious tissue of the host bone. Pain is very characteristic of this lesion and is accompanied by vasomotor disturbances, which occur long before characteristic radiographic and histopathology findings become evident. The lesion occurs predominantly in

children, adolescents and young adults between 10 and 25 years of age. It is distinctly rare in patients aged more than 30 years. We report a rare case of osteoid osteoma in a 43-year-old female in mandibular first molar area.

Clinical appearance. Extraoral examination did not reveal any swelling. Smetimes the submandibular lymph nodes are tender on palpation. Intraoral examination revealed tenderness on vertical percussion, no clinical mobility of the involved teeth nor were there any periodontal problems, wasting diseases, fracture of the involved teeth or any evidence of caries. Intraoral periapical radiograph and orthopantomogram revealed a well-defined small oval-to-round radiolucency surrounded by well-defined corticated border.

Histopathology of the lesional tissue revealed islands of mature bone containing osteocytes within the lacunae. Osteoblastic rimming was also seen. Scanty connective tissue stroma showed numerous fibroblasts, collagen fibers and vascular spaces.

Surgical enucleation is nesessery. Based on clinical and radiographic findings, benign cementoblastoma, cystic odontome, cementifying /ossifying fibroma, sclerosing osteitis, periapical cemental dysplasia were considered in the differential diagnosis.

Gardner syndrome is a genetic disorder characterized by the presence of multiple polyps in the colon together with tumors outside the colon. The extracolonic tumors may include osteomas of the skull, thyroid cancer, epidermoid cysts, fibromas and sebaceous cysts[1]. The countless polyps in the colon predispose to the development of colon cancer. Polyps can also grow in the stomach, duodenum and small bowel.

Gardner syndrome can be identified based on oral findings, including multiple impacted and supernumerary teeth, multiple jaw osteomas which give a "cotton-wool" appearance to the jaws, as well as multiple odontomas, congenital hypertrophy of the retinal pigment epithelium (CHRPE), in addition to multiple adenomatous polyps of the colon. Gardner syndrome is also associated with FAP (Familial Adenomatous Polyposis) and may manifest as aggressive fibromatosis (desmoid tumors) of the retroperitoneum.

Osteoma. An osteoma is a benign bone-forming tumour that almost always occurs in the skull and face. The common location in jaw includes the lingual side of the ramus or the inferior mandibular border below the molars. These lesions are usually asymptomatic and can occur at any age. They begin to develop in early adulthood and may very slowly enlarge over years Radiologically, an osteoma is seen as a well-defined, dense, radiopaque mass. Multiple osteomas should raise the possibility of Gardner syndrome.

They are painless and self-limiting, but occasionally may become several centimeters across and then contribute to periodontal disease of adjacent teeth by forcing food during chewing in toward the teeth instead of away from them, as is normally the case. They usually require no treatment, but for those possibly contributing to a peridontal condition they can be removed by

conservative surgical excision. There is no malignant potential to this lesion. Fewer than 3% occur in children. Taken as a group, these lesions are found in at least 3% of adults and are more common in females than in males. Lesions may become 3-4 cm. in greatest diameter, but are usually less than 1.5 cm. at biopsy. Pathology**:** On cut surface the torus and exostosis show dense bone with a lamellar or laminated pattern. They are usually comprised of dense, mature, lamellar bone with scattered osteocytes and small marrow spaces filled with fatty marrow or a loose fibrovascular stroma.

Treatment. **B**ony exostosis requires surgical treatment unless it becomes so large that it interferes with function, interferes with denture placement, or suffers from recurring traumatic surface ulceration.

Non-odontogenic, non-osteogenic jaw tumor. (**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. (presence of few to many multinucleated giant cells in a stroma composed of ovoid-shaped to spindle-shaped mesenchymal cells[5]. The giant cells typically possess four to eight randomly arranged nuclei that may be hyperchromatic, oval, stippled or any combination of the three, with prominent nucleoli. Vessels in the stroma often are engorged with red blood cells, and hemosiderin pigment is readily seen, particularly in areas of extravasated blood.)

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.

Melanotic neuroectodermal tumor of infancy (MNTI) is a relatively uncommon osteolytic-pigmented neoplasm that primarily affects the jaws of newborn infants. The typical melanotic neuroectodermal tumor of infancy (MNTI) begins as a nonulcerated, lightly pigmented, blue or black lesion on the anterior aspect of the maxilla and rapidly expands to form a swelling or a tumescence that is cosmetically obvious to the parents of the infant. MNTI presents as a rapidly growing bluish mass on the anterior aspect of the maxilla.

