Intralesional corticosteroid treatment of periocular xanthogranuloma associated with adult-onset asthma

Injection intralésionnelle de corticoïdes pour le traitement d'une xanthogranulomatose périoculaire avec asthme de l'adulte

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Abstract

Introduction: Adult-onset asthma and periocular xanthogranuloma (AAPOX) is a rare non-Langerhans cell histiocytic disorder.

Aim: To describe the periocular clinical findings in a patient diagnosed with AAPOX, treated successfully by intralesional corticosteroids.

Case Report: A 40-year-old woman presented with bilateral eyelid swelling and adult-onset asthma. Initial examination revealed bilateral yellow-orange, elevated, indurated, and nonulcerated masses at the upper eyelids. The laboratory data showed high level of IgG. Periocular biopsy samples showed xanthoma cells positive for CD68 and Touton giant cells. The patient received 2 intralesional 40 mg of triamcinolone acetonide with a local control. No complications were noted.

Commentaries: AAPOX is characterized by a histiocytic proliferation associated to an adult-onset asthma, systemic lymphadenopathy, salivary gland enlargement and elevated serum levels of IgG. Treatment options vary with no current consensus. Intralesional corticosteroids have been rarely reported in controlling the signs and symptoms of adult-onset xanthogranulomatous disease. Surgery was successful but demonstrated recurrence. Methotrexate has been proposed to treat refractory cases or as a potential corticosteroid-sparing therapy. In this case, intralesional corticosteroid was an effective and safe treatment for eyelid adult xanthogranuloma.

Keywords: Adult-onset Asthma; Periocular xanthogranuloma; Orbit; Corticosteroid

Résumé

Introduction : L'asthme de l'adulte et xanthogranulome périoculaire est une entité exceptionnelle appartenant aux histiocytoses non-Langerhansiennes.

Objectif: Décrire les manifestations palpébrales et périoculaires chez une patiente présentant un asthme de l'adulte avec xanthogranulome périoculaire traitée par injections intralésionnelles de corticoïdes.

Observation: Une patiente âgée de 40 ans nous a été adressée pour des masses palpébrales supérieures avec un asthme. L'examen ophtalmologique avait montré des plaques indurées jaunâtres non ulcérées au niveau des deux paupières supérieures. L'electrophorèse des protéines avait noté une élévation polygonale des Ig G. La biopsie des lésions palpébrales avait montré des histiocytes spumeux positifs au CD68 et des cellules géantes de Touton. La patiente avait reçu 2 injections intralésionnelles de 40mg d'acétone triamcinolone avec une régression des lésions périoculaires. Aucune complication n'a été notée, avec un recul de 24 mois.

Commentaires: L'asthme de l'adulte et xanthogranulome périoculaire est une entité exceptionnelle appartenant aux histiocytoses non-Langerhansiennes, associant un asthme de l'adulte et une dysfonction immunologique (lymphadenopathies et élévation des IgG). Il n'existe pas de consensus thérapeutique. L'utilisation des injections intralésionnelles de corticoïdes a été rarement rapporté pour les traitement des xanthogranulomes orbitaires de l'adulte. La chirurgie es associée à un haut risque de récidive. Le methotrexate peut être proposé dans les cas réfractaires ou comme agent d'épargne cortisonique. Dans notre cas, les injections intralésionnelles de corticoïdes ont permis de faire régresser les lésions.

Mots-clé: Asthme de l'adulte; Xanthogranulome périoculaire; Orbite; Corticoïdes

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INTRODUCTION

Adult-onset asthma and periocular xanthogranuloma (AAPOX) is a rare disorder that belongs to the group of adult orbital granulomatous disease, the latter comprises a heterogenous group of non-Langerhans cell histiocytosis (1-3). Only scarce case reports and series are reported in literature. Due to its rarity, there is no consensus on the treatment of AAPOX (4). Treatment options include surgery, local and systemic corticosteroids, immunosuppressive drugs and more recently rituximab. We herein present a case of eyelid involvement in a patient with AAPOX successfully treated with intralesional corticosteroids.

