Many extraocular masses involving the pediatric orbit have an osseous origin. The most common is the dermoid inclusion cyst; these cystic lesions may contain lipid and are most often found near the zygomaticofrontal suture, adjacent to an indolent-appearing erosion of bone. Some primary bone lesions may involve the orbit, producing a lytic or dense lesion with enlargement of the bone; these lesions include fibrous dysplasia, juvenile ossifying fibroma, and osteosarcoma. Fibrous dysplasia tends to produce a mass of ground-glass appearance with longitudinal osseous expansion, whereas juvenile ossifying fibroma is likely to produce a mixed lytic and sclerotic lesion and focal osseous enlargement. Osteosarcoma causes marked bone destruction and variable osteoid production. Langerhans cell histiocytosis, an idiopathic reticuloendothelial proliferative disorder, tends to involve the bones of the skull, especially the lateral orbital roof; it produces lytic destruction of bone with a sclerotic rim and a large intraorbital soft-tissue mass. Granulocytic sarcoma is a solid tumor that may occur in children with myelogenous leukemia. These tumors tend to arise in the subperiosteum of the lateral orbital wall, although they usually do not disrupt the bone. Finally, the orbit is a common site for bone metastases from neuroblastoma, which cause aggressive periosteal reaction in the orbital roof or lateral wall. The last three conditions are often bilateral. At imaging evaluation, osseous lesions may appear similar to each other and to nonosseous masses of the orbit. Knowledge of the pathologic features of these tumors and how these features are reflected in their imaging appearances may help radiologists differentiate them.
Introduction

Some extraocular masses that cause proptosis in children originate from the osseous orbit. These masses vary in histologic type and differ from those encountered in adults. They include congenital lesions associated with development of the osseous orbit (dermoid and epidermoid inclusion cysts), primary bone lesions that may involve the orbit (fibrous dysplasia, juvenile or psammomatoid ossifying fibroma, and Langerhans cell histiocytosis [LCH]), malignant tumors that involve multiple sites (granulocytic sarcoma), and hematogenous metastases. Most of these conditions also occur in adults, but they are more frequently found in children. Leukemia is much more likely than lymphoma to involve the orbit in children, whereas orbital lymphoma is common in adults. Ophthalmic metastases in children arise in the osseous or extraocular soft-tissue structures and virtually never involve the ocular structures; in contrast, metastases in adults often arise in the ocular choroid. Many common primary tumors in adults metastasize to the ocular structures, but the vast majority of orbital metastases in children arise from neuroblastoma.

At imaging evaluation, osseous orbital lesions may appear similar to each other and to nonosseous masses of the orbit. Knowledge of the pathologic features of these lesions and how these features are reflected in their imaging appearances may help radiologists differentiate them. Since the treatment and prognosis of osseous orbital lesions are widely varied, careful interpretation of the imaging studies may help in their diagnosis and management. In this article, the clinical, pathologic, and imaging features of these lesions are described and correlated, and the differential diagnoses are reviewed.

Dermoid and Epidermoid Inclusion Cysts

Dermoid inclusion cysts are congenital and perhaps the most common orbital tumor of childhood, accounting for the majority of such lesions (either sampled in biopsy or excised) (1). Unlike teratomas, these lesions are not neoplasms, but rather represent closed sacs lined by an ectodermal epithelium (2–9). Both dermoid and epidermoid inclusion cysts probably arise from the same mechanism: a failure of the surface ectoderm to separate completely from the underlying cephalic mesenchyme. They may arise when the surface ectoderm fails to separate completely from the developing neural tube (neuroectoderm) or when surface ectoderm undergoes complex infolding, invagination, and fusion as the ears, eyes, and face begin to form. In the orbital region, these cysts most commonly arise near the developing sutures of the orbital bones (5,8). Epidermoid cysts are thought to develop later in embryonic life, after the ectodermal cells become committed to a single cell type. They are lined only by squamous epithelium. In contrast, dermoid inclusion cysts have a more complex histologic make-up, with several types of cells, a characteristic that suggests these cysts arise from an earlier embryologic event involving undifferentiated pluripotential cells.

Clinical Features

Although they are congenital, less than one-quarter of dermoid and epidermoid inclusion cysts are diagnosed at birth (10). They grow slowly and often become apparent in the first decade of life (1,11). Most manifest as painless, visible masses and are usually found along the lines of embryologic fusion: the zygomaticofrontal and the frontoethmoidal sutures (5,11). Dermoid inclusion cysts are overwhelmingly superficial, occurring in the supraorbital ridge, in the lateral third of the eyebrow (12). More than 80% of orbital dermoid inclusion cysts are in the upper outer quadrant or the lacrimal fossa (12). Deeper lesions are often identified as incidental masses, or they may occupy much of the orbit and manifest with proptosis in older children or adults. Dermoid inclusion cysts may rupture spontaneously or following trauma, and the leaked keratinous contents may incite an intense inflammatory response in the surrounding tissues, a finding that suggests orbital cellulitis (13,14).

Pathologic and Histologic Features

Dermoid and epidermoid inclusion cysts are characteristically unilocular lesions. They expand over years or decades, slowly enlarging by the accumulation of debris into their enclosed space. The thin squamous cell lining of the epidermoid cyst produces material by desquamation and fills the sac with dry waxy or flaky keratin (Fig 1d, 1e). Epidermoid cysts are often described
as shiny or “pearly” tumors because of the whitish dry keratin material (Fig 1c, 1d). By definition, the lining of an epidermoid contains only squamous cells.