The intraoral lesion appears as a sessile, lobulated mass, often reaching 2-4 cm in diameter by the time of diagnosis. Bone destruction and displacement of teeth often occur because of the intraosseous location in the maxilla. No thrill or pulse can be elicited from the MNTI. Although the lesion expands rapidly, the overlying mucosa remains intact. More than 90% of MNTI occur in the head and neck region, with most on the anterior part of the maxillary ridge. Other common sites include the skull, the mandible, the epididymis, and the brain. Rare lesions have been reported in the shoulder, the skin, the femur, the mediastinum, and the uterus.

Consider clinical, radiographic, laboratory, and histologic findings when establishing a proper differential diagnosis for melanotic neuroectodermal tumor of infancy (MNTI). The MNTI often presents as a fast-growing lesion, suggesting a clinical impression of infection or malignant neoplasm. The location in the anterior aspect of the maxilla is consistent with a number of odontogenic cysts and tumors; however, the odontogenic cysts (eg, periapical cyst, dentigerous cyst, odontogenic keratocyst, calcifying odontogenic cyst) occur in an older age group, teenaged through middle-aged adults. The same age differential is noted with respect to the more common odontogenic tumors (eg, ameloblastoma, odontoma, adenomatoid odontogenic tumor, calcifying epithelial odontogenic tumor, ameloblastic fibroma, odontogenic myxoma, odontogenic fibroma).

In addition to a diagnosis of MNTI, the young age of the patient as well as the maxillary location is also compatible with a clinical diagnosis of congenital

epulis of the newborn. Many nonodontogenic tumors are possible in the jaws, including central giant cell granuloma, ossifying fibroma, fibrous dysplasia, hemangioma, arteriovenous malformation, craniopharyngioma, Langerhans cell histiocytosis, rhabdomyosarcoma, Ewing sarcoma, and lymphoma. However, only Langerhans cell histiocytosis, rhabdomyosarcoma, Ewing sarcoma, and lymphoma are common in young children.

The radiographic appearance of a maxillary alveolar low-density radiolucency, containing no evidence of calcification, is consistent with any of the odontogenic cysts or tumors. Additionally, many of the aforementioned nonodontogenic lesions may also present with a radiographic appearance similar to that of MNTI.

Once a differential diagnosis is established from the clinical and radiographic findings, histologic evaluation is necessary to determine the final diagnosis. The histologic appearance of MNTI is usually that of a small, dark, cell neoplasm suggestive of neuroblastoma, rhabdomyosarcoma, Ewing tumor, lymphoma, desmoplastic small round cell tumor, and peripheral primitive neuroectodermal tumor. Although the histologic appearance is characteristic, special immunohistochemical stains and electron microscopy may be necessary to make a definitive diagnosis.

The histologic appearance of MNTI is unique and characteristic in that a distinct biphasic pattern exists. A moderately vascular fibrous background supports the MNTI. The peripheral borders are faintly noted, at best, by a thin, delicate, fibrous layer; however, most often, this nonencapsulated tumor shows local infiltration into the adjacent bone.

One portion of the lesion contains large polygonal cells arranged in sheets or alveolarlike structures. These large cells appear, under hematoxylin and eosin staining, to have pale abundant cytoplasm and pale nuclei with finely dispersed chromatin. These cells often contain the melanin pigment that gives the MNTI its blue-black clinical appearance.

Fontana stain can be used to enhance the demonstration of the melanin pigment. The cuboidal polygonal cells are at the periphery of the alveolar spaces, while the central portion contains the second smaller characteristic cell type. These cells are lymphocytelike or neuroblastlike with small, dark nuclei and little, if any, cytoplasm. These cells occasionally also form isolated clusters of their own within the fibrous stroma. Throughout the lesion, mitoses are rare but, when present, are normal in appearance. Cellular pleomorphism is scant. The few reported malignant cases of MNTI have little variation from the description above other than an increase in mitoses (3 or more per high-power field), hypercellularity, and focal necrosis. The malignant diagnosis is more one of increased growth rate, infiltration, and metastases. Metastatic lesions have been described in the lymph nodes, the liver, the adrenal gland, the spinal cord, and a variety of other sites.

The treatment of choice for melanotic neuroectodermal tumor of infancy

(MNTI) is surgical excision, and it is usually curative. This treatment can usually be accomplished with a partial maxillectomy by using a Weber-Fergusson incision and a facial degloving approach. Teeth, developing teeth, and the adjacent bone must be sacrificed when they lie near the borders of MNTI, since many clinicians advocate that a 5-mm margin of healthy tissue be included with the surgical specimen.

