Differential Diagnoses of Diseases Involving the Extrinsic Ocular Musculature – A Pictorial Essay*

*Diagnóstico diferencial das doenças que envolvem a musculatura ocular extrínseca – Um ensaio pictórico**

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Abstract

Introduction There are some inflammatory, infectious, and neoplastic diseases affecting the extrinsic orbital musculature (EOM) that present with pain, decreased visual acuity, and proptosis. Imaging is fundamental to the differential diagnoses of these diseases with similar clinical presentations. The present case series report has as main objective to illustrate and discuss the main pathologies that affect the orbit.

Material and Methods The present series of cases discusses the main pathologies that can affect the extraocular musculature that can be characterized by computed tomography (CT) or magnetic resonance imaging (MRI) using cases from our institution.

Results and Discussion The present study compiled several cases of ophthalmopathy from our institution to illustrate and address some of these pathologies, such as orbital lymphoma, Grave disease, metastases, periorbital cellulitis, and idiopathic orbital inflammatory syndrome. The diseases are discussed according to the presentation of clinical cases with emphasis on the main imaging findings of each pathology.

Conclusion Computed tomography and MRI can help in the diagnosis and follow-up of the diseases that affect the EOM. We must be conversant with the main characteristics of the pathologies presented in the present case series report, since such findings together with clinical data can confirm the diagnosis of these diseases or at least help to narrow the differential diagnoses.

Keywords

- graves ophthalmopathy
- orbital lymphoma
- orbital pseudotumor
- orbital cellulitis
- sarcoidosis

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Resumo

Introdução Existem algumas doenças inflamatórias, infecciosas e neoplásicas que afetam a musculatura orbitária extrínseca que se apresentam com dor, diminuição da acuidade visual e proptose. Exames de imagem são fundamentais para o diagnóstico diferencial dessas doenças com apresentações clínicas semelhantes. A presente série de casos tem como principal objetivo ilustrar e discutir as principais patologias que afetam a órbita.

Material e métodos A presente série de casos discute as principais patologias que podem afetar a musculatura extraocular passíveis de caracterização por estudo de tomografia computadorizada (TC) ou de ressonância magnética (RM) utilizando casos próprios da nossa instituição.

Resultados e discussão O presente estudo compilou diversos casos de oftalmopatia da nossa instituição para ilustrar e abordar algumas destas patologias, como linfoma orbital, doença de Grave, metástases, celulite periorbital e síndrome inflamatória orbital idiopática. As doenças são discutidas de acordo com a apresentação dos casos clínicos, dando-se ênfase nos principais achados de imagem de cada patologia.

Conclusão A TC e a RM auxiliam no diagnóstico e no acompanhamento das doenças que acometem a musculatura ocular extrínseca. Deve-se estar familiarizado com as principais características das patologias apresentadas na presente série de casos, uma vez que tais achados, juntamente com os dados clínicos, podem confirmar o diagnóstico destas doenças ou, pelo menos, ajudar a estreitar os diagnósticos diferenciais.

Palavras-chave

- orbitopatia de graves
- linfoma orbital
- pseudotumor orbital
- celulite orbital
- sarcoidose

Introduction

The extraocular muscles (EOMs) occupy the retrobulbar space and are composed of six muscles: the superior, inferior, medial, and lateral recti and the superior and inferior oblique muscles.[1,2] They may be affected in different systemic and local diseases.

Except for the superior oblique and the lateral rectus, which are innervated by the trochlear nerve and the abducens nerve respectively, the other EOMs are innervated by the oculomotor nerve; in this way, the clinical presentation of patients will depend on the muscle or nerve affected by the disease.[1,2]

Pathologies that affect the retrobulbar space may have very similar clinical presentations; for example, for orbital inflammatory syndrome (OIS), orbital lymphoid lesions, and orbital cellulitis,[3–5] both computed tomography (CT) and/or magnetic resonance imaging (MRI) are required to make a definite diagnosis or to assist in the indication and orientation of biopsies.

