Soft Tissue Orbital Tumors

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Giulio Bonavolontà and Paola Bonavolontà

16.1 Introduction

The orbital cavity may harbor many types of mass lesions of neoplastic, vascular, congenital, and inflammatory origin. They may arise from different complex of vascular, neurogenic, mesenchymal, and secretory structures and are in close anatomical relationship with the eyelids, nasal sinuses, and brain [1–4].

Some lesions are benign and well differentiated and show slow clinical course; others are malignant and undifferentiated, with infiltrative aspect and rapid growth and can lead to death.

16.2 Classification

According to their initial location and growth, the lesions involving the orbit may be divided into three main groups: (1) Primary lesions arising in the orbital cavity; (2) Secondary lesions arising from adjacent structures; (3) Metastatic tumors to the orbit. The proposed classification is listed in Table 16.1.

Table 16.1 Classification of orbital mass lesions

1. Primary orbital lesions	Vascular Cystic Neurogenic Mesenchymal Lacrimal gland Lymphoproliferative and histiocytic
2. Secondary tumors arising from adjacent structures	Spheno-orbital meningioma Basal cell carcinoma Squamous cell carcinoma Melanoma Carcinoma of paranasal sinuses and nasopharynx Retinoblastoma Eccrine histiocytoid carcinoma Esthesioneuroblastoma Sebaceous carcinoma Lacrimal sac origin Unspecified origin
3. Metastatic tumors to the orbit	

This chapter discusses the tumors primary arising in the orbital cavity. Bone tumors are treated in Chap. 15 in this book. Tumors of the surrounding structures secondarily invading the orbit are excluded. On the other hand, we also discuss the metastatic tumors to the orbit because they are frequent and often indistinguishable at the initial diagnosis from primary tumors and cystic lesions.

G. Bonavolontà
Department of Neuroscience, University of Naples Federico II, Naples, Italy

P. Bonavolontà (✉)
Department of Clinical Medicine and Surgery, University of Naples Federico II, Naples, Italy
e-mail: paola.bonavolonta@unina.it

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16.3 Clinical Overview

Patients with an intraorbital mass must undergo a detailed diagnostic process, including clinical history, ophthalmological examination, correct selection of diagnostic tests, and finally a biopsy. Intraorbital lesions can present with different clinical symptoms and signs due to different mechanisms: mass effect, inflammation, infiltration, vascular, and functional mechanisms. The mass effect is characterized by compression and displacement of structures leading to functional deficits and proptosis. The inflammatory effect is characterized by orbital pain, redness, warmth, functional deficit and can be acute, subacute, or chronic. In case of tissue infiltration, a tumor can cause functional deficit such as limitation of the eye movements causing diplopia and sensory changes such as dysesthesias and hypo- and hyperesthesia. Finally, a neoplasia can cause loss of visual acuity and deficits of the visual field and color vision.

The type of eye displacement may aid to define the tumor location and the functional changes. Medial and inferior lesions mainly cause ocular displacement superiorly or laterally. Tumors that involve the lacrimal gland can cause an infero-medial displacement. Apical or intraconal lesions present with axial exophthalmos. The type of intra-orbital mass lesion may vary according to its anterior to posterior location. Anterior lesions are most commonly lymphoproliferative. The mid-orbit mainly harbors vascular malformations and different tumor types. Posterior lesions are most commonly neurogenic tumors.

The clinical onset may also be variable. The most common symptoms and signs of orbital lesions are due to the mass and infiltrative effect. Particularly, the neurogenic neoplasms are mostly associated with visual loss and mass effect. Lymphoproliferative lesions present with proptosis, orbital oedema, palpable mass, and ptosis. In cystic lesions, a palpable swelling is evident and the mass causes proptosis, followed by pain.

When the orbit is involved secondarily from adjacent structures, the neoplasia can cause pain, dysesthesia, proptosis, and globe displacement. Metastatic tumors to the orbit can present with diplopia, local swelling, ptosis, and pain.

16.4 Ophthalmological and Imaging Studies

Patients with orbital mass lesions must undergo a complete ophthalmological evaluation including eyelid malposition, orbital edema, swelling and palpable mass, visual acuity, fundus, globe displacement, exophthalmos, enophthalmos, color test; visual field examination and OCT are useful in selected cases. The extraocular muscle evaluation with Hess scheme is necessary in cases of muscular restriction.

The imaging studies must include orbital echography, computer tomography (CT), and magnetic resonance (MR).

The orbital echography is a rapid and easy noninvasive diagnostic technique [5]; it evidences the intra-orbital lesion and particularly defines the diameter of the optic nerve, which may increase as a result of increase of peri-optic CSF space, as occurs in several intra-orbital masses.

CT and MR with contrast administration are essential to diagnosis of orbital mass lesions [6, 7]. They allow to define the intra-orbital location, the size and margins of the lesion, its type of contrast enhancement, its relationship with the optic nerve, and other intra-orbital structures. Patients harboring orbital metastases or malignant lymphoproliferative and bone tumors must also be investigated by Positron Emission Tomography (PET, PET-CT) to staging the neoplastic disease.

