Abstract

A wide variety of lesions from the benign to aggressively malignant can present in the orbital region. Imaging is especially important in this highly specialized region. Computed tomography can provide data regarding bony involvement, and anatomical localization relative to the bony orbit, which is useful for surgical planning. Magnetic resonance imaging is superior in soft tissue resolution, lesion morphology, intensity, contrast enhancement, and for allowing localization in relation to vital orbital structures such as the optic nerve and extraocular muscles. Due to these structures and the closed orbital space, an orbital biopsy is not always easily performed and not without risk. Careful imaging with continual histopathological correlation can allow both the radiologist and surgeon to narrow the differential diagnosis of characteristic orbital tumors, which can ultimately guide management and potentially avoid risky surgery. We present the imaging characteristics of histopathologically proven neoplastic and inflammatory lesions of the orbit.

Keywords: Computed tomography, Magnetic resonance imaging, Orbit, Pathology

Introduction

The orbital region is subject to a variety of lesions that are most often evaluated with contrast material-enhanced computed tomography (CT) and magnetic resonance imaging (MRI). CT provides vital data regarding bony involvement and surrounding bony anatomy. MRI is superior in soft tissue resolution, distinguishing periorbital and orbital structures, as well as lesion morphology, intensity, and contrast enhancement. Often the combination of the two modalities can allow for localization, tissue composition, and sometimes diagnosis. As imaging technology advances, it is important to continually correlate imaging findings with histopathological diagnoses. Narrowing differential diagnoses can guide management, avoid unnecessary surgery, and if surgery is indicated, can aid in surgical planning.

INTRODUCTION

The orbit is the cavity of the skull in which the eye and its appendages are situated. In the adult, the volume of the orbit is 30 ml. The orbit is conical and consists of seven bones. Given the closed space, orbital occupying lesions can result in proptosis, impaired motility, diplopia, choroidal folds, and changes in visual acuity and fields.

Clinical history and the knowledge of key imaging features may narrow the differential diagnosis of orbital lesions.
Therefore, this information is vital for management and prognosis. We present the imaging characteristics of histopathologically proven neoplastic and inflammatory lesions of the orbit by anatomic compartments (Table 1).

**Imaging in orbital differential diagnosis**

A systemic radiological approach to examining the images is needed to reach a differential diagnosis. The images should be studied for lesion appearance, localization, contrast enhancement, bony orbit evaluation, and detection of calcifications.\[^{3,4}\]

The lesion appearance on imaging includes; solid or cystic, well circumscribed or ill-defined, and localized or infiltrative.\[^{4}\] Comparing the density of the lesion with that of the vitreous body can help to identify a solid lesion, whose density is higher than that of vitreous on CT images.\[^{4}\]

Orbital tumors can be localized anatomically within the globe/intraocular or intraconal or in the extracranal space, the orbital apex, the extraocular muscles, or the lacrimal gland. CT remains the modality of choice for evaluation of the bony orbit and paranasal sinuses. MRI is preferred to evaluate the optic nerve and chiasm.\[^{3,4}\]

Contrast enhancement aids in the characterization of orbital masses. Moderate to marked enhancement is usually noted in solid tumors as well as in acute inflammation, while minimal contrast enhancement suggests a chronic or sclerosing orbital inflammation, a fibrotic tumor or post-therapeutic scar tissue. No enhancement is documented in hemorrhagic processes, inflammation, a fibrotic tumor or post-therapeutic scar tissue.