In comparison to the epidermoid, the dermoid inclusion cyst is more complex. Dermoid inclusion cysts have a thicker lining that requires some scant vascularity, and they may develop dystrophic calcifications over time. The lining is composed of stratified squamous epithelium identical to that of the epidermis (Fig 2h). By definition, the wall of a dermoid inclusion cyst contains additional ectodermal features, such as hair follicles.
or sebaceous glands, which are typically arranged in pilosebaceous units (Fig 2h). Although these features are complex structures, they are all derivatives of ectoderm. Thus, a dermoid inclusion cyst is monodermal—that is, derived from a single germ layer—and is distinguished from a teratoma, which contains additional tissues of mesodermal or endodermal origin. The presence of lipid material in a dermoid inclusion cyst represents the oily secretion of ectodermally derived sebaceous glands and should not be confused with lipid from mesodermal fat. The lipid material within the cyst is lighter than its proteinaceous keratin debris, and it may float on top of the latter, like oil on water.

**Imaging Appearance**

Dermoid and epidermoid inclusion cysts slowly expand because of the accumulation of debris produced by the cutaneous lining. The increasing diameter and pressure of the cyst produce indolent periosteal and intradiploic remodeling of bone, usually with a reactive sclerotic margin or shell of dense bone. Because of these features, the cyst typically appears on radiographs and CT images as a sharply delimited, lucent lesion with a dense, surrounding rim of bone (Fig 2a) (14). Orbital dermoid and epidermoid inclusion cysts typically appear as encapsulated, well-circumscribed, unilocular cystic masses, and the appearance of the cyst contents varies depending on its composition.

Epidermoid inclusion cysts, probably because of their proteinaceous contents, are usually very similar in appearance to water or cerebral spinal fluid on both magnetic resonance (MR) and CT images (Fig 1); however, careful measurement of attenuation on CT scans may show that an epidermoid has a slightly higher attenuation coefficient compared with that of cerebral spinal fluid.

Use of MR images obtained with fluid-attenuated inversion recovery (FLAIR), diffusion-weighted, and apparent diffusion coefficient (ADC) sequences allows epidermoid cysts to be clearly distinguished from water. The internal signal of an epidermoid is not suppressed on FLAIR images, and epidermoid cysts have high signal intensity on diffusion-weighted images. Although this appearance is mostly caused by T2 shine through, epidermoid cysts do actually have reduced diffusion on ADC maps (3,15,16). Diffusion-weighted pulse sequences may be superior for delineating the margin or boundaries of these cysts (15).

Most dermoid inclusion cysts, in contrast to epidermoids and most other orbital masses, have the attenuation and signal intensity characteristics of lipid material because of their sebaceous secretions (Fig 2). Dermoid inclusion cysts may have CT attenuation coefficient values below zero, in the range of −60 HU to −90 HU. On MR images, their lipid components cause T1 shortening, and dermoid inclusion cysts often appear as bright as the subcutaneous fat. The lipid signal in a dermoid inclusion cyst also becomes dark on fat-suppressed images. Although the cyst contents do not enhance (Fig 2f), these lesions often have a discernable wall that may enhance on both CT and MR images. The wall may also contain high-attenuation foci of calcification on CT images.

**Differential Diagnosis**

Cephaloceles may also occur in the fronto-orbital region near the midline, often contain cerebral spinal fluid, and generally have adjacent osseous abnormalities, but these abnormalities are in the form of tracts that lead to the midline anterior cranial fossa. In addition, unlike dermoid inclusion cysts, cephaloceles do not contain lipid.

---

**Figure 2.** Dermoid inclusion cyst in a 21-year-old man with a 9-year history of facial asymmetry. (a) Nonenhanced coronal CT scan (bone window) shows a lucent tract through the right lateral frontal bone with a sclerotic margin (arrowhead) near the zygomaticofrontal suture. Note the scalloping of the adjacent superolateral orbit (arrow). (b) Coronal CT section slightly posterior to a shows the medial end of the lucent tract (arrowhead) leading to an intraorbital mass. Note the normal left zygomaticofrontal suture (arrow). (c) Coronal CT section (soft-tissue window) slightly posterior to b demonstrates the well-circumscribed mass adjacent to the scalloped portion of the orbital roof (arrowhead). Internal attenuation of the mass is less than that of the vitreous humor, a finding that suggests the presence of lipid. (d) Coronal spin-echo T2-weighted image demonstrates the well-circumscribed, predominantly high-signal-intensity mass in the right superolateral orbit (arrow), adjacent to the site of osseous scalloping seen in a and c. Pansinusitis is also apparent. (e) Coronal T1-weighted image depicts the well-defined mass with heterogeneous, predominantly high signal intensity, suggestive of fat (arrow). (f) Coronal fat-suppressed T1-weighted image obtained after intravenous administration of gadolinium at the same location as e shows suppression of the high signal within the mass, a finding that confirms its fat content (arrow). Enhancement is seen only in the rim and in adjacent, displaced extraocular muscles. (g) Intraoperative photograph shows the defect in the bone (arrowhead). (h) Photomicrograph (original magnification x100; H-E stain) of a specimen from a different patient demonstrates the cyst wall lined by keratinized squamous epithelium similar to epidermis (straight arrows) and deeper sebaceous gland lobules (arrowheads) and hair follicles and shafts (curved arrows). Note the keratin within the cyst lumen (©).
Figure 3. Polyostotic fibrous dysplasia with orbital involvement in a 15-year-old boy. (a) Coronal CT scan shows marked, expansile osseous remodeling with a ground-glass appearance (*) in the frontal bone, superior orbit, and nasal regions. The tissue encroaches on the left orbit and displaces the globe inferiorly. (b) Sagittal T1-weighted MR image reveals marrow replacement with expansion of the diploic space by extensive tissue with low to intermediate signal intensity (*). (c) Axial T2-weighted MR image demonstrates low signal intensity and mild heterogeneity of the fibrous dysplasia tissue (*). (d, e) Photograph of a sectioned whole-mount specimen (H-E stain) (d) and a photomicrograph (original magnification ×100; H-E stain) (e) show the diploic space marrow replacement by the fibrous dysplasia tissue (* in d), with the fibrous component (F in e) and trabecular bone (arrows in e) creating an alphabet-soup appearance.
Treatment and Prognosis
Small, asymptomatic dermoid and epidermoid inclusion cysts that remain stable for years do not require treatment. Treatment is indicated when they continue to grow or to prevent complications of rupture and infection. Inclusion cysts are completely surgically excised, preferably with the wall intact. Recurrence is unusual after complete excision (1,13,17).