16.5 Management Options

The management options for patients with intraorbital mass lesions include biopsy, surgical excision, radiotherapy, chemotherapy and, in rare cases, orbital exenteration.

The biopsy is often necessary to obtain the histopathological diagnosis, with the aim to decide the further management [8]. Different type of biopsy may be used, including fine needle

agobiopsy, incisional, or excisional biopsy. The excisional biopsy should be preferred, when possible.

The **surgical excision** of intra-orbital mass lesions may be realized by different approaches, orbital or cranio-orbital [9–11]. The less invasive orbital approaches include the anterior orbitotomy, the lateral orbitotomy (with or without lateral osteoplasty), the medial orbitotomy, and the trans-conjunctival approach [11, 12].

The cranio-orbital microsurgical approaches include the supraorbital-pterional [13], minipterional, orbito-zygomatic, lateral-supra-orbital, and supraorbital key-hole approaches [11].

More recently, the minimally invasive endoscopic approaches (trans-orbital, trans-eyelid, trans-sphenoidal endonasal, and combined endonasal-transorbital) have gained consensus [14–16]. The choice of the surgical approach depends on several factors, including intra-orbital location, size, and eventual intracranial or endonasal extension. The **orbital exenteratio** is the last surgical option in blind patients with very invasive orbital malignant tumors, mainly after multiple recurrences followed by radiotherapy; the severe proptosis with significant disfiguring change is an important indication. However, this radical and very invasive surgical procedure is associated with significant functional and psychological disability and is refused by several patients. Thus, the eye sparing surgery followed by radiotherapy is more widely considered [17].

The **radiotherapy and chemotherapy** are mainly indicated for malignant primary or metastatic orbital tumors as adjuvant or alternative treatments to surgery. Among benign intra-orbital tumors, the radiotherapy is indicated for optic nerve sheath meningiomas and the chemotherapy for benign optic nerve gliomas.

16.6 Specific Pathological Entities

16.6.1 Vascular Lesions

The group of vascular lesions includes proliferative lesions and arterial flow, venous flow, and no flow malformations (Table 16.2).

Table 16.2 Classification of intraorbital vascular lesions

1. Proliferative lesions
Cavernous malformation capillary hemangioma
Hemangioendothelioma
Intravascular papillary endothelial hyperplasia
2. Arterial flow lesions
Shunt/fistula carotid cavernous fistula
Arterial malformation
3. Venous flow lesions
Varix
Combined lymphangioma-varix
4. No flow malformations
Venous lymphatic malformation (lymphangioma)

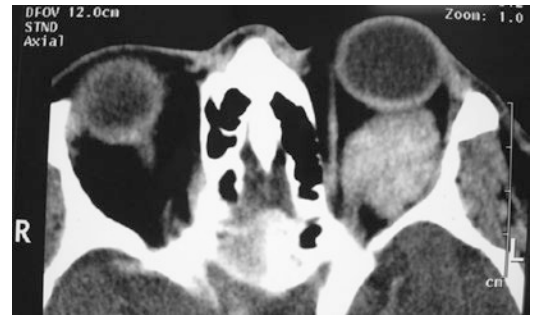

Fig. 16.1 CT scan of the orbits showing a large left **orbital venous malformation** causing axial displacement of the globe

The orbital venous malformation, also known as "cavernous malformation," is the most common vascular orbital lesion and the third more frequent after lymphoid tumors and orbit inflammatory syndrome [18, 19]. It accounts for approximately 5–15% of all vascular abnormalities of the central nervous system and 9% of orbital lesions, and usually occurs in middle age, with females more affected than males. Histologically, it is composed of endothelial-lined spaces surrounded by a well-delineated fibrous capsule.

The clinical presentation is variable. Many cases are asymptomatic and are incidentally discovered during radiological exams performed for other causes. In symptomatic patients, the onset is more often gradual, over years. The axial proptosis is the most common sign (about 70%) (Fig. 16.1). Other symptoms and signs include diplopia, visual field alterations, and rarely visual loss due to optic nerve compression. The diagnosis is performed by CT and MR.

The surgical resection is the gold standard treatment [19, 20]. Different surgical approaches can be used, from minimally invasive approaches to lateral orbitotomy (Fig. 16.2).

16.6.2 Cystic lesions

The cystic intraorbital lesions may be congenital or acquired (Table 16.3).