**Table 1: Orbital tumors by anatomic compartments**

<table>
<thead>
<tr>
<th>Intraconal</th>
<th>Extracranal</th>
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<tbody>
<tr>
<td>Distinct from optic nerve</td>
<td>Distinct from optic nerve-Schwannoma (neurilemmoma)</td>
</tr>
<tr>
<td>Cavernous venous malformation/cavernous hemangioma</td>
<td>Schwannoma</td>
</tr>
<tr>
<td>Contiguous with optic nerve</td>
<td>Contiguous with optic nerve-Schwannoma</td>
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<tr>
<td>Optic nerve sheath meningioma</td>
<td>Optic nerve sheath meningioma</td>
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<tr>
<td>Lacrimal-adenoid cystic carcinoma</td>
<td>Lacrimal-adenoid cystic carcinoma</td>
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<tr>
<td>Lymphoma</td>
<td>Lymphoma</td>
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<tr>
<td>Sarcoma</td>
<td>Sarcoma</td>
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<tr>
<td>Mucocele</td>
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<td>Mixed (intraconal/extracranal)</td>
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<td>Lymphangioma</td>
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<tr>
<td>Metastatic tumors</td>
<td>Metastatic tumors</td>
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<tr>
<td>Osseous</td>
<td>Osseous</td>
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<tr>
<td>Intraosseous hemangioma</td>
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<td>Neuroblastoma</td>
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Bony changes, such as cortical bone indentation, molding, bone erosion, bone lysis, or hyperostosis, can suggest the aggressive or non-aggressive nature of lesions. Molding of the bone by a well-circumscribed orbital mass is highly suggestive of a congenital lesion (e.g., dermoid cyst and lymphangioma) or slowly growing benign lesion (i.e., cavernous malformation, neurofibroma, neurilemmoma, and benign lacrimal gland tumor). Bone erosions or scalloping and destruction are seen in more aggressive inflammatory or neoplastic primary or secondary lesions.\[^{3,4}\]

Calcifications can also be characteristic of certain etiologies. CT is the modality of choice to evaluate calcifications that can be seen in trauma, vascular tumors, optic nerve sheath tumors (meningioma), epithelial lacrimal gland tumor, retinoblastoma, and osteosarcoma.\[^{4}\]

**Typical intraconal orbital tumors**

**Distinct from optic nerve – Cavernous venous malformation (also known as cavernous hemangioma)**

Cavernous venous malformations are considered the most commonly occurring primary tumor of the orbit. Histologically, they are encapsulated masses with a complex network of dilated vascular channels lined with flattened endothelial cells surrounded by fibrous stroma. Thus cavernous venous malformation is considered more accurate nomenclature than “hemangioma”.\[^{1}\] They commonly are slowly progressive, benign, and occur more often in females, between the ages of 20 and 60 years. Rootman et al. found the far majority of these lesions to be intraconal and separate from the optic nerve.\[^{3}\] Patients can present with painless axial proptosis; however, these tumors are more often found as incidental findings on imaging done for other symptoms.\[^{3}\] On CT imaging, these lesions are well circumscribed, oval, or round in shape, and homogenous. Calcifications may be present and these lesions generally demonstrate mild to moderate enhancement. On MRI, cavernous malformations are typically isointense to muscle and cortical gray matter, and hypointense to fat, on T1-weighted imaging (Figure 1a). They are often hyperintense to fat and brain on T2 (Figure 1b). Complete enhancement with gadolinium is typically seen (Figure 1c). Most cavernous malformations can be observed clinically. If surgical excision is performed, en bloc removal, often with the aid of a Cryoprobe is done. There is some emerging evidence that stereotactic fractionated radiotherapy may be useful in treating surgically complicated cavernous malformations.\[^{6}\]

