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Short communication

IgG4-related orbital disease☆

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ABSTRACT

Case report: The case is presented of a 64-year-old woman with bilateral palpebral swelling and dacryoadenitis, exophthalmos, and a history of chronic rhinitis and asthma. An increase in serum IgG4 was observed, and an incisional biopsy of lacrimal glands was performed, which showed fibrosis and a lymphoplasmacytic infiltrate with IgG4 producing cells.
Discussion: Orbital involvement in IgG4-related disease is frequent. Bilateral dacryoadenitis is the most common manifestation. Histopathology is essential for the diagnosis and to exclude malignancy.

Enfermedad orbitaria relacionada con Ig-G4

Palabras clave:
Enfermedad relacionada con IgG4
Dacrioadenitis
Inflamación orbitaria inespecífica
Órbita

RESUMEN

Caso clínico: Presentamos el caso de una mujer de 64 años con tumefacción palpebral, dacrioadenitis bilateral y exoftalmos, e historia de rinitis crónica y asma bronquial. Se evidenció aumento de IgG4 sérica y se realizó biopsia incisional de glándulas lagrimales que demostró fibrosis e infiltrado linfoplasmocitario con células productoras de IgG4.
Discusión: El compromiso orbitario en enfermedad relacionada con IgG4 es frecuente. La dacrioadenitis bilateral es la manifestación más común. La histopatología es esencial para el diagnóstico de la enfermedad y excluir malignidad.

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Introduction

IgG4-related disease (ER-IgG4) is characterized by diffuse inflammatory or tumor lesions that exhibit a dense lymphoplasmacytic infiltrate and IgG4-producing plasma cells, obliterative phlebitis and evolution toward fibrosis.[1,2] It can appear heterogeneously with synchronic or metachronic systemic compromise, simulating neoplastic, inflammatory or selfimmune diseases.[2] Orbital disease related to IgG4 (EOR-IgG4) is frequent, with dacryoadenitis being the main expression.[2] One case of EOR-IgG4 is presented, describing clinic, serologic and histological findings together with a review of the literature.

Clinic case report

Female, 64, who visited due to xerophthalmia without xerostomy, painful palpebral tumefaction and bilateral dacryoadenitis (Fig. 1A and B), left exophthalmos and limitation of abduction and inferior gaze with 6 months evolution. The patient referred chronic rhinitis and recently diagnosed asthma. Ocular fundus was normal. Blood tests showed slight normocytic normochromic anemia, normal leukocytes (5600/mm^3) with slight eosinophilia (10%), accelerated erithrosedimentation (97 mm/h), elevated C-reactive protein (3.19 mg/dl) and transaminases, dyhydrogenase lactate, amilase, lipase, normal kidney function and thyroid hormones. Antinuclear antibodies, anti-Ro/SS-A, anti-La/SS-B, anti-DNA, ANCA, anti-Trab, antiperoxidase, and rheumatoid factor were normal. Viral serologies for hepatitis B, C and HIV were negative. The patient exhibited polyclonal hypergammaglobulinemia (IgG total 1612 mg/dl), with increased IgE in serum (730 mg/dl) and IgG4 (144 mg/dl), and normal complementemia. Orbital magnetic resonance evidenced increased lacrimal glands, predominantly on the left side. Biopsy of minor salivary gland was taken, which revealed slight sialadenitis, and incisional biopsy of left lacrimal gland which showed lymphoplasmacytic infiltrate (Fig. 1C) and extensive collagen fibrosis (Fig. 1D). Immunohistochemistry was positive for plasmatic cells for CD138 (Fig. 1E), for IgG (Fig. 1F) and immunoperoxidase IgG4, evidencing >100 cells of IgG4 + per high zoom field (40× lens and field greater than 20 mm) con with a IgG4/IgG ratio above 40%.

Chest, abdomen and pelvis tomographies did not reveal compromise of other organs. On the basis of the clinic findings mentioned above, eosinophilia, increased IgE and IgG4 in serum and histological changes of the lacrimal gland, EOR-IgG4 was diagnosed (definitive diagnostic as per Umehara et al. criteria).[3] Treatment was initiated with prednisone 40 mg/day. The patient exhibited partial improvement but symptoms were exacerbated when diminishing the glycocorticoid dose. Mycophenolate mofetil 2 g/day were added with significant reduction in the gland size verified by resonance and normalization of analysis parameters.

Discussion

Orbital compromise in ER-IgG4 has been described in 29% of patients with systemic disease.[1,2] It affects males and females similarly, with a mean debut age of 55.[1] Studies focused on EOR-IgG4 reveals that the most frequent involvement is bilateral dacryoadenitis, which can be observed in 50% of cases.[2] The most frequent clinic presentation is painless palpebral tumefaction, followed by exophthalmos without visual alterations. Association with anopsia or hemianopsia due to optic nerve compromise is infrequent.[2,4,5] Other expressions described in the literature include restrictions of ocular movement due to pain, ptosis and infrequently scleritis, corneal ulceration, epiphora and uveitis.[2] The present patient debuted with progressive tumefaction of the left eyelid, secondary to lacrimal gland infiltration and evolved with pain, exophthalmos, ocular movement restriction and palpebral ptosis.