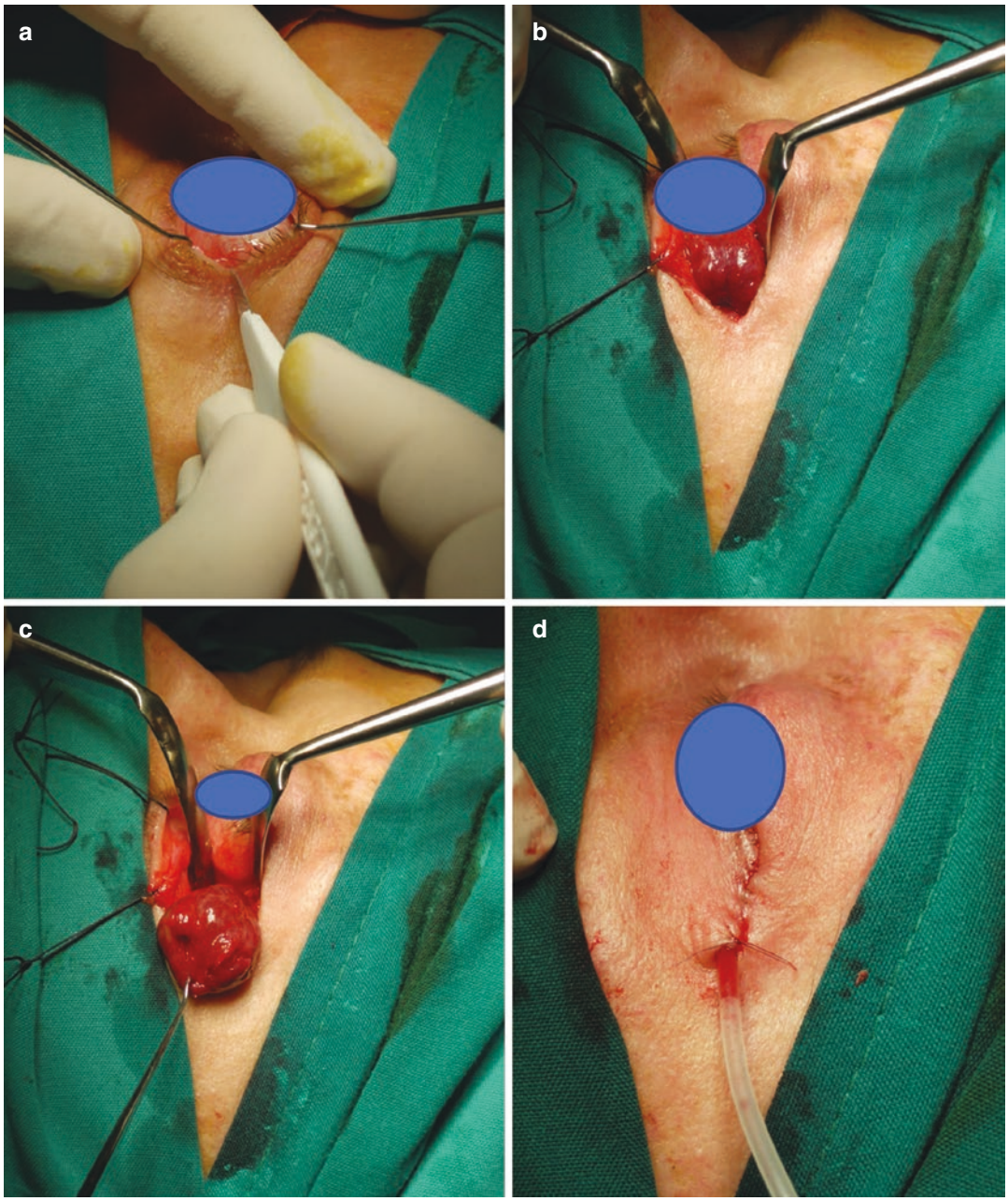

Fig. 16.2 Surgical resection of an **orbital venous malformation** through left orbitotomy: (**a**) Lateral canthotomy. (**b**) Orbital exploration and exposure of the lesion. (**c**) Resection of the malformation. (**d**) Suture and drainage

Table 16.3 Classification of orbital cystic lesions

1. Congenital lesions
Dermoid and epidermoid cyst
Dermolipoma
Sweat gland cyst
Hematic pseudocyst
Arachnoid cyst
Microphthalmos with muscle cyst
2. Acquired lesions
Mucocele
Encephalocele
Lacrimal sac mucocele
Implantation

Orbital epidermoid and dermoid cysts have been classified into juxtasutural, sutural, and soft tissue types and further subdivided according to their relationship to bone [21, 22]. Dermoid cysts arising from congenital rests of epithelial and subepithelial tissue are commonly located in the supero-temporal quadrant of the orbit, near the zygomatic-frontal suture, although they can also occur at other bony sutures. They are present at birth and can rarely remain asymptomatic. They tend to become symptomatic during the first decade [22] or more rarely at a later age. The first clinical manifestation is a slow-growing painless mass, which develops progressively over time and occupies the supero-external quadrant of the orbit. It is most commonly located deep to the epidermis and is fixed to the underlying bone. Only large cysts can cause downward and medial displacement of the globe. In case of perforation of the cyst wall, a strong inflammation can be triggered due to the extravasation of the cystic material in the neighboring tissues. In these cases, the diagnosis can be more complex, mimicking a primary inflammation of the orbit.