**Distinct from optic nerve-Schwannoma (neurilemmoma)**

Schwannoma is a benign tumor of the nerve sheath that arises from Schwann cells of the peripheral nervous system. It is important to make this distinction, as the optic nerve is part
of the central nervous system, and thus schwannomas are lesions that do not arise from and are distinct from the optic nerve. They typically occur between the ages of 20–60 years old. 10–15% occur in patients with neurofibromatosis. They are slow growing and present with painless proptosis and malpositioning of the globe. Most are intraconal, and well circumscribed. They often are located in the superior orbit originating at the frontal branch of the ophthalmic nerve. On CT, the lesions appear smooth, well defined. Mucinous cystic degeneration can appear as low attenuation. The lesions vary between moderate to marked enhancement with contrast (Figure 2). On MRI, they appear well circumscribed with heterogeneous signal intensity. This differs from cavernous venous malformations, which are typically homogenous. On T1-weighted imaging, the lesions appear isointense to hyperintense to muscle. On T2-weighted imaging, they generally appear hyperintense to muscle and fat. The lesions moderate to markedly enhance with gadolinium. Histologically, these tumors are characterized by two distinct cellular patterns: Antoni A and Antoni B. Antoni type A areas consist of well-differentiated spindle cells with ovoid nuclei that are often arranged in a palisading fashion or in an organoid arrangement called Verocay bodies. Antoni type B areas consist of abundant edematous fluid or loose myxoid matrix separating tumor cells. If treatment is pursued, en bloc surgical excision is preferred.

**Contiguous with optic nerve-Optic nerve sheath meningioma**

Meningiomas of the optic nerve sheath are contiguous with the optic nerve. They arise from the meningotheial/ arachnoid cap cells surrounding the optic nerve. It is seen more frequently in females, in their fifth decade. They can be associated with neurofibromatosis (NF-2), radiotherapy, or meningiomatosis. Patients present with gradual vision loss with evidence of optic disc atrophy and optociliary shunt vessels with the relative afferent pupillary defect. On CT, the tumor shows tubular enlargement of the optic nerve. It is isodense to cortical gray matter and may show calcification 20–50% of the time. There is homogenous enhancement with contrast surrounding the optic nerve of lesser density, demonstrating “tram-track” sign. On MRI, on T1, meningiomas are isointense compared to the optic nerve and gray matter. On post-gadolinium, T1 images, shows marked enhancement, best appreciated on fat suppression sequences (Figure 3a). MRI can also demonstrate the encasement of the optic nerve (Figure 3b). Intraorbital meningiomas are most frequently either meningotheial or transitional subtypes and WHO Grade I. Management of optic nerve sheath meningiomas involves clinical follow-up with serial visual function testing and imaging. Radiation, both conventional and stereotactic, therapy may be used to slow progression. Surgery invariably results in loss of vision and is typically only considered when posterior growth threatens the contralateral eye.

**Typical extraconal tumors**

**Lacrimal-Adenoid cystic carcinoma**

Adenoid cystic carcinoma is the most common primary epithelial malignancy of the lacrimal gland. It is most often seen in middle-aged adults. Due to perineural invasion, patients often present with pain, as well as downward and medial displacement of the globe. Bony destruction is characteristic and best seen on CT. On CT, these tumors show heterogeneous density in the lacrimal gland fossa and range from irregular to well-demarcated lesions. Calcification can be present. On MRI, these tumors demonstrate heterogeneous signal on T1-weighted imaging and are generally hyperintense to muscle and hypointense to fat (Figure 4a). On T2, the lesions are hyperintense to fat (Figure 4b). Areas of necrosis may be seen as an increased signal on T2-weighted imaging. Moderate enhancement can be seen with gadolinium administration (Figure 4c). MRI can also demonstrate perineural spread. Adenoid cystic carcinoma is typically a poorly circumscribed and uncapsulated solid tumor with an infiltrative pattern of growth. Histologically, the most common growth pattern
described as “cribriform” shows nests and columns of cells arranged concentrically around gland-like spaces. Primary treatment includes surgical resection with clear margins, with adjuvant radiation therapy often used. In general, adenoid cystic carcinoma may recur several times and many years after the initial resection. Intra-arterial cytoreductive chemotherapy has recently been introduced with putatively improved results over conventional therapy.\[1\] Despite aggressive surgical intervention, the long-term prognosis is poor. Radiation can also be used in patients when surgery is not an option, and chemotherapy is used for metastatic disease.