Fibro-osseous Lesions
Fibrous dysplasia and juvenile ossifying fibroma are variants in a spectrum of histologically similar but biologically diverse fibro-osseous lesions that affect the craniofacial bones (the group also includes cementifying fibroma). These lesions vary in location (gnathic vs sinonasal), clinical behavior (aggressive vs indolent), and composition of mineralized component (cementum vs osteoid); however, there is a great deal of overlap in their histologic features, and clinical and radiologic correlation is often necessary to render a precise pathologic diagnosis (19). Differentiation of fibrous dysplasia from juvenile ossifying fibroma, both of which affect a similar age group, has important clinical implications, because the former condition is self-limited and rarely requires surgery, whereas the latter behaves aggressively and requires complete surgical resection.

Fibrous Dysplasia
Fibrous dysplasia represents a benign developmental anomaly in which the osteoblast fails to undergo normal differentiation and maturation. This process leads to replacement of the normal bone marrow by immature fibro-osseous tissue. Fibrous dysplasia is a slowly progressive disease centered in the medullary canal and may involve one or multiple bones, including the facial bones and orbit (19-21).

Clinical Features.—Fibrous dysplasia most frequently affects children (older than 2 years of age), adolescents, and young adults, although it has a wider age distribution. Fibrous dysplasia is monostotic in 70%–80% of cases (19-21). Polysototic disease occurs in 20%–30% of cases, with a variable extent of involvement, from only a few osseous sites to most of the skeleton (19-21). The sex distribution of fibrous dysplasia has been variably reported, from a mild female predilection (1.2:1 ratio) to a male predominance (almost 2:1 male-to-female ratio) (19-23). Craniofacial involvement is common, with the craniofacial region being affected in 10%–27% of cases of monostotic disease and 50% of cases of polyostotic disease (22,24–28). Frequently affected craniofacial sites include the frontal, sphenoid, ethmoid maxilla, zygoma, parietal, occipital, and temporal areas (in decreasing order of frequency) (22,24–28). The orbit is affected in 20%–39% of patients with craniofacial involvement (22,24–28).

Clinical symptoms of ocular involvement of fibrous dysplasia have been divided into primary and secondary processes (29). Primary complications result from osseous orbital involvement and include facial asymmetry, hypertelorism, proptosis, exophthalmos, diplopia, extraocular muscle palsies, and visual impairment (29,30). Visual symptoms may result from osseous expansion and compression of the optic nerve or chiasm. Secondary ocular complications of fibrous dysplasia include development of a mucocele or rare malignant transformation (20).

Additional clinical findings may include café-au-lait spots whose configuration resembles the coast of Maine and multiple endocrinopathies related to hypothalamic dysfunction, including the McCune-Albright syndrome of precocious puberty in girls with polyostotic fibrous dysplasia and cutaneous pigmentation.

Pathologic Features.—Lesions of fibrous dysplasia are composed of mixtures of fibrous and osseous components in varying proportions. The osseous component consists of woven bone and varies from solid round areas to curved, serpentine, or curlucie shapes (Fig 3d, 3e). The irregular shapes of these trabeculae usually predominate, leading to a histologic appearance described as “Chinese characters” or alphabet soup (20,29).
Osteoblastic rimming about the trabeculae is usually absent (20,29). The fibrous component or stroma surrounding the osseous trabeculae is typically of low cellularity and mitotic rate, and it has a variable degree of collagen and myxoid component (Fig 3e). Hemorrhage and cystic change may be apparent.

**Imaging Appearance.**—Radiographs of fibrous dysplasia typically demonstrate a medullary-based lesion with expansile osseous remodeling. In the calvaria, the outer table is usually more prominently affected, compared with the inner table. A characteristic “ground-glass” appearance is created by the mixture of woven bone and fibrous components that replace the medullary space (Fig 3a). The overall density of bone is determined by the amount of woven bone present and the degree to which it is mineralized (20,23,31,32). Areas of sclerosis are particularly common in craniofacial lesions, particularly those in the skull base and in the orbit. This sclerosis may be diffuse and obscure the ground-glass appearance of craniofacial lesions.

CT reveals features similar to those seen on radiographs, but it provides better anatomic delineation of the extent of involvement. Typical attenuation values of fibrous dysplasia are 70–130 HU, with areas of sclerosis demonstrating higher values (33–35). Intermixed areas of sclerosis and characteristic ground-glass appearing regions are more easily appreciated with the superior contrast resolution of CT (Fig 3a).

At MR imaging, fibrous dysplasia has a variable appearance. The predominant signal intensity is low to intermediate on T1-weighted images. On T2-weighted images, the signal intensity may be low (18%–38% of cases), intermediate (18%), or high (62%–64%) (20,23,36,37). In our experience, craniofacial lesions are more likely to have low signal intensity on T2-weighted MR images, a finding that likely corresponds to the increased sclerosis seen with other imaging modalities (Fig 3). Lesions are often relatively homogeneous on T1-weighted images, with more heterogeneity seen on long repetition time images. MR imaging performed after intravenous administration of contrast material demonstrated two patterns, as described by Jee and co-workers (36). In the majority of cases (73%), central enhancement was seen, whereas 27% revealed a peripheral rim pattern (36).