The present case series discusses the main pathologies that can affect the EOMs and that appear in the daily practice.

Objectives

The present series of cases aims to review the main orbital diseases that affect the extrinsic musculature of the orbit, illustrating with cases of our institution.

Material and Methods

The present study was approved by the ethics committee of the Hospital Universitário Cassiano Antônio Moraes (HUCAM, in the Portuguese acronym).

Patients with classic presentations of the main diseases that affect the extrinsic musculature of the orbit who underwent CT and/or MRI in the HUCAM imaging sector were selected.

A literature review was carried out using the PubMed and SciELO databases to elaborate the discussions of the cases.

Results and Discussion

Orbital Cellulitis

Seen more commonly in children and young adults, orbital cellulitis can be divided into five stages: type I, inflammatory edema; type II, diffuse orbital cellulitis; type III, subperiosteal abscess; type IV, orbital abscess; type V, cavernous sinus thrombosis.[5–7]

The differentiation between the infection limited to the preseptal tissue and the infection that affects the postseptal tissue is fundamental because patients with infection of the preseptal tissue alone can be treated in an outpatient setting, whereas patients with postseptal tissue involvement should be admitted for intravenous antibiotic therapy and drainage when indicated.[1,5,6,8,9]

Patients with orbital cellulitis usually present with edema and eyelid erythema, pain, proptosis, and limitation of ocular movements.[7]

In MRI, the collection of cellulite presents as isointense to EOM and hypointense to the orbital fat in T1, and hyperintense in T2, with peripheral and annular impregnation by the contrast enhancement medium (►**Fig. 1**).[3,5,10] In the presence of an abscess, diffusion restriction is observed, which may aid in its identification in the absence of contrast enhancement.[11]

In CT, the abscess presents as hypodense, with orbital fat densification and peripheral contrast enhancement.[9,10] When the etiologic agent is fungal or bacterial, the cellulite presents in a similar way in both cases on radiographic examination; in these cases, mass effect, bone erosion, and calcifications can be observed in the CT image. However, in MRI, the fungal lesion can be hypointense in T2 due to the impregnation of paramagnetic substances and free radicals released by fungi.[10]

In cases in which cavernous sinus thrombosis (type V) occurs, the "black turbinate sign" may be an early predictor of mucormycosis.[12]

Idiopathic Orbital Inflammatory Syndrome

Also known as inflammatory pseudotumor, its etiology is not yet defined, and its diagnosis is one of exclusion.[1,13–16] Unilateral presentation is most common in adults, and although rare, bilateral occurrence is more prevalent in the pediatric group.[17] Treatment is done with corticosteroid therapy.[15]

The most typical clinical presentation is acute pain, edema, and periorbital erythema, with or without reduction of visual acuity and diplopia.[14,16] It can be divided into five subgroups: lacrimal, anterior, posterior, diffuse, and myositic pseudotumor.[16,18]

It may present as a focal intraorbital lesion or with infiltrative features similar to lymphoma. In MRI, it is hypointense in T1 and T2 with contrast enhancement, evidencing inflammation of the muscles, tendons, and adjacent fat (►**Fig. 2**).[1,13,16]

Orbital myositis, one of the subtypes of idiopathic orbital inflammatory syndrome (IOIS), may involve one or two EOMs (the inferior rectus being the most affected); it is typically unilateral and affects tendinous insertions (unlike orbital involvement due to thyroid disease, which usually spares the tendinous insertions).[1,16]

One variant is the Tolosa-Hunt syndrome, an idiopathic syndrome that is characterized by inflammation of the superior orbital fissure and/or of the cavernous sinus, with consequent recurrent painful ophthalmoplegia, which responds to corticosteroid therapy.[13,19,20] In MRI, it presents as hypointense lesions in T1 and T2 in the cavernous sinus, the orbital apex, or the superior orbital fissure with impregnation by contrast enhancement medium.[13,20] Computed tomography findings are not specific but may aid in differential diagnoses. It may present asymmetric enlargement of the cavernous sinus and nodular enhancement in the prepontine cisterna, the cavernous sinus, and the orbital apex by the contrast medium.[17,19]