**Lymphoma**

Most orbital lymphomas are low-grade proliferations of monoclonal B lymphocytes. They can occur anywhere in orbit but tend to occur in the lacrimal gland. They are seen in patients between 50 and 70 years of age. Orbital lymphoma accounts for 55% of malignant orbital tumors in adults.\[12\] More than half of patients with a primary orbital lymphoma may have systemic involvement.\[13\] Systemic involvement is higher with lymphoma of the conjunctiva. On CT, lymphoma appears as a homogenous, diffuse to moderately defined mass, arising in the lacrimal fossa, and molding to tissues around.\[1\] Mild to moderate homogenous enhancement is seen in contrast. Moon et al. described a two-phase dynamic enhanced CT technique, which can help differentiate lymphoma from inflammatory disease.\[14\] On MRI T1-weighted images, lymphoma is hyperintense to muscle and hypointense to fat (Figure 5). On T2 images, lesions are hypointense to isointense to muscle with enhancement with gadolinium, best seen with fat suppression. Diffusion-weighted imaging demonstrates reduced diffusion due to hypercellularity of the tumor.\[11\] Management will depend on the type of lymphoma and extent of disease. Most primary orbital lymphomas can be treated primarily with radiation therapy. Massive orbital involvement or systemic disease can be treated with both radiation and chemotherapy. Monoclonal antibody therapy can also be used.
Sarcoid

Sarcoidosis is classified as non-caseating granulomatous inflammation of unknown etiology that can affect multiple systems. Ocular tissue is involved in 20% and may be the only manifestation. It is more common in patients of African American race, and females. It can affect any ocular or orbital structure, but more commonly seen in the lacrimal gland.\(^1\)\(^2\) On CT, the lacrimal gland can show diffuse enlargement with irregular borders. On MRI (Figure 6), on T1 images, the lesions are isointense to muscle. On T2-weighted images, they are hypointense to muscle. There is a marked enhancement with gadolinium.\(^1\)\(^2\) Histologically, the lesion is typically a non-caseating granuloma composed of epithelioid cells with Langhans multinucleated giant cells and lymphocytes.\(^1\)\(^3\) Systemic corticosteroids have been the mainstay of treatment. Steroid injections can be considered for localized disease. Immunomodulatory agents can be used in patients refractory to corticosteroids.

Mucocele

Mucoceles are cysts that originate extraconally, in the paranasal sinuses. They most often arise in the frontal or ethmoid sinus. As mucus and inflammatory tissue accumulate, the cyst can enlarge and displace the globe.\(^3\) Patients typically have a history of sinusitis. A nontender mass may be seen on examination at the superomedial orbital rim. They can cause proptosis and displace the globe, down, and out. On sinus CT, opacification is seen with a defined cystic mass into the orbit. Bone may be remodeled or eroded. The cyst cavity is homogenous and low density. There is no enhancement with contrast. On MRI, the presentation is variable (Figure 7). With mucoceles of high water content, T1 images show low signal intensity, with hyperintensity on T2. On lesions with higher protein content, they are hyperintense on both T1 and T2 images. With increasing protein content, mucoceles may become hypointense on both T1 and T2. They do not enhance with gadolinium. Microscopically, the cyst wall is composed of chronically inflamed subepithelial and granulation tissue with the inner contents consisting of an accumulation of inflammatory exudates and mucin secretion.\(^1\)\(^5\) Treatment is typically surgical and involves removing as much of the cyst lining as possible. Some mucoceles can resolve with primary sinus surgery alone.