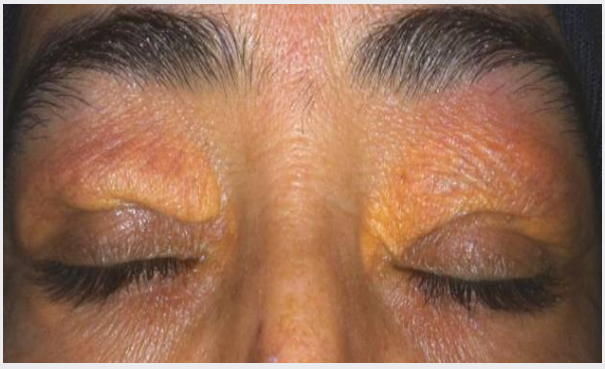


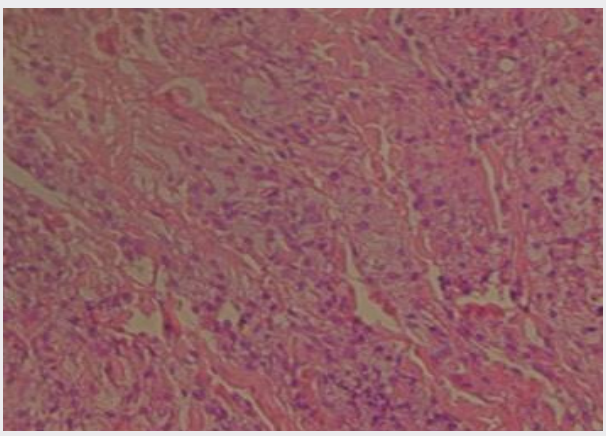
Figure 1. Bilateral yellow-orange, indurated and non-ulcerated lesions at the upper eyelids

CASE PRESENTATION

A 40-year-old woman was referred to our center for bilateral xanthelasma. She presented with bilateral swollen eyelids that had gradually worsened over 5 years. She was diagnosed with asthma 5 years previously, treated by inhaled bronchodilator. Initial examination revealed bilateral painless yellow-orange, indurated and nonulcerated lesions at the upper eyelids (Figure 1). Best corrected visual acuity was 20/20 in both eyes and slit lamp examination was unremarkable. Magnetic resonance imaging showed enhancing lesions the upper eyelids extending into anterior orbital fat. No extra ocular or optic nerve abnormalities were shown.

Physical examination revealed a mandibular lymphadenopathy. The laboratory tests showed elevated polyclonal gamma globulin with a high level of IgG. We performed incisional biopsy of the eyelid masse. Histopathological examination showed an infiltration of xanthoma cells (mononucleated foamy histiocytes) and Touton giant cells (Figure 2a). On immunohistochemical staining, foamy histiocytes were strongly positive for CD68 (Figure2b) and negative for CD1a and S100.

The patient received 2 intralesional injections of 40 mg triamcinolone acetonide at 2-month interval, using a 25-gauge needle, in the involved eyelid subcutaneous tissue, with a considerable reduction of the palpebral lesions at 24-month follow-up (Figure 3). No complications occurred especially no ocular hypertonia or skin discoloration.



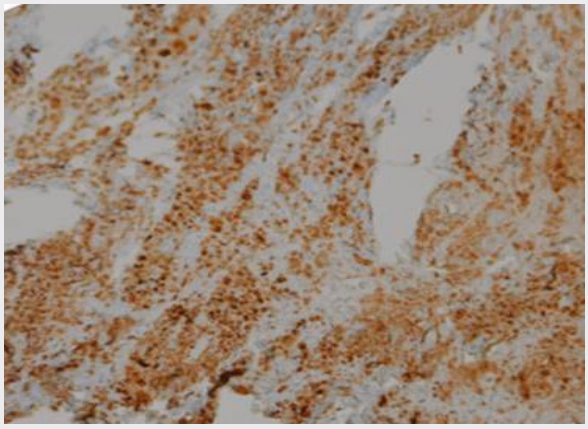


Figure 2. Eyelid biopsy samples in a patient with adult-onset asthma Fiand periocular xanthogranuloma (AAPOX)
Figure 2A. Infiltration of xanthoma cells (mono nucleated foamy histiocytes) and Touton giant cells (stain: Hematoxylin and eosin)
Figure 2B. Foamy histiocytes strongly positive for CD68 (stain: immunoperoxidase)

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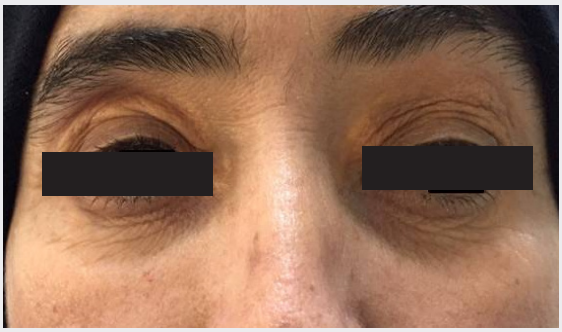