Histologically, the cyst wall is composed by epithelial-lined structure with dermal tissue; the cyst contains keratin and hairs in its lumen.

The diagnosis should include ultrasound and CT to better define the cyst relationship. At CT, the cyst usually appears as a well-defined round lesion with enhancing wall and non-enhancing lumen.

Small cysts may be treated conservatively with serial follow up, since they can remain stable for a long time and may even become smaller. Most commonly, however, the cyst enlarges and tends to break, thus requiring a prompt surgical treatment.

The goal of the treatment should be the complete surgical excision of the cyst, while preserving the integrity of its wall. The anterior orbital epidermal-dermoid cysts are best removed by an anterior approach (Fig. 16.3).

16.6.3 Neurogenic Tumors

Neurogenic orbital tumors include more common types, such as the benign optic nerve glioma (described in Chap. 12 of this book), neurofibroma, and schwannoma (approximately 1% of all orbital tumors) and more rare types such as ganglioma, neuroblastoma, and malignant peripheral nerve sheath tumors [23] (Table 16.4).

Schwannomas are benign peripheral nerve sheath tumors that may occur as sporadic forms or associated with neurofibromatosis. They usually arise from superior ciliary nerves or more rarely from smaller peripheral nerves [24]. The tumor typically appears as a globular and encapsulated enlargement of the involved nerve causing nerve displacement (Figs. 16.4 and 16.5).

The schwannoma clinically manifests with slow-growing exophthalmos in young or middle-aged patients; when the lesion occurs in the orbital apex (Fig. 16.6), the symptoms appear early.

The treatment consists in the radical surgical resection (Fig. 16.5) [25].

16.6.4 Mesenchymal Tumors

Primary mesenchymal tumors of the orbit are relatively rare despite the high prevalence of mesenchyme in this region. These include the meningioma of the optic nerve sheath (described in Chap. 12 of this book), several fibrocytic and fibro-osseous lesions, malignant bone tumors and myogenic tumors, mainly the rhabdomyosarcoma (Table 16.5).

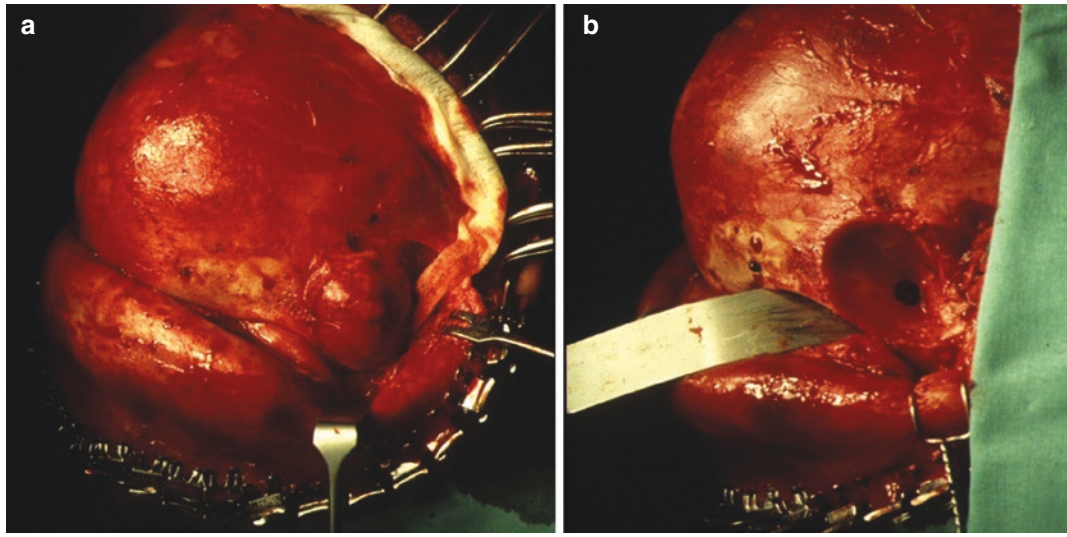

Fig. 16.3 Patient with a large **dermoid cyst** of the left orbit located supero-laterally near the zygomatic-frontal suture (**a**) Coronal approach used to completely remove the large cyst with bony involvement of the temporal fossa. (**b**) At the end of resection, the bony erosion due to the lesion is evident

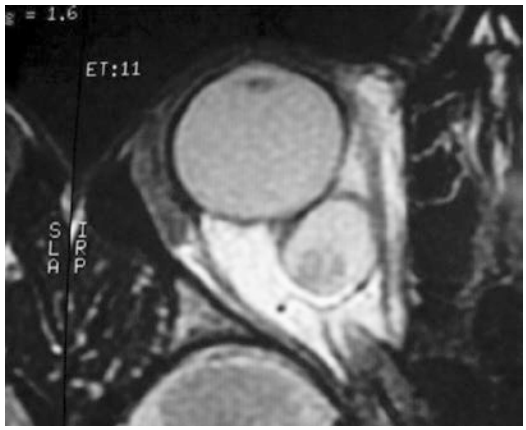

Fig. 16.4 MR of the right orbit: retrobulbar **schwannoma** located between the medial rectus and the optic nerve, causing nerve displacement

Table 16.4 Classification of orbital neurogenic lesions

Optic nerve glioma
Schwannoma
Neurofibroma
Glioneural tumor
Neuroblastoma

The rhabdomyosarcoma is a highly malignant tumor, most commonly found in children; the orbit is involved in 10% of cases.