Several pathologies may manifest as an orbital pseudotumor, such as IgG4-related disease, idiopathic hypereosinophilic syndrome (HES), sarcoidosis, granulomatosis with polyangiitis (GPA), and Churg-Strauss syndrome. The IgG4-related orbital pseudotumor has an estimated incidence of

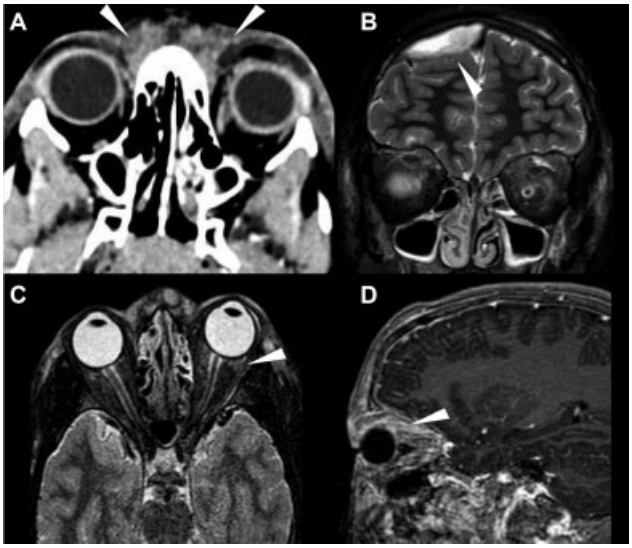

Fig. 1 Orbital cellulitis. A – Computed tomography without contrast: Thickening and heterogeneity of bilateral periorbital soft tissue with extension of the nasal and malar region (arrows). B, C and D – T2WI and T1 postcontrast show preseptal and postseptal compartments. The inflammatory process involves the orbital musculature (arrows). Extradural empyema is also noted in the right frontal convexity (arrow in b).

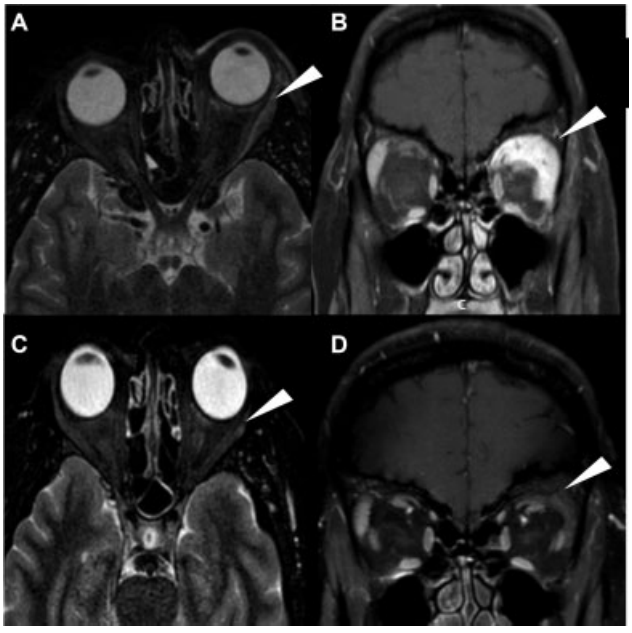

Fig. 2 Orbital inflammatory pseudotumor. A and B – T2-WI and T1 postcontrast show an extraconal expansive lesion in the superolateral aspect of the left orbit, involving the superior and lateral rectus complex surrounding the lacrimal gland, with a low T2-WI sign and with an intense homogeneous contrast enhancement (arrows). C and D – T2-WI and T1 postcontrast after 1 year showing resolution after corticoid treatment

between 5 and 20% among inflammatory orbital lesions[21] and has predilection for the lacrimal gland and nerves.[21,22] The HES is characterized by prolonged eosinophilia with no definite cause, leading to visceral damage.[23]