Fibroosseous Lesions. *Fibrous Dysplasia*. Fibrous dysplasia is a skeletal developmental anomaly of the bone-forming mesenchyme that manifests as a defect in osteoblastic differentiation and maturation. Virtually any bone in the body can be affected. It is a nonhereditary disorder of unknown cause.

The primary symptom in 90% cases was swelling, including deformation of the jaw. All cases displayed buccolingual expansion; all mandibular cases exhibited downward displacement of the lower border of the mandible; and almost all maxillary cases involved the maxillary antrum.

In fibrous dysplasia, the medullary bone is replaced by fibrous tissue, which appears radiolucent on radiographs, with the classically described *ground-glass appearance*. Trabeculae of woven bone contain fluid-filled cysts that are embedded largely in collagenous fibrous matrix, which contributes to the generalized hazy appearance of the bone.

There are two forms, monostotic form, occurring in 70%, which is more common in the jaws and cranium, and polyostotic, occurring in 30%, with is often associated with McCune-Albright's syndrome (cutaneous pigmentation, autonomic hyper-functioning endocrine glands, and precocious puberty). It only occur in 3% of cases. The neck and head are involved in half of these patients. Skull involvements occuers in27% of monostotic and up to 50% of polyostotic patients. 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 lession 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. Fibrous dysplasia involving the face and skull is called "Leontiasis ossea". Without treatment, one or more bones progressively increase in size, and move into the cavities of the eye,mouth, and or the nose and its sinuses. Also, abnormal protrusion of the eyeball (exophthalmos) may develop and eventually cause complete loss of sight because its presses on the optic nerve. In addition, there may be interference of the nasal passage and with eating. It may also cause facial nerve paralysis or dizziness. However, any of 12 nerves can be involvedwith fibrous dysplasia. The more common results could include cranial nerve problems, and sight, and hearing loss.

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.

Eosinophilic granuloma (EG) is the benign form of the 3 clinical variants of Langerhans cell histiocytosis, which include Letterer-Siwe disease, Hand-Schüller-Christian disease, and EG (formerly termed histiocytosis X).

Eosinophilic granuloma, which is classified with tumors of histiocytic origin, may be an isolated bony lesion or parenchymal, or may be part of systemic disease. EG is characterized by single or multiple skeletal lesions, and it predominantly affects children, adolescents, and young adults. Solitary lesions are more common than multiple lesions. When multiple lesions occur, the new osseous lesions appear within 1-2 years. Any bone can be involved; the more common sites include the skull, mandible, spine, ribs, and long bones. The age range of patients with EG is 2-30 years. The highest frequency occurs in patients aged 5-10 years; 75% of patients with EG are younger than 20 years.

Symptoms include localized pain, tenderness, swelling, fever, and leukocytosis. Lesions usually begin to regress after approximately 3 months, but they may take as long as 2 years to resolve. Most patients have no symptoms.

The distinctive morphologic lesions of the entire group of Langerhans histiocytosis disorders consist of expanding erosive accumulations of histiocytes, usually within the medullary cavity. Microscopically, proliferation of foamy and vacuolated histiocytes is associated with a variable admixture of neutrophils, eosinophils, lymphocytes, and plasma cells. The concentration of eosinophilic infiltrate varies from scattered mature cells to sheetlike masses of cells. Occasionally, areas of bone necrosis may interrupt the cellular infiltrate. The foamy cells may also be amassed in clumps, but because these clumps

represent phagocytosis of lipid debris, they are of no clinical significance. The diagnosis is usually based on radiographic demonstration of a destructive bone lesion arising from the marrow cavity and on characteristic morphologic findings.

Mandibular involvement may present as gingival and continuous soft tissue swelling. Eosinophilic granuloma may masquerade as an aggressive periodontitis. Eosinophilic granuloma should therefore be considered when an expanding lytic jaw lesion is encountered. Mandibular lesions may be associated with gingival and soft tissue swelling and floating teeth.

The differential diagnosis includes osteomyelitis, non hodgkin's lymphoma, and hodgkin's disease. Most patients have no symptoms, and the diagnosis is normally based on radiographic show of a harmful ivory lesion arising from the marrow cavity and on distinctive morphologic findings.

This disorder is treated with corticosteroids, which suppress immune function. Smoking may worsen the response to treatment and should be stopped. Radiation therapy or limited surgery may also be used to treat bone lesions. Treatment may include antibiotics, breathing assistance with a respirator, physical therapy, selenium-based shampoo for scalp problems, and hormone replacement to deal with hormonal dysfunction.

Cherubism. *Disease characteristics***.** Cherubism was first described as "familial multilocular cystic disease of the jaws" by Jones in 1933; however, shortly thereafter he renamed the condition cherubism because of the resemblance of affected individuals to the cherubs in Renaissance art.