Three variants of rhabdomyosarcoma are recognized: embryonal, alveolar, and pleomorphic. The embryonal variant is the most common in childhood, ranging between 50 and 70% of the orbital rhabdomyosarcomas [26]. The alveolar subtype accounts for approximately 20–30% of cases. The pleomorphic subtype almost exclusively occurs in adults [27].

Histologically, the embryonal subtype shows bipolar cells with tapered cytoplasmic processes and less commonly cells "tadpole-like" with long cytoplasmic extensions.

The alveolar subtype is a highly cellular tumor composed of a monotonous population of small round primitive cells; they form solid sheets or nests separated by thin fibrous septa. The nests classically show loss of cohesion centrally.

The rhabdomyosarcoma of the orbit clinically presents with rapidly progressive exophthalmos within a few weeks, impairment of extraocular movements, visual deficit, pain, and globe displacement. Parameningeal tumors can cause headache as well as focal neurologic symptoms related to mass effect. If cranial nerve palsies occur, they can indicate skull base erosion and intracranial extension.

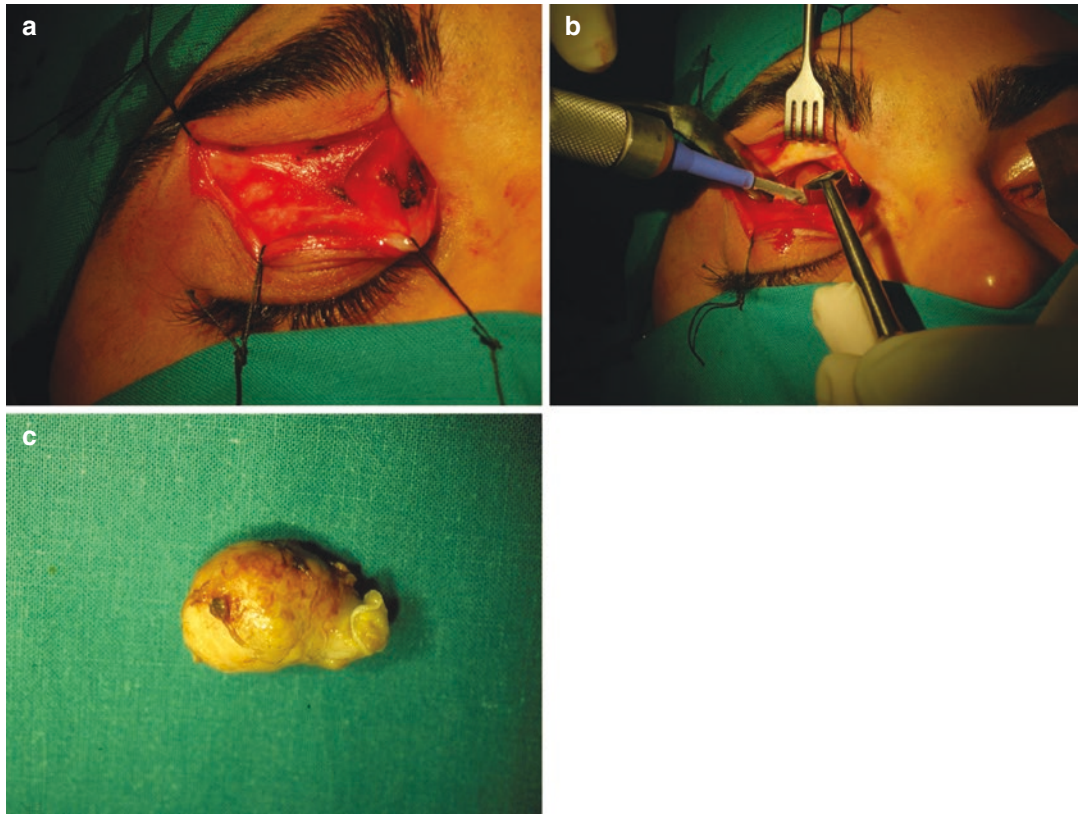

Fig. 16.5 Operative images of the patient of fig. 16.4. (**a**) Anterior orbitotomy by skin crease incision. (**b**) The tumor is easily removed with the aid of Cryo probe without damage of optic nerve and extraocular muscles. (**c**) Surgical specimen