Bone scintigraphy of fibrous dysplasia typically reveals intense radionuclide uptake (20,38). The increased radionuclide activity is seen on blood flow and blood pool images, but it is most intense on static delayed images. Recently, positron emission tomographic (PET) images of fibrous dysplasia have demonstrated its marked radiotracer avidity (standardized uptake value, 3–19), a finding that simulates the appearance of malignant disease (39).

**Differential Diagnosis.**—The radiologic differential diagnosis of craniofacial fibrous dysplasia in children includes ossifying fibroma, cherubism, and renal osteodystrophy.

Juvenile ossifying fibroma, which is discussed in the next section, is a round to oval mass that causes focal expansile remodeling at a single osseous site. In contradistinction, fibrous dysplasia is often polyostotic, with more extensive and elongated bone involvement, characteristics that reflect its developmental rather than neoplastic etiology. Ossifying fibroma also may reveal multiple focal punctate areas of calcification within the fibrous tissue without a ground-glass appearance, whereas fibrous dysplasia typically contains some ground-glass density without punctate areas of sclerosis.

Cherubism is a benign disease of childhood with a pathologic appearance similar to that of fibrous dysplasia (40). The radiologic appearances of fibrous dysplasia and cherubism are similar; however, cherubism is limited to involvement of the jaw (40).
Renal osteodystrophy may cause expansion and sclerosis in the medullary space of the craniofacial bones, characteristics that simulate those of polyostotic fibrous dysplasia (41). This involvement can become extensive and may be referred to as leontiasis ossea (41). Additional manifestations of renal osteodystrophy and hyperparathyroidism and a clinical history of chronic renal failure help to distinguish renal osteodystrophy from fibrous dysplasia.

**Pathologic Features.**—At gross inspection, juvenile ossifying fibroma is a yellow-white or pink mass, which may appear gritty or cheesy (Fig 4f). Cystic spaces may be filled with serous or hemorrhagic fluid (45).

At histologic analysis, the mass consists of mineralized bodies formed from osteoid within a cellular fibrous stroma. The most conspicuous osteoid component is the uniform, small, round, lamellated, “psammoma-like” ossicles (Fig 4g). With H-E staining, the psammomatoid ossicles appear blue-black, surrounded by a pinkish osteoid rim. The population of these ossicles ranges from sparse to quite dense. Another common osteoid component is the irregular spicules or trabeculae of lamellar bone that are surrounded or rimmed by osteoblasts (Fig 4g, 4h). Osteoclasts may be seen within these spicules (Fig 4h).

The fibrous component of juvenile ossifying fibroma consists of a densely cellular stroma, which is predominantly nuclear with inapparent cytoplasmic borders and little production of collagen (Fig 4g). The cells vary from round to spindle shaped. Focal, cystic degeneration may be identified, particularly in tumors larger than 5 cm (50). A few mitoses may be seen within the cellular stroma, but no atypical mitoses or anaplasia is observed (13,47,48,50,51).

At the interface of the tumor with adjacent normal bone, osteoblastic activity is observed on the convex outer margin of the bone, whereas osteoclastic activity is seen on the concave inner margin. These findings account for the ballooned or bowed appearance of the sclerotic margin seen at radiography (50).

**Juvenile Ossifying Fibroma**

Juvenile (psammomatoid) ossifying fibroma is a nonmetastasizing, benign tumor that arises in the sinonasal region of young patients and often involves the orbit. The condition is distinguished clinically by its tendency for locally aggressive behavior and histologically by a substantial component of small, round, psammomatoid ossicles.

**Clinical Features.**—Juvenile ossifying fibroma most commonly affects children and adolescents, but it occurs in patients with a wide range of ages (44,45). It has no gender predilection (46). Facial bones are involved in 85% of cases, with the paranasal sinuses being affected in the vast majority of these (47) and more than one sinus being involved in half of them (47,48). Juvenile ossifying fibromas that involve the orbit usually arise in the ethmoid region or superior orbital plate of the frontal bone and enlarge to invade the orbit (45,48).

The most common symptom is proptosis (45). Less frequent presenting symptoms include facial swelling, nasal obstruction, visual or ocular motility disturbance, headache, and sinusitis (45,47,49). Intracranial extension is not uncom-
**Imaging Appearance.**—On radiographs, juvenile ossifying fibroma appears as a monostotic, round or ovoid, well-demarcated, expansile lesion of mixed lytic and sclerotic density (Fig 4). The internal density varies depending on the relative content of the mass, the type of cystic changes, and the osteoid components (45,48).

On CT scans, the lesions usually have predominantly soft-tissue attenuation with multiple foci of calcification (Fig 4b). Lower-attenuation areas represent areas of cystic change (50,51). The internal composition may appear multiloculated, with sclerotic septa or enhancing soft-tissue attenuation septa (52). Juvenile ossifying fibroma frequently involves multiple anatomic spaces, often with bowing and ballooning of the osseous margins; however, the tumor is usually surrounded by a sclerotic rim or shell that may be partially disrupted (Fig 4b) (50). This shell and the solid portions of the tumor enhance with intravenously administered contrast material (48–52).

On T1-weighted MR images, juvenile ossifying fibroma is generally isointense relative to muscle (Fig 4c, 4d). On T2-weighted images, the tumor appears hypointense relative to muscle, and foci of high signal intensity representing fluid-filled cystic spaces may be seen (Fig 4e). Solid portions enhance with gadolinium (18,51,53,54).

