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Intraconal Tumor-like mass as first manifestation of IgG4-related disease

Dear Editor

A great variety of tumors and tumor-like lesions can involve the orbit. Benign and malignant neoplasms, inflammatory diseases, vascular and congenital lesions take part of this heterogeneous group that creates many challenges for diagnosis, management, and treatment. [1]

Obviously, symptoms and clinical history are fundamental to establish a differential diagnosis, and imaging is mandatory to distinguish between lesions that have similar clinical presentations in most cases. With this report, the authors highlight the diagnostic difficulties and the importance to include not only tumors but also vascular inflammatory process into the differential diagnosis of this unilateral orbital lesion type.

CT scan availability and efficacy in detecting masses makes it the first imaging exam used, although MRI is accurate for describing the anatomic location and vascular components and it may reveal additional informations in order to distinguish similar appearing lesions, especially when these do not involve the bone but soft tissues. Sometimes this does not happen and there is no certain diagnosis until post-biopsy histological result. [2] This is the case of a 43 years-old Caucasian male, who presented with a progressive unilateral painless right exophthalmos without eye kinetics alteration or visual acuity compromission. Medical history was unremarkable; he only referred chronic traumatism (boxer).

MRI with gadolinium revealed the presence of an endorbital intraconal expansive lesion (3 cm), "crescent moon" - like morphology, tightly adherent to the posterior surface of the eye. The margins were regular and sharply defined. The mass showed hypointensity on T1-weighted and marked hypointensity on T2-weighted images and after contrast media demonstrated absent or very low vascularization. No significative restricted diffusion was found in DWI. MRI features suggested a fibrotic-granolumatous tissue without aggressive behaviour, according with chronic inflammatory process. (Fig. 1 A-B)

Thyroid disfunction and infection were excluded after laboratory tests. Due to low vascularization detected after MRI, vascular malformation was not considered.

Definitive histopathological examination after incisional biopsy was consistent with a rare case of a tumour-like intraconal vasculitic lesion IgG4-related disease (IgG4-RD) with unifocal involvement of the right orbit and a probable chronic traumatic cause. (Fig. 1 C–F) Hystopathological diagnosis was confirmed after laboratory test. IgG4-RD is a newly recognized fibroinflammatory disease presenting with many unexplained aspects and multiple features including mass forming lesion. Only few reports that describe ocular tumor-like mass lesions IgG4-related diseases can be found in literature. [3,4]

In our case the mono-lateral presentation and the similar clinical and radiological features led to an initial misdiagnosis of malignancy (particularly of primary orbital sarcoma) as frequently happens in this uncommon disease. [4]

Even if the typical presentation is low-grade proptosis with minimal pain, the hypotheses of orbital lymphoid tumor was discarded, due to the absence of systemic disease and unaltered blood values , the less common unilateral presentation and the discordant imaging. [2] Moreover, negative DWI excluded lymphoma.

The hypothesis of a secondary tumor was abandoned as well: even if orbital metastases are the most common primary breast, lung, and prostate malignancies, the empty tumor anamnesis and the no signs of muscle infiltration or bone erosion were not in favor to this diagnosis. [5]

Therefore, the hypothesis of primary orbital low-grade sarcoma was supposed, given the common clinical presentation, as a painless one-sided mass with variable growth rate depending on the biologic behavior and grade of the tumor and the unknown etiology in which traumatic or infectious causes may play a role. [6,7]

Due to chronic traumatism history, a second hypothesis of benign chronic haematic cyst was considered. As orbital hemorragies, trauma is the usual ethiology but the difference being that the initial event is often subclinical; an inapparent hemorrhage could lead an incomplete resorption that may cause a progressively mass effect and chronic inflammatory reaction. [8]

We decide to perform an incisional biopsy through transconjunctival approach and histopathological examination revealed fibroadipose tissue with intense and diffuse inflammatory infiltrate consisting of lymphocytes (T and B), plasma cells (IgG4) and small vessels with thickened wall and activated endothelium with transmural eosinophilia infiltration as a vasculitis in reactive phase.

The immunohistochemistry showed CD1a, S100, CD207 and CKAE1/AE3 negatives markers discarding the hypotheses of epithelial malignancies. [7] Laboratory investigations revealed elevated IgG4 serum level at 423 mg/dl (normal: 8–140mg/dL) [4] that confirmed, with the morphological and clinical appearance, the diagnosis of IgG4-related disease (IgG4-RD) ocular manifestation. Systemic steroid therapy led to a rapid mass reduction and improvement in the patient's overall condition.