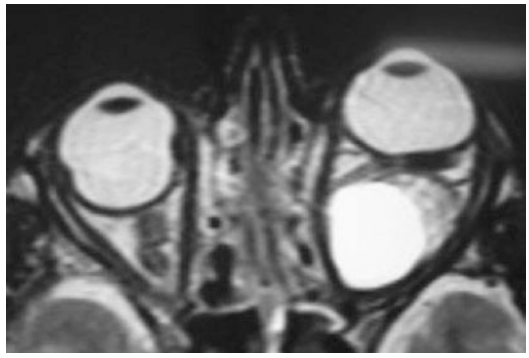

Fig. 16.6 MRI of a patient with severe left exophthalmos showing large apical lesion of the left orbit between optic nerve and lateral rectus muscle (**orbital schwannoma**)

CT and MR are important for the diagnosis and tumor staging. MR with multiplanar reconstructions, using routine spin-echo pre- and post-contrast T1 and T2 sequences, can provide excellent tumor definition (Fig. 16.7).

The treatment of rhabdomyosarcoma includes surgery, chemotherapy, and irradiation depending on its stage.

Complete excision of the primary tumor should be performed when it can be done safely. On the other hand, in patients with aggressive tumor, the radical surgery is not recommended.

Vincristine, actinomycin D, cyclophosphamide, doxorubicin, isofosfamide, and etoposide are the most used chemotherapy drugs; topotecan and irinotecan are also active against this type of cancer.

Radiation is used with doses of 3600–5400 cGy over 4–5 weeks. In cases with parameningeal extension, the irradiation must be extended to the perilesional tissues for at least 2 cm.

Table 16.5 Classification of orbital mesenchymal lesions

1. Fibrocytic lesions
Benign fibrous histiocytoma/solitary fibrous tumor
Fibroma
Fibrosarcoma
Angiofibroma
2. Benign fibro-osseous lesions
Osteoma
Fibrous dysplasia
Ossifying fibroma
3. Malignant bone lesions
Ewing sarcoma
Osteosarcoma
Chondrosarcoma
4. Reactive bone tumors
Giant cell granuloma
Aneurysmal bone cyst
5. Myogenic lesions
Rhabdomyosarcoma
Rhabdoid tumor
6. Lipocytic or myxoid lesions
Lipoma
Liposarcoma
Dermolipoma
Epithelioid sarcoma

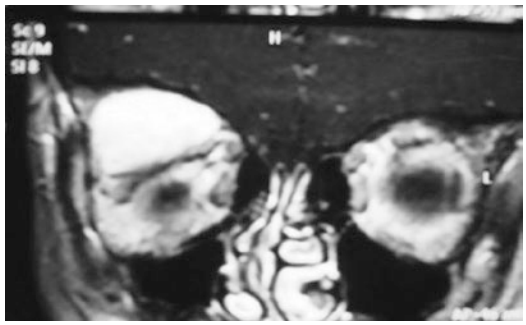

Fig. 16.7 Post-contrast coronal MR of a patient with orbital **rhabdomyosarcoma**: large enhancing lesion occupying the superior part of the right orbit and causing inferior displacement of the globe

16.6.5 Lacrimal Gland Lesions

Lacrimal gland lesions can originate from different cell types [28] (Table 16.6).

The neoplasms are classified into two types: epithelial and non-epithelial. Non-epithelial tumors are the most common, accounting for 70–80% of solid lacrimal gland masses; lymphomas are the most common tumors of this group. Epithelial lacrimal gland tumors mainly include the adenoid cystic carcinoma (60% of cases), followed by pleomorphic adenocarcinoma (20%), and adenocarcinoma -ex-pleomorphic adenoma (10%). Other types of lacrimal gland carcinomas (mucoepidermoid, primary squamous cell, sebaceous gland carcinoma, basal cell adenocarcinoma) are extremely rare.

Table 16.6 Classification of lacrimal gland lesions

1. Benign neoplastic lesions
Adenoma (monomorphic and pleomorphic)
Warthin tumor
Oncocytoma
2. Non-neoplastic lesions
Nonspecific inflammation
Atypical lymphoid hyperplasia
Lacrimal cyst
3. Malignant tumors
Adenoid cystic carcinoma
Non-Hodgkin lymphoma
Carcinoma ex-pleomorphic adenoma
Adenocarcinoma
Mucoepidermoid carcinoma
Squamous cells carcinoma
Ductal cell carcinoma
Acinic cell carcinoma
Unclassified carcinomas

Histologically, the adenoid cystic carcinoma is characterized by solid areas or cords of bland-appearing malignant epithelial cells. The infiltrative borders of the epithelial areas can be distinguished from the surrounding connective tissue and typically show perineural invasion.

The pleomorphic adenocarcinoma is characterized by myoepithelial cells in the surrounding connective tissue.

The adenocarcinoma (ex-pleomorphic adenoma) is characterized by areas of malignant degeneration in a pleomorphic adenoma, with variable amount of myxoid and chondroid structures; the epithelial cells also show carcinomatous changes.