**Differential Diagnosis.**—As previously discussed, the most prominent lesion in the differential diagnosis of juvenile ossifying fibroma is fibrous dysplasia. Other lesions include cementifying fibroma and aneurysmal bone cyst. Cementifying fibroma is a histologically similar lesion that arises from the periodontal ligament; however, this pattern of disease spread follows a substantial juxtaneural or intracranial extension; granuloma (58). This form of LCH may include bone in older children or adults (56,57). Eosinophilic granuloma may manifest as an indolent disease limited to bone in older children or adults (56,57). Orbital LCH most commonly manifests as eosinophilic granuloma (58). This form of LCH may include substantial juxtaneural or intracranial extension; however, this pattern of disease spread follows a relatively benign course (59).

**Treatment and Prognosis.**—Most authors agree that the treatment of choice for juvenile ossifying fibroma is complete local excision, preferably by means of an open procedure, because the tumor tends to recur after incomplete resection (13,50,52,53). There have been no reports of metastases.

**Langerhans Cell Histiocytosis**

The three clinical syndromes included within the designation Langerhans cell histiocytosis (formerly called histiocytosis X) are part of a spectrum of disorders with a common underlying etiology: the proliferation of the Langerhans cell, an immature dendritic cell of bone marrow origin (55). It is useful to classify the possible patterns of disease of each of these entities, even though these syndromes often clinically overlap. Letterer-Siwe disease is the acute disseminated form of LCH that affects infants and involves vital organs, often with fatal consequences. Hand-Schüller-Christian disease is a disorder found in young children and is characterized by a classic triad of diabetes insipidus (due to involvement of the posterior pituitary stalk), osteolytic calvarial defects, and exophthalmos. Eosinophilic granuloma may manifest as an indolent disease limited to bone in older children or adults (56,57). Orbital LCH most commonly manifests as eosinophilic granuloma (58). This form of LCH may include substantial juxtaneural or intracranial extension; however, this pattern of disease spread follows a relatively benign course (59).

---

**Figure 4.** Juvenile ossifying fibroma involving the orbit in a 17-year-old girl. (a) Frontal radiograph shows a mixed lytic and sclerotic lesion involving the left nasal and orbital region (arrows). (b) Axial CT scan reveals the expansile lesion with a partial thin sclerotic rim (arrows); the lesion contains small, focal punctate areas of mineralization (arrowheads). (c, d) Sagittal (c) and coronal (d) T1-weighted MR images demonstrate the oval configuration and intermediate signal intensity (e) of the lesion, which displaces and effaces the orbit. (e) Axial T2-weighted MR image shows predominantly high signal intensity within the mass, with small lower-signal-intensity regions (arrowheads) that correspond to areas of focal calcification better seen in b. (f) Photograph of a sectioned gross specimen reveals the mass, which contains small focal regions of punctate calcification (arrowheads) that correspond to the imaging appearance. (g) Photomicrograph (original magnification ×200; H-E stain) demonstrates multiple ovoid and irregular osteoid spicules within a background of densely cellular stroma consisting of round to spindle-shaped cells with prominent nuclei. Also shown are multiple, lamellated, psammoma-like bodies dispersed within the stroma but also within the spicules (arrowheads). (h) Higher-power photomicrograph (original magnification ×400; H-E stain) shows small, flat osteoblasts that rim a spicule (arrows). A few osteoclasts are also seen at the edge of the spicule (arrowhead).
large mononuclear histiocytes, with abundant eosinophilic cytoplasm and grooved, indented, coffee bean– or kidney-shaped nuclei with bland, stippled chromatin and inconspicuous nucleoli (Fig 5c) (61). Lymphocytes, plasma cells, multinucleated giant cells, and eosinophils are often scattered within the proliferation (Figs 5c, 6d) (13,61).

**Imaging Appearance**

At radiography, LCH appears as osteolytic lesions with beveled or irregular margins, with or without sclerosis (Fig 5) (61). At ultrasonography (US), the proliferation of LCH is seen as a well-defined, heteroechoic mass in the supratemporal orbit (10).

On CT scans, LCH appears as soft-tissue masses that replace and destroy the osseous structures; these masses are well-defined (Fig 5a) or diffuse with a somewhat homogeneous appearance. The lesions exhibit moderate to marked enhancement following intravenous injection of contrast material (61). Common sites of osteolytic lesions include the superior or superolateral orbital region (Fig 6), although similar osseous defects may be seen in other cranial bones (59,61). In addition to its osseous destruction, an

---

**Clinical Features**

Histiocytic lesions of the orbit are rare (60), but among patients with LCH, orbital involvement is fairly common. LCH may occur at any age, but it most frequently develops in children less than 4 years of age (58,61).

The most common presenting sign of orbital LCH is unilateral or bilateral proptosis (58). Other typical clinical manifestations include ptosis, palpebral and periocular erythema, and enlargement of the associated palpebral fissure (58,61).

LCH involvement of the orbit most frequently occurs in the supratemporal frontal bone (13). Stem cell precursors of Langerhans cells are located in hematopoetic bone marrow, which is found in the frontal bone. As the frontal sinus develops, the marrow space is crowded into the lateral orbital roof (62). The finding of orbital LCH in children should prompt a full work-up for more generalized disease (59).

**Pathologic Features**

At gross inspection, LCH appears as a soft, friable, hemorrhagic, tan-yellow mass (58,61). The histiocytic proliferation manifests with sheets of

---

**Figure 5.** Langerhans cell histiocytosis in a 13-year-old boy. (a) Axial CT image (bone window) shows a small soft-tissue mass and beveled erosion of the adjacent greater wing of the sphenoid bone (arrowhead). (b) Axial proton density–weighted MR image, obtained after intravenous administration of gadolinium, shows the well-circumscribed, hyperintense mass, which replaces the bone and extends into the orbit and middle cranial fossa (arrowhead). (c) Photomicrograph (original magnification ×400; H-E stain) of a specimen from another patient shows multiple cells with indented or reniform nuclei (arrowheads) and multinucleated giant cells (straight arrows), as well as a few eosinophils (curved arrows).
Scintigraphic evaluation of patients with suspected LCH includes technetium 99m (\textsuperscript{99m}Tc) diphosphonate skeletal scintigraphy. Radiographic skeletal survey may also be helpful. These methods yield complementary information. Fluorine 18 (\textsuperscript{18}F) fluorodeoxyglucose PET/CT can localize lesions not detected with the routine evaluation. LCH may have a standardized uptake value greater than 2, a finding suggestive of a malignant lesion (65–67).

