Short communication

Necrobiotic xanthogranuloma. Differential diagnosis, treatment and systemic involvement. Case report


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ARTICLE INFO

Article history:
Received 24 January 2011
Accepted 7 November 2012
Available online 6 August 2014

Keywords:
Xanthogranuloma
Necrobiotic xanthogranuloma
Xanthogranulomatosis
Corticosteroids
Monoclonal gammapathy

ABSTRACT

Case report: A 48-year-old male was referred to our hospital for further evaluation of eyelid edema with bilateral yellowish ulcerated nodules. Suspecting a xanthogranulomatosis, imaging tests and biopsy were performed with diagnosis of necrobiotic xanthogranuloma. IgG monoclonal gammapathy was diagnosed in a systemic study. Systemic corticosteroids and cyclosporine were initiated unsuccessfully; therefore, intra-lesional injections of triamcinolone were started, which controlled the orbital disease.

Discussion: Necrobiotic xanthogranuloma is a rare condition that usually affects the eyelids and anterior orbit. Its diagnosis is important as it is associated with malignant lymphoproliferative processes. Intra-lesional corticosteroids were effective in our patient.

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Xantogranuloma necrobiótico. Diagnóstico diferencial, tratamiento e implicaciones sistémicas. A propósito de un caso

RESUMEN

Caso clínico: Varón de 48 años remitido por edema palpebral con nódulos ulcerados amarillentos en ambos párpados superiores. Las técnicas de imagen demostraron infiltración en ambas órbitas anteriores que fueron biopsiadas con el resultado de xantogranuloma necrobiótico. En el estudio sistémico se halló una gammapatía monoclonal IgG no conocida. Se inició tratamiento con corticoides y ciclosporina orales sin éxito, por lo que se pautaron inyecciones intralesionales de triamcinolona que controlaron la enfermedad orbitaria.

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Introduction

There are 4 types of orbital xanthogranulomae: necrobiotic xanthogranuloma (NBX), adult onset xanthogranuloma (AOX), asthma-associated adult periocular xanthogranuloma (AAPOX) and the Erdheim–Chester disease (ECD).

AOX affects the eyelids and the anterior orbit without systemic involvement.\textsuperscript{1,2} AAPOX exhibits periocular and anterior orbit lesions, typically associating asthma, benign lymphadenopathy and IgG polyclonal paraproteinemia IgG.\textsuperscript{2}

ECD is the most severe form, which is lethal between 3 months and 15 years despite different therapies and is characterized by medium and posterior orbital xanthogranulomatous fibrosclerosis with proptosis and progressive visual acuity loss,\textsuperscript{3,4} together with fibrosclerosis of long bone metaphysis and of deep organs.\textsuperscript{3,4}

NBX is characterized by bilateral palpebral, orbital and periocular lesions, including the conjunctiva, which can infiltrate other bodily areas and deep organs. Said lesions tend to greater ulceration and fibrosis vis-à-vis the previous subtypes.\textsuperscript{3,4} Systemic involvement is frequently associated to monoclonal gammopathy and malignant lymph proliferative processes.

A necrobiotic xanthogranuloma case is presented with the systemic involvement and good response to intral esional corticoid treatment.

Clinical case

A male, 48, referred to our hospital due to bilateral palpebral tumors of unknown origin with recurring inflammation episodes (Fig. 1). The patient history included smoking habit (20 cigarettes per day) with a diagnosis of idiopathic thrombocytopenic purpura.

Upon exploration the patient exhibited bilateral yellowish injuries in upper eyelids, aponeurotic ptosis and increased intraocular pressure (IOP) (27/26 mmHg) in both eyes, in combined treatment with cu simolol and dorzolamide (Fig. 1); in addition, 2 orange infiltration-like lesions were observed in the left elbow and the right pretilibial region.

Orbital MR was carried out due to suspected xanthogranulomatosis (Fig. 2), observing occupation of the anterior half of both orbits by multiple soft tissue lesions.

Palpebral biopsy revealed the presence of Touton-type multinucleated cells together with lymphoplasmocitary infiltrates rich in interstitial cells and collagen necrobiosis; biopsy suggested NBX and matched the result of pretilibial and elbow biopsies (Fig. 3).

Systemic study revealed IgG monoclonal gammopathy (1960 mg/dl) and elevation of β2-microglobulin (3.4 mg/dl), together with thrombopenia (169,000 platelets/mm\textsuperscript{3}), leukopenia (2700 leukocytes/mm\textsuperscript{3}) with neutropenia (800 cells/mm\textsuperscript{3}) and VSG 100 mm/h. In addition, the patient presented non-nephrotic proteinuria. Bone marrow biopsy was negative for myeloma and skin biopsy was negative for amyloidosis. Accordingly, monoclonal gammopathy of uncertain significance (MGUS) was diagnosed.