Clinically, the tumor causes enlargement of the lacrimal gland; it results in "S-shaped" deformity of the eyelid margin, globe displacement, and limited ocular motility causing diplopia (Fig. 16.8).

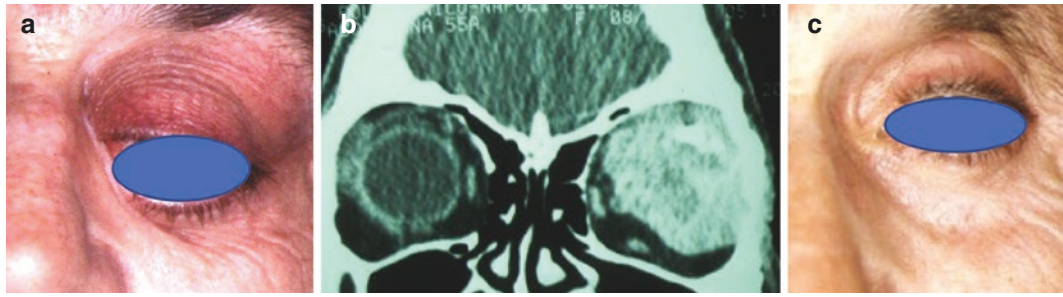

Fig. 16.8 (**a**) Patient with **adenocarcinoma ex pleomorphic adenoma** of the left lacrimal gland showing left orbital proptosis with inferior globe displacement. (**b**) Post-contrast coronal CT: large enhancing lacrimal gland tumor. (**c**) Aspect of the patient after the treatment (surgical excision and radiation therapy): remission of orbital proptosis and displacement

MR is important for the tumor definition and for evaluation of soft tissue involvement. CT is necessary for the evaluation of the bony changes.

Malignant epithelial tumors of the lacrimal gland are characterized by aggressive biological behavior. Thus, also aggressive local surgical treatments, such as the orbital exenteration, do not result in better long-term survival [17]. Perineural and bone invasion are frequently observed; the recurrence and metastases rates are high. The best treatments for malignant tumors of the lacrimal gland seems to be eye-sparing procedures and radiotherapy.

16.6.6 Lymphoproliferative and Histiocytic Lesions

Lymphoproliferative orbital lesions frequently present as orbital masses (24%–49%) in the adult and include a wide spectrum of benign and malignant lesions [29, 30] (Table 16.7).

Lymphoma is the most common orbital neoplasm (55% of the cases in adults). Most orbital lymphomas are primary, low-grade, B-cell, non-Hodgkin lymphomas; the extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT) is the most common subtype.

In recent years, the classification of lymphoproliferative lesions is considerably changed; several benign, noninfectious, chronic inflammatory diseases have been added, such as IgG4-related ophthalmic disease, reactive lymphoid hyperplasia, and idiopathic orbital inflammation [31, 32]. In particular, the IgG4-related ophthalmic disease is increasingly recognized and accounts for 50% of benign lymphoproliferative orbital lesions. Therefore, obtaining a correct diagnosis and differentiating orbital lymphomas from the different lymphoproliferative lesions are fundamental steps to decide the correct therapy, since the clinical behavior of the various pathologies is very different.

Table 16.7 Classification of orbital lymphoproliferative and histiocytic lesions

Lymphoma	Plasmacytoma
Diffuse lymphoma	Histiocytic lymphoma
MALT-type lymphoma	Burkitt lymphoma
Marginal zone lymphoma	Unknown histology lymphoma
Small lymphocytic lymphoma	Atypical lymphoid hyperplasia
Follicular lymphoma	Xanthogranuloma
Mantle cell lymphoma	Eosinophilic granuloma

The therapy of orbital lymphomas consists of low-dose radiation therapy, whereas others lymphoproliferative lesions are expected to show good response to corticosteroid therapy.

The primary orbital lymphoma originates from the eyelids, extraocular muscles, soft tissue orbital adnexa, conjunctiva, or lacrimal glands. It is typically located in the anterior orbital compartment or beneath the conjunctiva in the extraconal space. It presents with proptosis, slowly growing palpable mass, or painless swelling of the eyelids, with a "salmon-patch appearance" beneath the conjunctiva (Fig. 16.9).

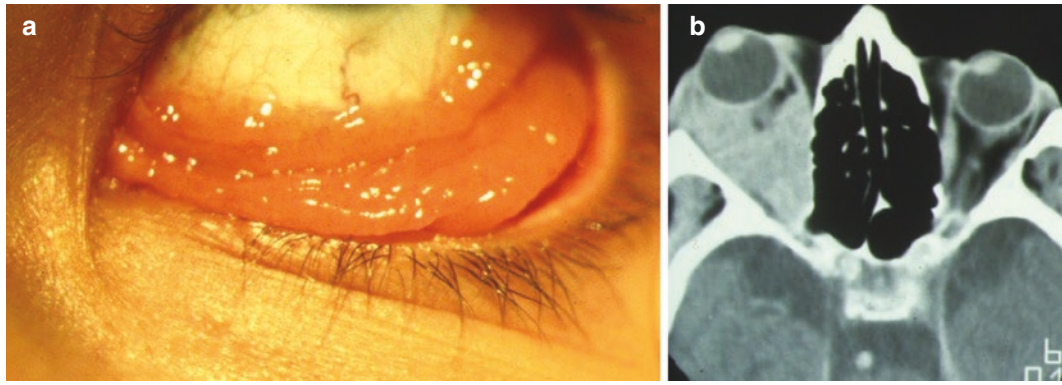

Fig. 16.9 Patient with right **orbital lymphoma**. (**a**) Typical "salmon-patch appearance". (**b**) CT: large right orbital involvement