Orbital involvement in patients with systemic sarcoidosis is not rare. In these cases, involvement of the lacrimal gland, of the optic nerve, and of soft tissues may occur, with anterior uveitis being the most common manifestation, followed by dacryoadenitis.[24,25] Although uncommon, patients may develop strabismus due to involvement of bilateral EOMs, usually with dacryoadenitis.[26,27]

Granulomatosis with polyangiitis (GPA) typically affects the kidneys and lungs, but up to 60% of the patients may present with orbital involvement including the optic nerve, and it may be the first or only manifestation of the disease.[28] Clinically, it can manifest with pain, erythema, conjunctival injection, limited extraocular muscle movements, and vision loss.[28,29]

The imaging findings are nonspecific, presenting more commonly in CT as an infiltrative lesion of the orbit with adjacent fat obliteration and, in some cases, sclerosis and bone erosion with or without sinus pathology. In MRI, it usually presents as a hypointense lesion in T2 with contrast enhancement.[28,29]

Churg-Strauss syndrome (CSS) is a systemic vasculitis characterized by hypereosinophilia, asthma, and allergic rhinitis. Orbital manifestations are rare, but when present, may appear as an inflamed mass or inflammation of the orbital structures.[30]

Orbital Lymphoma

Orbital lymphoma corresponds to up to ~ 12% of all orbital tumor lesions and is typically non-Hodgkin lymphoma. It can occur anywhere in the orbit.[1,31]

The EOMs lymphomas affect the muscular tendons (unlike thyroid ophthalmopathies), and the most common location of involvement is the superolateral quadrant, followed by the superomedial quadrant of the orbit.[32]

Clinically, the patient may present with proptosis, palpable mass, and reduction of ocular mobility, with pain being an uncommon finding (unlike in cases of pseudotumor).[16,33]

Extraocular muscles lymphomas are hyperdense expansive lesions in CT (►**Fig. 3**) and have moderate contrast enhancement; it is difficult to differentiate them from orbital myositis. A study published in 2003 observed that lymphomas show a decrease in CT density with dual-phase contrast-enhancement protocol, whereas orbital myositis shows an increased density in the late phases.[32,33]

In MRI, lymphomas are hypointense in T1 and hypo- to isointense in T2 with a homogeneous appearance on contrast enhancement.[1,34]

Orbital Metastasis

Orbital metastasis represents 2% of all orbital lesions, with the breast being the most common primary site. The EOM is most commonly affected by orbital metastases from cutaneous melanoma.[1,31,35,36]

Generally, the symptoms are related to mass effect. A great majority is unilateral[1,36,37] and can range from well-defined focal lesions to infiltrative lesions.[36]

In the case of an already established metastatic cancer, biopsy of the orbital lesion is often not indicated.[36]

Breast metastases often present with diffuse and irregular growth along the rectus muscles and fascial planes.[38]

Computed tomography assists mainly in the diagnosis of prostatic metastases due to its predilection for bone with development of osteoblastic orbital metastases (►**Fig. 4**).[37]

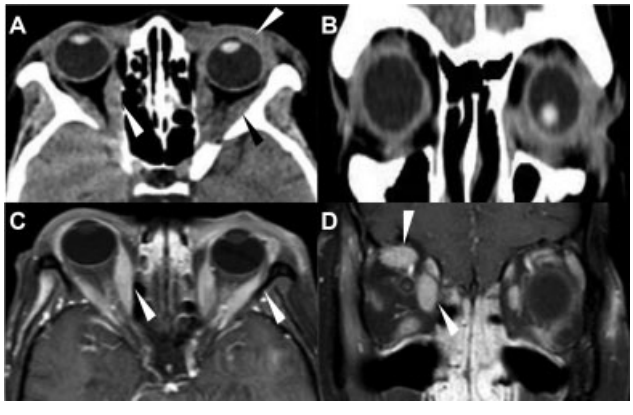

Fig. 3 Orbital lymphoma. A and B – Computed tomography without contrast shows left eyelid involvement with thickening of the bilateral extrinsic musculature (arrows). C and D – T1 postcontrast shows intense homogeneous contrast enhancement of the bilateral extrinsic musculature (arrows).