Mixed (intraconal/extraconal) tumors

Lymphangioma

Lymphangiomas are hamartomas of the venous-lymphatic channels and tend to hemorrhage from small vessels. This can cause an expansion of vascular networks into “chocolate cysts.” The can comprise both deep orbital and preseptal tissues. They most often present in children and teens. During events of hemorrhage, motility can be impaired as well as compressive optic neuropathy seen. On CT scan, these lesions are irregular, heterogeneous, and poorly defined. Enhancement with contrast is variable. On MRI, a diffuse infiltrative mass is seen, and cystic cavities may be present (Figure 8). T1 images show heterogeneous signal hyperintense to muscle and hypointense to fat. T2 is highly variable with blood cysts with high intensity. Serpentine signal voids represent vessels. Acute hemorrhage is seen as hypointense to muscle on T1. Older blood is seen as hyperintense on T1 and T2. Even older blood is seen as low signal on MRI. There...
is slight to moderate enhancement with contrast. Fluid-fluid levels can be seen as well. Microscopically, lymphangioma consists of large lymphatic channels filled with serum in loose connective tissue. Most lymphangiomas are observed due to the difficulty and risks associated with surgical removal. Optic nerve compression and severe proptosis are indications for surgery; however, due to the poorly defined nature of the tumor, complete excision is rarely attained. Recent reports in the New England Journal of Medicine and the Journal of the American Medical Association Ophthalmology, show promising medical treatment of lymphangiomas with sildenafil. [16,17]

**Metastatic tumors**

Different carcinomas may reach the orbit and present as metastases. The most common orbital metastases include breast (Figure 9), prostate, lung, followed by cutaneous melanoma, kidney, and gastrointestinal [Figure 10] tumors. Shields et al., on reviewing 100 consecutive cases of metastases to the orbit, found that metastatic involvement was typically unilateral, and ophthalmic presentation often included limited motility, proptosis, blepharoptosis, and palpable mass. In 19% of cases, patients had no known primary. [18] Breast metastases typically involve soft tissue such as the orbital fat and extraocular muscles, whereas prostate tends to involve orbital bones. On CT scan, metastases are ill-defined, infiltrating with moderate density. Enhancement is minimal to moderate with contrast. Bony destruction can be present. On MRI, the metastases can appear as diffusely infiltrating to moderately well-defined. They are typically isointense to muscle, hypointense to fat on T1, and hyperintense to muscle and fat on T2-weighted images. Moderate to marked enhancement may be seen with gadolinium, appreciated best with fat suppression. [13] Treatment is guided by the primary tumor and can include radiotherapy, chemotherapy, hormone therapy, surgery, and immunotherapy. Prognosis is poor. [18]

**Osseous**

**Intraosseous hemangioma**

Intraosseous hemangiomas are expansile osseous lesions that rarely occur in the orbit. Less than 50 cases have been reported in literature to date. [19] They have an insidious course and may cause mass effect on the surrounding structure. They are typically found in adults but can affect any age. Patients can present with painless proptosis, diplopia, or optic neuropathy. On CT, a sunburst of radiating trabecula is typically seen, although this can be seen in other more aggressive tumors as well (Figure 11a). On T1 and T2 images (Figure 11b-e), hemangiomas have high signal intensity. [11] Histologically, the lesion consists of dilated thin-walled vessels lined by flattened endothelial cells extending between scattered bone trabeculae similar to cavernous malformation (Figure 11f). [6] Treatment is reserved for symptomatic lesions and can include radiation, embolization, surgery, and intrallesional ethanol injection.
Neuroblastoma

Neuroblastoma is the most common metastatic orbital tumor in children. The tumor is made up of malignant neuroblasts from neural crest cells. It typically is found in the first 2 years, with the primary typically found in the adrenal medulla and the sympathetic or parasympathetic tissues of the abdomen or chest. The far majority of cases found in orbit are in children with a known primary in the abdomen or chest. Rarely, orbital neuroblastoma is found to be the primary. The clinical presentation is typically proptosis with periorbital ecchymosis and globe dystopia. It can rarely present in adults. On CT the tumor is large, irregular, lobulated, hyperdense, with more lucent areas of necrosis and hemorrhage. Destruction of bone is typically seen (Figure 12a). On MRI, the mass is ill-defined with the invasion of adjacent orbital structures, including bone (Figure 12b-e). On T1 the signal can be hetero or homogenous with hypointensity to cortical gray matter. On T2, the tumor is isointense of slightly hyperintense to gray.