It has been described that bilateral EOR-IgG4 is significantly associated to extra-ophthalmic compromise of the disease.[6,7] For this reason it is suggested to carry out systemic imaging studies.[6] The only systemic expressions exhibited by the patient were allergic rhinitis and bronchial asthma, present in up to 40% of patients with ER-IgG4.[1,2] She also evidenced eosinophilia, high IgE and IgG4 levels in serum and polyclonal hypergammaglobulinemia. These analytical data match those reported in the SMART records.[5] It is worthy of note that up to 30% of patients could exhibit normal levels of serum IgG4 which in some cases could be due to the prozone phenomenon.[1,2] For this reason, tomography and nuclear magnetic resonance of the orbits are useful to demonstrate dacryoadenitis, compromise of the extraocular muscles, subcutaneous cell tissue, eyelids and nasolacrimal duct.[4,7] EOR-IgG4 lesions are not generally destructive.[1] There are multiple differential diagnostics, including B-cell ocular lymphoma, Graves ophthalmopathy, Sjögren syndrome, sarcoidosis, granulomatosis with polyangeitis (ex-Wegener), orbital pseudotumor and malign tumors, among others.[4–7] For this reason histopathological analysis is crucial.[1,2] Findings in dacryoadenitis due to ER-IgG4 are different from the lesions evidenced in other organs.[7,8] Fibrosis is frequent and usually exhibits a collagen pattern, in contrast with the typical storiform pattern exhibited in the majority of the other organs. Obliterating phlebitis is infrequent in lacrimal compromise (0–10%).[7] The threshold of IgG4 + plasmatic cells in lacrimal gland biopsy should be >100 cells per high zoom field as definitive criterion.[7–10] However, in evolved lesions exhibiting abundant fibrosis and scarce cellularity, the threshold can be highly variable.[10] In these cases, a number of >50 cells of IgG4 + per high zoom field and an IgG4/IgG ratio> 40% suggests EOR-IgG4 in the appropriate clinical context.[8–10]

Induction treatment consists in 0.6 mg/kg/day prednisone during 4 weeks, subsequently diminishing at 3 and 6 months to reach the maintenance dose of 5 mg/day.[1,10] Azathioprine, methotrexate or micofenolate can be associated in cases

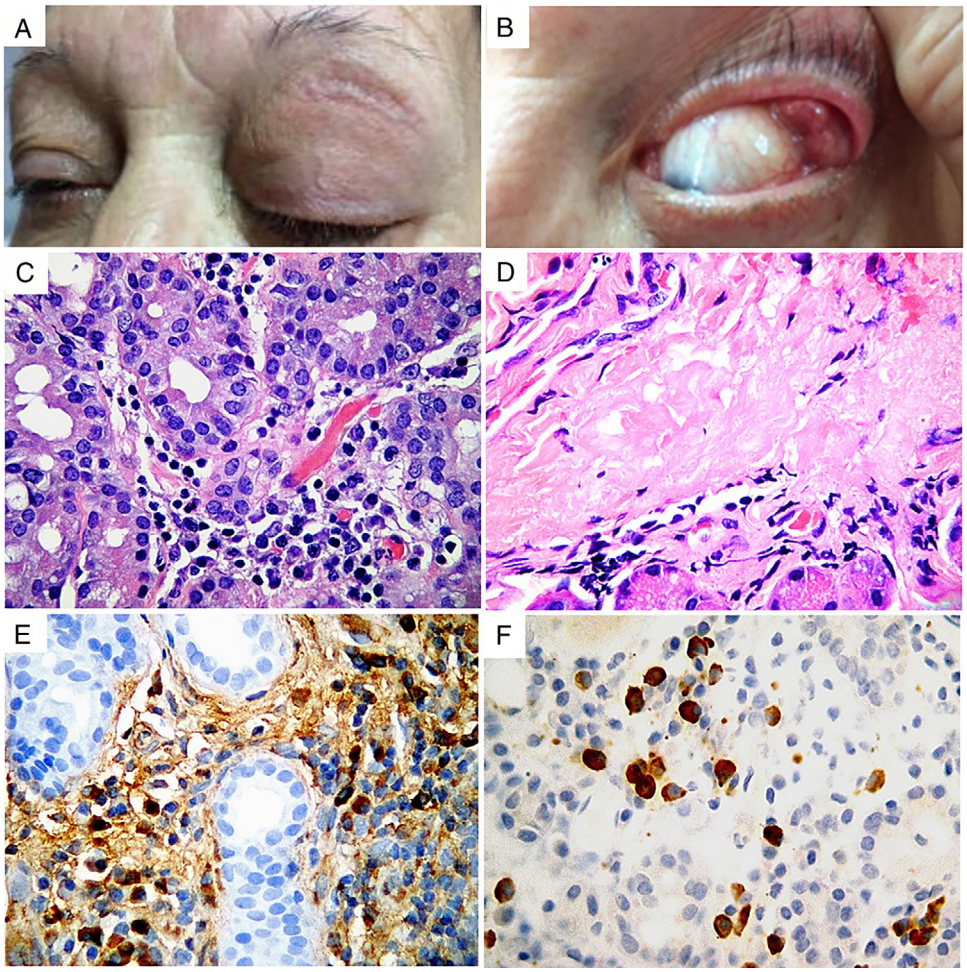

Fig. 1 – (A) Left palpebral tumefaction. (B) Left dacryoadenitis. (C) Lacrimal gland tissue with lymphoplasmocitary infiltrate. (D) Non-storiform fibrosis. (E) Positive immunohistochemistry for IgG. (F) Positive immunohistochemistry for IgG4.

requiring high glycocorticoid dosis for controlling the disease. Rituximab is useful in Sofia and resistant cases.[10]

EOR-IgG4 must be taken into account in the differential diagnostic of dacryoadenitis and tumor orbital lesions.[4–6] Biopsy is crucial to support clinic and image-based diagnostic as well as to exclude malign diseases.[8–10]

Conflict of interests

No conflict of interests was declared by the authors.

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