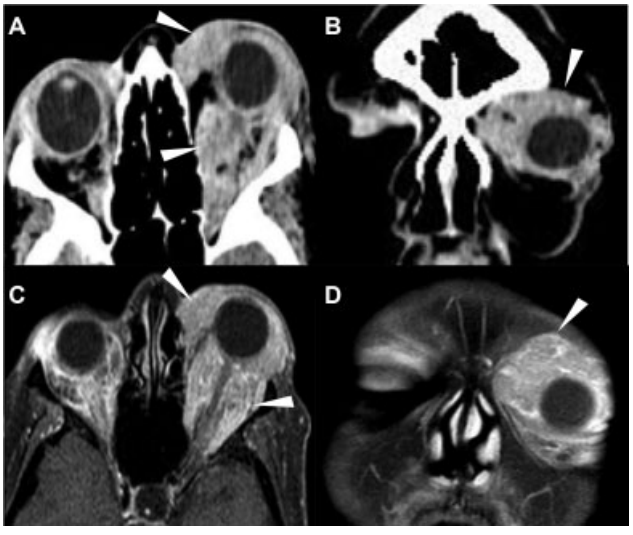

Fig. 4 Orbital metastasis in computed tomography. A and B – Computed tomography without contrast shows thickening and densification of the periorbital soft tissues in the left orbit, with extension to the intraconal fat (arrows). C and D – Mass with left orbital infiltrative aspect showing intense enhancement after contrast, with intra- and extraconal components infiltrating the extrinsic musculature and involving the greasy planes and optic nerve, determining reduction of the caliber of the same and proptosis (arrows).

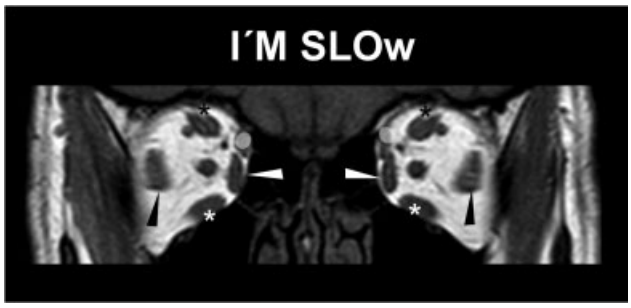

Fig. 5 Mnemonic "I'M SLOW" Magnetic resonance imaging showing the inferior rectus (white asterisk), the medial rectus (white arrow), the superior rectus (black asterisk), the superior oblique (circle), and the lateral rectus (black arrow).

Signal intensity in MRI exhibits some degree of contrast enhancement and varies depending on the primary site of metastasis.[39]

Thyroid Ophthalmopathy

Graves ophthalmopathy is the main cause of proptosis in adults. It is usually bilateral and with symmetrical involvement of EOMs. The muscle most commonly involved is the inferior rectus, followed by the medial, superior, and lateral recti, usually known by the mnemonic "I'M SLOW" (►**Fig. 5**).[1,32]

It is more commonly seen in patients with hyperthyroidism but can also be found in patients with hypothyroidism or normal thyroid function.[1,40]

Computed tomography and MRI examinations evidenced thickening of the EOMs with relative preservation of the tendon insertions, increase of retro-ocular orbital fat, and may present contrast enhancement. Muscle bellies are typically hypodense in CT and hyperintense in T2 (►**Fig. 6**).[1,40,41]