The occurrence of orbital lymphoproliferative lesions in immuno-compromised patients, such as those affected by AIDS or those who have undergone immunosuppressive therapies, is an important problem. Some studies of the recent literature have confirmed the involvement of some pathogens, such as Chlamydia psittaci, H. pylori, and some viruses in association with orbital lymphoma.

The correct diagnosis by open biopsy is necessary. The staging of the disease must also include the FDG-PET/CT of chest, abdomen and pelvis, the cranial MRI, and the bone marrow biopsy [33].

16.6.7 Metastatic Tumors to the Orbit

Orbital metastases are rare, accounting for 1–13% in the reported series of orbital tumors and for 2–5% among patients with systemic cancers [34] (Table 16.8).

The breast and the lung are the most frequent sites of primary tumors causing orbital metastases, followed by the prostate. Although the prevalence of colorectal cancer is rather similar to breast and lung cancers, its tendency to develop orbital metastases is significantly lower, maybe due to a different metastatic pathway. On the other hand, metastases arising from tumors of the gastrointestinal tract, kidney, and from skin melanoma occur rarely [34].

Table 16.8 Metastatic tumors to the orbit

Breast carcinoma	Prostate carcinoma
Renal cell carcinoma	Bladder carcinoma
Lung carcinoma	Gastric carcinoma
Nasopharyngeal carcinoma	Hepatocarcinoma
Melanoma	Adrenal neuroblastoma
Parotid gland carcinoma	Carcinoma of the penis
Squamous cell carcinoma	Undetermined primary site
Neuroendocrine carcinoma	

Patients who develop orbital metastases may have extremely, rapidly growing exophthalmos followed by double vision due to extraocular muscle involvement, decreased vision, and pain. The diplopia can be caused by direct muscle infiltration or by mass effect. When the metastasis involves the orbital apex, ophthalmoplegia and blindness can occur.

The diagnostics imaging protocol must include ultrasound, CT, and MRI of the orbit. Orbital metastases from breast cancer present diffuse and irregular infiltration along the rectus muscles and fascial planes. Standardized B- and A-scan echography can be used to obtain a fast and accurate differential diagnosis in cases of muscle involvement or more superficial lesions. CT commonly shows a solid enhancing mass often located within the orbital fat and/or the muscles associated with bone erosion. MRI may provide a more accurate definition of the mass (Fig. 16.10).

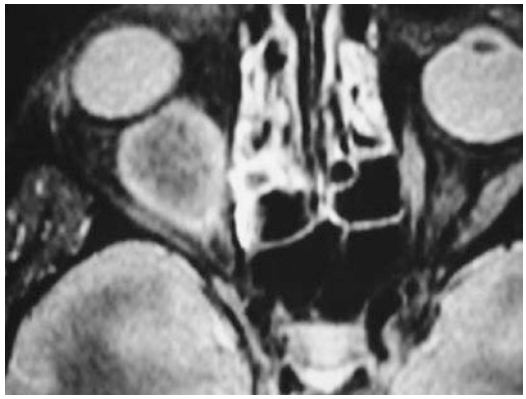

Fig. 16.10 MR of the orbits, T2 -weighted axial sequence: hyperintense right orbital mass involving the inferior rectus muscle (**metastasis** from undifferentiated breast cancer)

The definitive diagnosis of orbital metastases is made by biopsy and histopathological examination. The fine needle aspiration biopsy is a valid procedure in patients with systemic malignancy or in poor condition and when the mass is located deeply within the orbit. When the lesion is in the anterior orbital compartment, an incisional biopsy through transconjunctival or transcutaneous approach should be preferred. In cases with well circumscribed tumor, an excisional biopsy can be performed.

The therapy of orbital metastases is closely linked to the patient's general condition, the clinical staging of the neoplastic disease, the type of primary tumor, as well as the use of radiotherapy and chemotherapy protocols [35].

The mass effect can lead to worsening of vision; thus, the surgical removal or debulking of lesion could be a valid strategy. The exenteration orbitae, which was once considered the first-choice treatment, is currently no longer used, as it does not significantly affect the survival.

Unfortunately, despite all the efforts in the management of orbital metastases, the therapies are effective for local palliation and disease control, but the systemic prognosis remain poor.

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