IgG4-RD is an emerging fibroinflammatory disease entity characterized by expansive lesions or tissue infiltration by IgG4-positive plasma cells and elevated serum IgG4 concentration. This disease can involve a variety of organs and tissues and the characteristic presentation includes different degrees of tumor-like mass, tissue fibrosis and perivascular lymphocytic infiltration rich in IgG4-positive plasma cells. [8,9] There are few reports in literature that report orbital involvement as first manifestation of IgG4-RD, and only 30% of them has had

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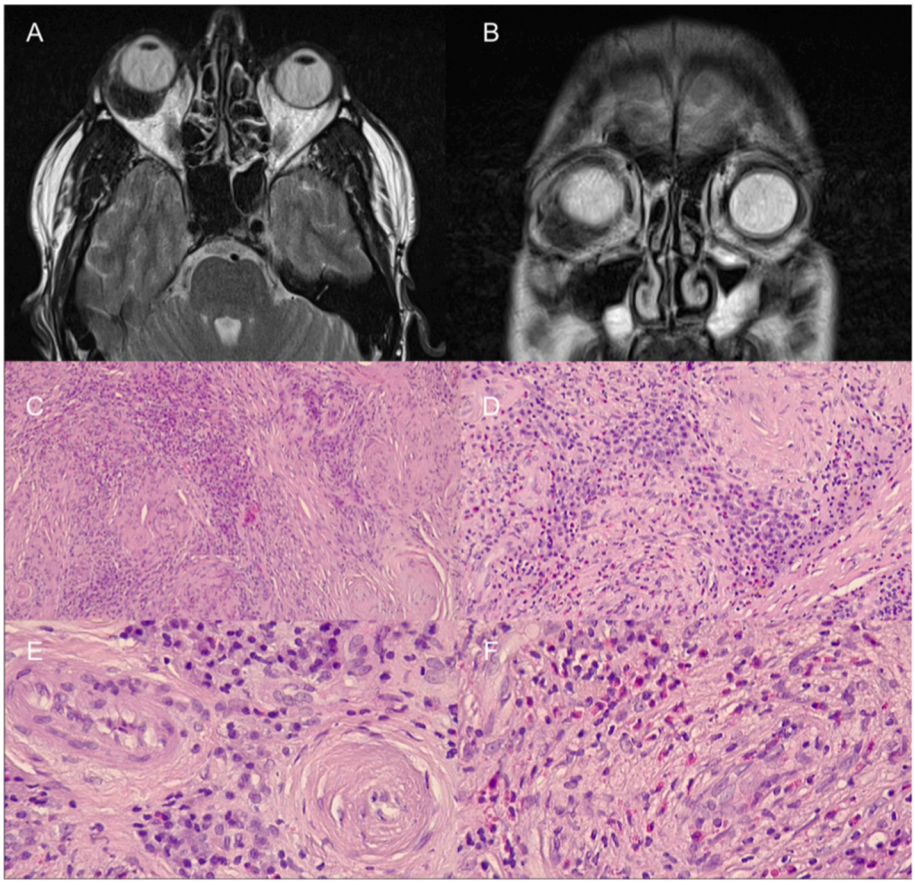

Fig. 1. A-B) Hypointense endorbital intraconal expansive lesion (3 cm), "crescent moon" - like morphology, tightly adherent to the posterior surface of the eye - T2 axial and coronal sequences; C-D) Histological sections showing sclerotic nodules surrounded by massive inflammatory infiltrates. Original magnification 10× and 20X. Hematoxylin and eosin staining; E) Higher magnification of the nodules showing small vessels with thickened wall; D) Higher magnification of the nodules showing small vessels with transmural infiltration of eosinophils.

proptosis as clinical presentation. [4–9]

The etiology is not clear, but the possible mechanism of mass lesion formation is the rupture of small vessels due to the infiltration of inflammatory cells, resulting in the enlargement of the lesion mimicking the mass, [10] and in our case chronic traumatism may has been a contributing factor.

Monolateral tumor-like IgG4-RD cases are rare and often misdiagnosed with malignancies; [4] preoperative radiological differential diagnosis is often challenging. Sharply defined margins and marked T2 hypointensity are the most specific MRI signs for granulomatous lesion in the head and neck region in patients without story of previous surgery. With this report we want to highlight that the differential diagnosis of a monolateral orbital masses should not include only tumors but also inflammatory process to avoid misdiagnosis. In particular, the relevance in reporting IgG4-RD cases, especially in unusual scenarios, such as monolateral orbital mass presentation, remains an important contribution to differentiate this condition still underdiagnosed, in which medical treatment may lead to remission and prevent significant morbidity and mortality.

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Ethical approval

The methods were carried out in accordance with the approved guidelines.

No Ethical Committee approval was required for this study. The research was conducted ethically, with all study procedures being performed in the accordance with the requirements of the World Medical Association's Declaration of Helsinki. Written informed consent was obtained from each participant/patient for study participation and data publication.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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