Fig. 1 – Xanthomatous tumors in both upper eyelids, with adjacent soft tissue inflammation and secondary mechanical ptosis. Top image, first visit; bottom image, one month after the first visit.

Fig. 2 – Bilateral tumors with soft tissue consistency involved in the anterior portion of the orbit, without surrounding fatty and muscular inflammation. (a) Axial T2; (b) sagittal T1 image; (c) coronal STIR; (d) coronal image with gadolinium.
The patient of this case who exhibited palpebral and anterior orbit involvement leads to consider NBX, AOX and AAOX, discarding ECD which usually affects the posterior half of the orbit.

The biopsy confirmed the diagnosis with the presence of non-Langerhans histiocytes and Touton-type cells; in ECD proliferative fibroblasts with areas of fibrosis would appear together with dispersed lymphocytes and histiocytes; in AXG

The orbital lesions were treated without initial response with high doses of methylprednisolone (1 g/kg/day) and subsequently with cyclosporine 150 mg/day for one year, suspended due to nephrotoxicity, after which 2 monthly intralesional triamcinolone injections were administered (Fig. 4). After 6 injections, IOP was controlled without medication and the number and size of the lesions had diminished (Fig. 5) without local (cataracts, ocular perforation, etc.) or systemic complications (cushingoid reactions, and adrenal suppression). Two years after treatment the lesions remained stable (Fig. 6) and the patient is being followed up by hematology due to MGUS.

Discussion

Differential diagnosis is important in lesions similar to large xanthelasmas; depth, orbit involvement and adhesion to keep levels are distinctive signs of xanthogranuloma. Classification in the 4 subtypes is based on clinic and biopsy.

Fig. 3 – Histopathological image with hematoxylin–eosin staining (400 increases, HE 400×). Giant multinucleated cells over background with geographic areas of necrosis, mononucleated cells and histiocytes.

Fig. 4 – After treatment with systemic corticosteroids and cyclosporine, no lesion size reduction was appreciated at the macroscopic level.

Fig. 5 – After 6 corticoid injections a significant reduction of palpebral lesions was observed together with mechanical ptosis resolution.

Fig. 6 – The patient remains stable up to 2 years of treatment with intralesional corticoid injection, with good esthetic-functional results. (a) Photograph; (b) axial T1 with contrast; (c) axial T2; (d) coronal T1; (e) coronal STIR.
and AAPOX, mostly lymphocytes aggregates and germinal centers; and in NBX, geographic areas of necrosis surrounded by epithelioid histiocytes palisades as in this case.\(^2\)

For NBX, concomitant lymphoproliferative disorder must be discarded as in the present patient who exhibited IgG monoclonal gammopathy (1,960 mg/dl). In the presence of a monoclonal component exceeding 1,500 mg/dl, malign hemopathy must be discarded with spinal biopsy, bone radiology light chains in urine and in patients with cutaneous injuries as in this case, amyloidosis with skin biopsy. The present patient did not exhibit malignity symptoms or signs and therefore the diagnosis was MGUS, in which case it is advised to carry out 6 monthly and subsequently the annual checkups without requiring baseline treatment.

The low prevalence of this type of lesions hinders the assessment of different treatments, most of which are not very effective, particularly for ECD, with multiagent chemotherapy treatments being most efficient.\(^4\) In what concerns cyclosporine, it has been observed that the lymphocyte-T population is more numerous\(^2\) and therefore should be more efficient. In the present case, cyclosporine was not efficient and caused nephrotoxicity without slowing the disease progression. In contrast, intralesional corticoid injections, an option described in the literature with contradictory results,\(^3\) turned out to be effective. Corticoids could slow down the inflammatory cascade which appears to be involved in these tumors and for this reason might reduce lesion size.

In what concerns IOP reduction, attendant to diminished lesion size, the authors suspect that it could be due to the reduction of hypothetical ocular compression caused by the orbit xanthogranulomae. However, it is not possible to confirm this hypothesis as it could simply be a casual finding.

Finally, it is important to diagnose the different xanthogranulomatous entities due to their possible systemic involvement which, in NBX, could involve early diagnosis of a malignant lymphoproliferative disorder. As regards treatment, the use of intralesional triamcinolone was efficient to control palpebral and orbital lesions. Even so, subsequent studies are necessary to verify this observation.

**Conflict of interests**

No conflict of interests has been declared by the authors.

**References**