Figure 3. Clinical response to two intralesional triamcinolone acetonide injections in a patient with adult-onset asthma and periocular xanthogranuloma (AAPOX). Considerable regression of the palpebral lesions at 24-month follow-up

DISCUSSION

Adult orbital xanthogranulomatous disease is an uncommon subgroup of non-Langerhans cell histiocytic disorder (1-3). It is classified into 4 subtypes, based on systemic associations: adult-onset xanthogranuloma, necrobiotic xanthogranuloma, Erdheim-Chester disease, and adult-onset asthma and periocular xanthogranuloma (AAPOX). Histological features are common to all adult orbital xanthogranulomatous disease. Systemic manifestations allow to differentiate these disorders as management and prognosis are different. Only about 50 cases of AAPOX are reported in literature.

AAPOX was first described by Jacobiec et al. in 1993 (1). It includes a triad with periocular swelling, adult-onset asthma and immunological dysfunction. It affects adults in fourth and fifth decades. Male to female ratio in AAPOX is 2:1 (3). Periocular involvement in patients with AAPOX is typically bilateral, characterized by indurated yellowish xanthomatous eyelid lesions which extend to the anterior orbit. Unilateral involvement is possible at the onset of the disease (1). Extra-ocular muscles and lacrimal gland are rarely involved (2,3). Patients with extra ocular muscles infiltration present with diplopia and ocular motility limitation. In most cases of AAPOX, patients already have mild to severe asthma. Other systemic associations include lymphadenopathy, paraproteinemia, IgG4-related disease and hematologic malignancies especially lymphoma (2-8). A systemic evaluation is mandatory. Adult-onset asthma starts often at the same time as orbital manifestations or could be delayed after months to many years (1). It usually responds well to bronchodilators (7). Recently, an increasing interest to the association between AAPOX and IgG4-related disease may suggest that AAPOX could be a manifestation of IgG4-related disease. For some authors, this association could just suggest a non-specific reaction to xanthogranulomatous infiltration (9,10).

Differential diagnosis of orbital involvement in AAPOX include Langerhans cell histiocytosis, non-specific orbital inflammation, thyroid orbital disease, IgG4-related orbital disease, ocular adnexal lymphoma and xanthelasma (8-10). Biopsy with histological examination and immunohistochemical staining rules out easily these conditions.

Histological features in AAPOX are common to all adult orbital xanthogranulomatous disease and comprise a periocular tissues infiltration of mono nucleated foamy histiocytes with Touton giant cells. These histiocytes are strongly positive for CD68 and CD 163 on immunohistochemical staining and negative for CD1a and S100, the latter are specific to Langerhans cells (2). In AAPOX, large lymphoid follicles with reactive germinal centers are common (1,3).

Due to its rarity, there is no consensus on the treatment of periocular involvement in AAPOX (4,7). For most authors, systemic corticosteroids are considered as the mainstay of treatment. Prednisolone is administrated as first-line therapy at 1mg/Kg daily and tapered gradually. Surgery is associated to a great rate of recurrence and scarring lesions (1,3,4). Methotrexate have been used in refractory diseases or as a steroid-sparing agent (7). Recently, Maeng et al. reported a case with a spontaneous regression of xanthogranulomatous orbital lesions and considered observation in patients with adult orbital xanthogranuloma without systemic findings (4).

Intralesional corticosteroids have been rarely reported in the treatment of eyelid involvement in patients with AAPOX and other adult orbital xanthogranulomatous diseases such as necrobiotic xanthogranuloma (1,8,9). Literature showed mixed results. Elner et al. reported a case series of 6 patients successfully treated with intralesional injection of triamcinolone acetonide alone: four patients with necrobiotic xanthogranuloma

and two patients with adult-onset xanthogranuloma (8). Patients received 2 to 25 injections with a local control in all cases. None of previously reported local complications of steroids were found, especially eyelid necrosis, glaucoma or fat atrophy. Attention should be paid to the importance of a biopsy-proven diagnosis before treatment. This treatment option avoids side effects of systemic corticosteroids. However, Green et al reported a case of AAPOX, that didn't respond neither to systemic nor to five intralesional injections of corticosteroids (9). The patient showed improvement after surgical treatment (9). More recently, Rituximab has been used for treatment of AAPOX, added to steroids, showing a long-term remission (10,11). CD20 positivity may be associated with a better response to Rituximab. Singh et al recommended it as first-line therapy but its use may be limited by its high cost (11).

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