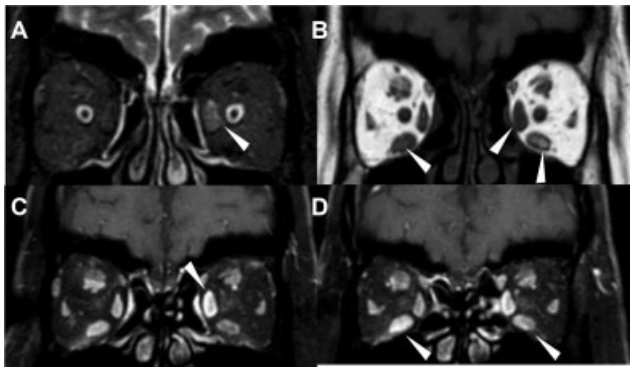

Fig. 6 Thyroid ophthalmopathy. A and B – T2-WI and T1-WI show thickening of the extrinsic ocular musculature, especially of the inferior and medial recti, associated with an increase in the fat component (arrows). C and D – T1 postcontrast shows an intense homogeneous contrast enhancement (arrows).

Miscellaneous

Less common diseases, such as Crohn disease, Behçet disease, rheumatoid arthritis, Lyme disease, and systemic lupus erythematosus can also affect the extrinsic ocular musculature.

Patients with Crohn disease may exhibit ocular manifestations, mainly episcleritis and uveitis and, less commonly, orbital myositis.[42]

The ocular involvement in Behçet disease is already well established in the literature and is usually considered when uveitis and vasculitis occur simultaneously. Patients with Behçet disease may also present with orbital myositis, although there are few reports on its occurrence.[43]

Rheumatoid arthritis, systemic lupus erythematosus, and Lyme disease may also manifest with orbital myositis.[44–46] ►**Table 1** summarizes the main imaging features of the pathologies mentioned in this iconographic essay.

Table 1 Main imaging features

	Clinics	Computed tomography	Magnetic resonance imaging
Cellulitis	Edema, pain, and proptosis	Abscess presents as hypodense with orbital fat densification, and peripheral impregnation	T1-isointense T2- hyperintense peripheral and annular impregnation
IOIS	Acute pain, edema, and erythema	Focal or infiltrative with tendon thickening	T1- hypointense T2- hypointense Contrast enhancement - muscle, tendons and fat.
Lymphoma	Proptosis, palpable mass	Moderate contrast enhancement	T1-hypointense T2- hypo/isointense homogeneous enhancement
Metastasis	Symptoms related to mass effect	Varies	T1-varies T2-varies some degree of contrast enhancement
Thyroid ophthalmopathy	Bilateral, symmetrical involvement of EOM	Thickening of the EOM with relative preservation of the tendon insertions. Muscle bellies are hypodense.	T2- Muscle bellies are hyperintense.

Abbreviations: EOM, extrinsic orbital musculature.

Conclusion

Computed tomography and MRI help in the diagnosis and follow-up of the diseases that affect the EOMs. We must be conversant with the main characteristics of the pathologies presented in the present case series since such findings together with clinical data can confirm the diagnosis of these diseases or at least help to narrow the differential diagnoses.

Ethics Approval and Consent to Participate

Ethical approval was provided by the HUCAM Institutional Review Board (CAAE - 08119819.8.0000.5071), Brazil.

Availability of Data and Materials

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request. All data generated or analyzed during the present study are included in the present published article (and its supplementary information files).

Contributions of the Authors

Santana L. M. and Rosa-Junior M analyzed and interpreted the patient data regarding CT and MRI and were major contributors in the writing of the manuscript. Martins L. A. analyzed and interpreted the patient data regarding CT and MRI and made the figure slides. All authors read and approved the final manuscript.

Conflict of Interests

The authors have no conflict of interests to declare.

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