Cherubism is characterized by painless bilateral, symmetrical enlargement of the mandible and/or maxilla resulting from replacement of bone with multilocular cysts (cyst-like growths) composed of fibrotic stromal cells and osteoclast-like cells. The phenotype ranges from no clinical manifestations to severe mandibular and maxillary overgrowth with respiratory, vision, speech, and swallowing problems. Onset is typically between ages two and five years. Other bones are usually not affected and the affected person is otherwise normal. The jaw lesions progress slowly until puberty when they stabilize and then regress. Dental abnormalities include congenitally missing teeth, premature exfoliation of the deciduous teeth, and displacement of permanent teeth by the jaw lesions. Othen, interfere with normal tooth development. By age 30 years, facial abnormalities are no longer apparent; residual jaw deformity is rare.

Diagnosis depends on typical clinical findings and radiographic findings of well-defined, often extensive bilateral multilocular areas of diminished density, with few irregular bony septa. in the mandible and/or maxilla. *SH3BP2* is the only gene currently known to be associated with cherubism. Histologic manifestations of lesions in the mandible and/or maxilla: non-neoplastic fibrotic lesions that contain numerous multinuclear giant cells and occasionally cysts. Increase in osteoid and newly formed bone matrix is observed in the periphery.

Differential Diagnosis. Central giant-cell granuloma. Central giant-cell

granuloma is a rare benign lesion that usually occurs in the mandible and maxilla. The lesions can lead to facial deformity and displacement of the teeth. The condition occurs in children and young adults, with a higher frequency in females. Histologically, central giant-cell granuloma cannot be separated from cherubism. The two conditions can be distinguished by radiologic findings because the majority of lesions in cases of central giant-cell granuloma are unilocular, whereas in cherubism the lesions are usually multilocular [De Lange & Van den Akker 2005]. No mutations in the *SH3BP2* gene have been identified in individuals with aggressive central giant-cell granuloma [de Lange et al 2006]. The etiology of central giant-cell granuloma is unknown.

Fibrous dysplasia**.** Fibrous dysplasia of the jaw is characterized by benign giant-cell lesions localized asymmetrically in maxilla rather than mandible. The condition usually presents in childhood and is progressive until after adolescence [Zenn & Zuniga 2001]. Cherubism can be distinguished from fibrous dysplasia on a clinical basis.

Hyperparathyroidism. Brown tumors are rare benign giant-cell lesions that arise as a result of parathyroid hormone effects on bone tissue in persons with hyperparathyroidism. Brown tumors can occur in both the maxilla and mandible [Lessa et al 2005]. The age of onset is usually in adulthood. Hyperparathyroidism can be distinguished from cherubism with biochemical investigations, since serum concentrations of calcium, parathyroid hormone, and alkaline phosphatase are elevated in hyperthyroidism [Silva et al 2002]. Cherubism has also been reported in association with neurofibromatosis type 1 and in a single case of coronal and sagittal craniosynostosis, which is likely to be a coincidental association.

Management. *Treatment of manifestations:* care by a craniofacial team in a major pediatric medical center; surgery (curettage with or without bone grafting) as needed between ages five to 15 years for disfiguring enlargement of jaws or locally aggressive lesions; orthodontic treatment; ophthalmologic treatment for displacement of the globe or vision loss. A mouse model for cherubism demonstrated that increased cytokine tumor necrosis factor α(TNF-α) production by myeloid cells is causative [Ueki et al 2007]. If TNF-α were found to be pathogenic in humans, anti-TNF therapies could provide new treatment options for cherubism. *Prevention of secondary complications:* Early orthodontia and/or jaw reconstruction may reduce risk for upper airway obstruction, obstructive sleep apnea, tooth displacement. *Surveillance:* long-term follow-up with clinical, radiographic, dental, orthodontic, ophthalmologic evaluations. *Testing of relatives at risk:* When the disease-causing mutation in the family is known, molecular testing can be used to identify mildly affected relatives who may benefit from early intervention; otherwise use clinical and radiographic evaluations to identify relatives at risk. *Other:* Results of studies using calcitonin are not promising.

Genetic counseling. Cherubism is inherited in an autosomal dominant

manner. The proportion of cases caused by *de novo* mutations is unknown because of variable expressivity and reduced penetrance. Each child of an individual with cherubism has a 50% chance of inheriting the mutation. Prenatal diagnosis for pregnancies at increased risk is possible when the *SH3BP2* disease-causing mutation has been identified in the family.

1. Melanotic neuroectodermal jaw tumor in infancy.