Figure 9: Metastatic breast carcinoma. (a) Axial T1-weighted fat-saturated magnetic resonance (MR) image shows enhancing soft tissue involving the intraconal and extraconal orbital contents, left greater than the right (white arrow). (b) Coronal T1-weighted post-contrast fat-saturated MR images show diffuse enhancing soft tissue involving the left orbital soft tissues (white arrow) with lesser involvement of right orbit.

Figure 10: Metastatic mucinous carcinoma (colorectal primary). (a) Axial T1-weighted magnetic resonance (MR) image shows a mass within the right anterior superior orbit, which is relatively homogenous and hypointense relative to the orbital fat. (b) Coronal T2 fat-saturated MR images show that the mass is mildly heterogeneous but hyperintense relative to the adjacent extraocular muscles. (c) Low-power photomicrograph (original magnification, ×10; hematoxylin-eosin stain) shows several signet ring cells (arrow) from metastatic colorectal cancer in a background of fibrous stroma. (d) High-power photomicrograph (original magnification, ×60; mucicarmine stain) shows signet rings cells strongly positive for mucicarmine stain (pink) confirming a mucinous carcinoma.

Figure 11: Intraosseous Hemangioma. (a) Axial non-contrast CT image shows destructive lesion with large soft tissue component involving right lateral orbital wall and zygomatic arch (white arrow). A sunburst type pattern of new bone formation is seen (white arrowhead). (b) Axial T1-weighted pre-contrast fat-saturated MR images show mild enhancement of these lesions (white arrow). Right globe ptosis. (c) Axial T1-weighted post-contrast fat-saturated MR images show avid heterogeneous enhancement of the soft tissue component (white arrow) as well as the intraosseous components (white triangles). (d) Axial T2-weighted fat-saturated MR images again show heterogeneous T2 hyperintense soft tissue as well as hypointense osseous components involving the right orbit (white arrow). (e) Coronal T2 fat-saturated non-contrast image shows the mass (white arrow) with multiple septations/cystic components (arrowhead). (f) Low-power photomicrograph (original magnification, ×4; hematoxylin-eosin stain) shows dilated thin-walled vessels lined by flattened endothelial cells extending between scattered reactive bone trabeculae.
matter and muscle. Heterogeneous enhancement can be mild to marked with gadolinium. Diffusion-weighted imaging demonstrates reduced diffusion due to hypercellularity of the tumor. Neuroblastomas are composed of small, primitive-appearing cells with hyperchromatic nuclei, scant cytoplasm, and poorly defined cell borders growing in solid sheets (Figure 12f). Mitotic activity, nuclear breakdown (“karyorrhexis”), and pleomorphism may be prominent. The background often demonstrates a background of eosinophilic fibrillary material (neuropil) that corresponds to the neuritic process of the primitive neuroblasts. Typically, Homer-Wright rosettes can be found.[15] Treatment often includes a combination of surgery, radiation, chemotherapy, autologous bone marrow transplantation, and postchemotherapy retinoic acid.

CONCLUSION

The orbit is subject to a wide variety of lesions. Often, the clinical presentation with the combination of both CT and MRI can localize and characterize these lesions. Aviv et al. described how localizing orbital pathology to an anatomic compartment might narrow differential diagnoses.[4] Characterizing a mass as homogenous or heterogeneous, well versus ill-defined, molding or infiltrative, associated with bony remodeling or destruction, and enhancement patterns can point to a diagnosis. Imaging advancements and changes in protocols may differentiate between malignancy and inflammation.[3,4,14] As imaging technology advances, it is important to continuously correlate imaging characteristics with confirmed histopathology to check that we are making the correct diagnoses. We have presented a pictorial imaging review of common histopathologically diagnosed orbital tumors. This information can allow the physician to narrow the differential diagnosis, improve management, and potentially avoid risky surgery.

REFERENCES