Treatment and Prognosis
The prognosis of LCH depends on multiple factors. Negative prognostic indicators include diffuse, multisystem disease with the presence of organ dysfunction and an onset during infancy (58,59). Orbital histiocytosis most commonly manifests in the form of eosinophilic granuloma;
The temporal relationship between the manifestation of granulocytic sarcoma and the onset of systemic disease evident in the peripheral blood or bone marrow is variable. Granulocytic sarcoma may occur in a patient with a known diagnosis of myelogenous leukemia, possibly heralding relapse; may be the presenting sign of coincident systemic disease; or may antedate the development of systemic disease by months or even years (71–74).

**Clinical Features**

The peak prevalence for orbital granulocytic sarcoma occurs in patients aged 7–8 years (68,69,71); three-quarters of the patients in a large series were younger than 10 years of age (68). Some authors report that the tumor has no gender predilection (69,70), whereas others have observed a slight male predominance (68,71,75). Orbital granulocytic sarcoma has a higher prevalence among African, East Asian, Latin American, and Middle Eastern populations (68,71,74). The most common presenting symptom of orbital disease is proptosis (68,70). Other presenting symp-
Tons include periorbital cellulitis or swelling and a mass in the lacrimal gland or eyelid. Orbital involvement may be bilateral (68,74).

Granulocytic sarcoma of the orbit usually arises in the subperiosteal region of the osseous wall of the orbit (68,70), but it may involve the extraocular muscles, intra- or extraconal spaces, or the lacrimal gland.

**Pathologic Features**

Granulocytic sarcoma is composed of immature myelocytic precursor cells, supporting connective tissue, and vascular stroma. Most tumors are predominantly composed of uniform, undifferentiated cells with little cytoplasm and round to ovoid nuclei. The finding of histologic features of myeloid differentiation, such as eosinophilic cytoplasmic granules and indented nuclei (Fig 7c), in some of the cells facilitates making the diagnosis, but the precursor cells are frequently poorly differentiated and these features are often absent (68,71,75).

**Imaging Appearance**

Granulocytic sarcomas of the orbit usually arise from the lateral orbital wall (Fig 7) (73,74).

They tend to encase, rather than invade, normal structures, including bone and sclera (Figs 7, 8). They usually do not disrupt the bone, although the lamina papyracea may be breached by a mass arising in the ethmoid air cells or nasal cavity and secondarily invading the orbit (Fig 8) (74,76).

At radiography, granulocytic sarcoma usually appears as a soft-tissue mass. Less commonly, bone erosion or demineralization or periosteal reaction may be seen (69). At US, a nonspecific, homogeneous, hypoechoic or echogenic solid mass is seen. The borders may appear infiltrative (10,69).

On unenhanced CT scans, granulocytic sarcomas are generally homogeneously isoattenuating to slightly hyperattenuating relative to muscle or brain and less attenuating than the sclera. Invasion of the orbital fat and extension to the eyelid are commonly observed (Fig 7b). No calcification is detected. Uniform enhancement is seen after intravenous administration of iodinated contrast media (Fig 7) (63,69,74,76).

On T1-weighted MR images, granulocytic sarcomas are iso- to hypointense relative to gray matter or muscle (Fig 8a), and they replace the high signal intensity in the yellow bone marrow.
They are heterogeneously iso- to slightly hyperintense on T2-weighted images. The signal intensity of the tumor, which contains little fibrous stroma, is quite different from the very dark signal of the highly collagenized sclera (Fig 8b) (76). Homogeneous enhancement is seen after intravenous administration of gadolinium (64,69,74,76).

Differential Diagnosis
In patients with a known diagnosis of leukemia, differential diagnosis of a solid mass includes several complications of the disease: abscess, hematoma, or secondary malignancy. The diffuse enhancement seen in granulocytic sarcomas distinguishes them from abscesses, which enhance only in the wall, and hematomas, which do not enhance at all. Differentiation of granulocytic sarcoma from another malignancy is more challenging. When a uniformly enhancing orbital mass develops in this patient group, it is reasonable to presume a diagnosis of granulocytic sarcoma and to treat it with chemotherapy. If the tumor does not respond, biopsy should be pursued.

In patients with no history of leukemia, the differential diagnosis of a retrobulbar orbital mass that causes rapid progression of proptosis includes malignant and inflammatory processes. Rhabdomyosarcoma is the most common extraocular malignancy of the orbit in children. Rhabdomyosarcoma is much more likely than granulocytic sarcoma to cause bone erosion. In contrast to granulocytic sarcoma, which usually involves the lateral orbit, rhabdomyosarcoma usually arises in the superior orbit.

Patients with granulocytic sarcoma may present with inflammatory signs including redness and swelling of the orbit, infiltration of the conal fat, and diffuse enhancement at imaging. These findings suggest the much more common condition of orbital cellulitis. Symptoms of systemic disease in patients with synchronous onset of leukemia, such as paleness, lethargy, or epistaxis, or the finding of well-defined masses with central enhancement may suggest the proper diagnosis.

Orbital granulocytic sarcomas may be bilateral, which suggests another differential diagnosis, including LCH and metastatic neuroblastoma. LCH may involve both orbits. However, LCH is associated with bone erosions with beveled edges in the skull, concomitant lytic lesions of other bones, or the syndrome of diabetes insipidus related to involvement of the infundibulum.

Metastatic neuroblastoma also has a predilection for the orbits, is frequently bilateral, and also originates in the osseous walls of the orbits. But this tumor contains calcifications and may be accompanied by aggressive periosteal reaction, lytic lesions elsewhere in the skeleton, abdominal masses, and excess urinary levels of catecholamines.

Treatment and Prognosis
Early diagnosis and induction chemotherapy are critical for achieving complete remission in cases of leukemia. In patients with no hematologic evidence of leukemia, the finding of granulocytic sarcoma portends its development, and some authors support initiation of chemotherapy upon diagnosis of isolated granulocytic sarcoma to abort the leukemic process (13,68).

Neuroblastoma Metastases
Neuroblastoma, the most frequent extracranial solid tumor of childhood, often metastasizes to bone, and it is the most common primary tumor to involve the orbit. Other primary tumors of childhood, including Ewing sarcoma and Wilms tumor, only rarely metastasize to the orbit (77,78).

Clinical Features
Ophthalmic manifestations occur in 19.8–54.7% (78–80) of patients with neuroblastoma and include signs and symptoms of orbital metastasis, Horner syndrome due to local mass effect of the primary tumor, and opsoclonus/myoclonus (a paraneoplastic syndrome of “dancing eyes” and cerebellar ataxia). Ophthalmic findings are often bilateral and occasionally are the first presenting sign of the tumor (77–80).

The most common ophthalmic findings in neuroblastoma are proptosis and periorbital ecchymosis (“raccoon eyes”). These manifestations of metastatic disease are bilateral in about half of cases (78–80). Less frequent clinical features include periorbital swelling, subconjunctival hemorrhage, ocular mobility disturbance, strabismus, and atrophy of the optic head (57,79,80).

Most patients are less than 2 years old; they are rarely over 8 years of age (80). There is no definite gender bias. Most patients with orbital metastatic neuroblastoma have abdominal primary tumors (78,79). In three-quarters of patients, excessive amounts of catecholamine metabolites are found in the urine (79).
of the tumor is composed of primitive, small, round cells with scant cytoplasm and round to ovoid, hyperchromatic or densely speckled nuclei. Scattered among these primitive cells may be a variable number of cells differentiating toward ganglion cells, which are larger round cells with abundant eosinophilic cytoplasm and prominent nucleoli (Fig 9d).

**Pathologic Features**

Generally, neuroblastoma metastases arise in the marrow of the bony orbit, especially in the roof and lateral wall (81,82). The tumor, which may be circumscribed or infiltrative, is usually extracanal and may be contained by the periosteum of the orbital bone. The pathologic appearance of neuroblastoma metastases is similar to that of the primary tumor. The cut surface varies from gray-tan and mucoid to deep red and grossly hemorrhagic. The internal content may be solid, lobular, hemorrhagic, necrotic, or gritty due to small, coarse calcifications (83,84).

At histologic examination, the tumor contains neuroblasts, which are small round cells, supported by stroma composed of Schwann cells and a framework of fibrovascular tissue (Fig 9c). Most of the tumor is composed of primitive, small, round cells with scant cytoplasm and round to ovoid, hyperchromatic or densely speckled nuclei. Scattered among these primitive cells may be a variable number of cells differentiating toward ganglion cells, which are larger round cells with abundant eosinophilic cytoplasm and prominent distinct nucleoli (Fig 9d).

A highly characteristic feature of neuroblasts is the formation of fine eosinophilic, cellular processes that create the appearance of a fibrillary extracellular network called **neuropil**. Homer-Wright rosettes are a highly characteristic arrangement of these cells; they consist of round or ovoid clusters of cells surrounding a central core.
Figure 10. Neuroblastoma metastases in a 10-month-old boy with right proptosis. (a) Axial T1-weighted MR image shows a homogeneous mass that is isointense relative to gray matter and that arises from the right sphenoid bone. It extends into the lateral extraconal space, temporal fossa, and middle cranial fossa (arrowheads). (b) Axial T2-weighted image shows that the mass causes right proptosis (arrowheads). The tumor is slightly heterogeneous and mostly hyperintense relative to the medial rectus muscle (arrow). (c) Axial T2-weighted image obtained inferior to b shows bilateral masses of the lower sphenoid bones (arrowheads). The left mass extends into the inferior orbit. (d) Contrast-enhanced axial T1-weighted image reveals diffuse enhancement of the mass (arrowheads). (e) Anterior image of the upper body from a bone scintigraphic study shows a mask of increased radiotracer uptake around both orbits (arrowhead) and radiotracer accumulation in the left adrenal primary tumor (arrow).
of light pink neuropil. In addition to the neuropil, groups of neuroblasts are also surrounded by a stroma of fusiform cells with elongated nuclei that represent Schwann cells and are supported by incomplete fibrovascular septa that confer a lobular appearance to the tumor as a whole. The relative composition of these cellular components of the tumor determines its gross appearance: Abundant stroma or neuropil is seen in tumors with a gray to tan mucoid appearance, whereas abundant neuroblasts are seen in grossly hemorrhagic tumors (80,83,84).

**Imaging Appearance**

Radiographic findings of orbital neuroblastoma metastases include destruction or spiculated thickening of the orbital roof or lateral orbital wall, a soft-tissue mass, or orbital calcification (Fig 9) (80,85). At US, these masses have a nonspecific appearance of variable echogenicity and infiltrative margins (10).

At CT and MR imaging, neuroblastoma metastases appear as circumscribed or poorly defined, extraconal masses that usually arise from the lateral wall of the orbit (Figs 9, 10). Frequently, these masses are bilateral. Adjacent permeative bone destruction is commonly seen on CT scans (Fig 9b). On unenhanced CT scans, the mass may show high attenuation relative to that of muscle, and small calcific foci may be noted (82). The tumor may infiltrate adjacent structures, including the infratemporal fossa, the face, and the intracranial contents, but preseptal extension is uncommon.

On T1-weighted MR images, orbital neuroblastoma typically has low signal intensity compared with that of muscle; it appears slightly hyperintense relative to muscle on T2-weighted images (Fig 10). The mass may appear heterogeneous because of necrosis or hemorrhage. Heterogeneous enhancement is typical following intravenous administration of contrast material (Fig 10d) (63,81,82,85,86).

Several scintigraphic studies are used to evaluate patients with orbital neuroblastoma. Bone metastases show increased radiotracer uptake on 99mTc diphosphonate bone scintigrams (Fig 10e). This study is a sensitive screen for bone metastases, but it does not allow cortical involvement to be differentiated from medullary involvement. Iodine 123 metaiodobenzylguanidine (MIBG) is a radiolabeled catecholamine analog that is highly sensitive and specific for the primary tumor and its metastases and is routinely used in staging and follow-up. Somatostatin receptor scintigraphy with indium 111 pentetreotide shows radiotracer accumulation in the primary tumor and its metastases, but it is not as sensitive nor as specific as 123I MIBG. 18F-fluorodeoxyglucose PET/CT and immunoscintigraphy are also sensitive and specific for neuroblastoma and its metastases (83,87).

Additional findings that may be observed in patients with orbital neuroblastoma include dural metastases, which may cause sutural widening; permeative lesions of other bones, including the metaphyseal region of long bones; and an adrenal or sympathetic chain mass representing the primary tumor.

**Differential Diagnosis**

Rhabdomyosarcoma, which also manifests with rapidly progressive proptosis, is the most common tumor of the extraocular soft tissues in children and often erodes the osseous orbit, causing an appearance similar to that of neuroblastoma metastases. Rhabdomyosarcoma is the more likely diagnosis if the mass involves the anterior orbit, because neuroblastoma typically does not extend into the preseptal soft tissues. On the other hand, hyperattenuation of the mass compared with that of muscle on CT scans or bilateral findings are suggestive of neuroblastoma rather than rhabdomyosarcoma (82).

**Treatment and Prognosis**

The prognosis for patients with neuroblastoma depends on many factors, but particularly age and stage at presentation. Patients who, at presentation, are less than 1 year old; have surgically resectable disease (stage I or II); or have metastases limited to the liver, skin, and bone marrow (stage IVS) have a good prognosis with therapy. Metastatic orbital involvement is stage IV disease, which is considered high risk (79) and is treated with polychemotherapy at high doses.

**Primary Malignant Bone Tumors**

Primary malignant bone tumors arising in or near the orbit are rare, but the most common of these is osteosarcoma. About 10% of orbital osteosarcomas arise in the craniofacial region, most frequently from the gnathic bones (18).
They may also arise from the paranasal sinuses and extend to involve the orbit. In young children, osteosarcomas generally occur in normal bone, but they may also develop in bone affected by such conditions as fibrous dysplasia or osteogenesis imperfecta. Children with hereditary retinoblastoma have a mutation of the **RB1** gene, which also places them at risk for developing osteosarcoma and other mesenchymal tumors. This risk is increased if the retinoblastoma was treated with radiation, in which case the second primary tumor usually, but not always, arises within the radiation port, in or near the orbit.

Osteosarcomas are mainly formed of two components, matrix and sarcomatous stroma. Depending on the amount and degree of mineralization of its matrix component, the tumor may be grossly firm and sclerotic or soft and fleshy (18,88). Craniofacial osteosarcomas may be osteoblastic or chondroblastic. At histologic analysis, osteoblastic osteosarcomas are formed from irregular foci of pinkish hyaline osteoid material surrounded by spindled to polygonal stromal cells. Chondroblastic osteosarcomas contain lobules of cartilage with malignant cells within the lacunae.

On radiographs and CT scans, osteosarcomas appear as destructive, expansile lesions of bone, which may be sclerotic, lytic, or both. Dense mineralized matrix may be prominent or minimal. On MR images, especially those obtained with T2-weighted pulse sequences, these tumors appear heterogeneous. Fluid levels may be seen (89). On T1-weighted images, osteosarcomas have intermediate signal intensity and they enhance heterogeneously after administration of gadolinium (18,89).

**Conclusions**

Orbital lesions of osseous origin represent a wide histologic spectrum, from developmental anomalies to neoplastic and proliferative disorders. These conditions share imaging features with each other and with nonosseous lesions of the orbit, but their pathologic features often influence their radiologic appearances and may allow them to be distinguished at imaging.

**References**


Pediatric Orbit Tumors and Tumorlike Lesions: Osseous Lesions of the Orbit

Ellen M. Chung, MD, et al

Most dermoid inclusion cysts, in contrast to epidermoids and most other orbital masses, have the attenuation and signal intensity characteristics of lipid material because of their sebaceous secretions (Fig 2).

Juvenile ossifying fibroma, which is discussed in the next section, is a round to oval mass that causes focal expansile remodeling at a single osseous site. In contradistinction, fibrous dysplasia is often polyostotic, with more extensive and elongated bone involvement.

Orbital LCH most commonly manifests as eosinophilic granuloma (58). This form of LCH may include substantial juxtaneural or intracranial extension; however, this pattern of disease spread follows a relatively benign course (59).

Granulocytic sarcomas are more common in children than in adults; are often multifocal; and most frequently arise in bones, especially the skull and orbit (68–70).

Neuroblastoma, the most frequent extracranial solid tumor of childhood, often metastasizes to bone, and it is the most common primary tumor to involve the orbit.