Case Report

Adult-Onset Asthma with Periocular Xanthogranuloma (AAPOX), a Variant of Periorbital Xanthogranulomatous Disease: An Uncommon Entity

Abstract

Adult orbital xanthogranulomatous disease (AOXGD) is a rare granulomatous disorder. Adult-onset asthma with periocular xanthogranuloma (AAPOX) which is a subtype of AOXGD is very rare and a realtively unknown entity among dermatologists. Very few cases had been reported in literature. Clinically recurrent periorbital swelling and its location may mimic other dermatological conditions like sarcoidosis, necrobiotic xanthogranuloma, dermatomyositis, and rarely amyloidosis. Herein we report a female with recurrent periorbital swelling with brownish yellow papulonodular lesions on periorbital area with adult-onset asthma. Histopathology and immunohistochemistry proved the diagnosis. She was started with systemic methylprednisolone and methotrexate and improved significantly after 4 months. We report this case because of its rarity and to create awareness among dermatologists about this uncommon entity.

Keywords: *Asthma, periorbital swelling, xanthogranulomatous disease*

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Introduction

Adult orbital xanthogranulomatous disease (AOXGD) is a rare granulomatous disorder, which has four subtypes: Adult-onset xanthogranuloma (AOX), adult-onset asthma with periocular xanthogranuloma, necrobiotic xanthogranuloma and Erdheim–Chester disease. We report a 48-year-old woman who presented with periorbital brownish yellow swelling with yellowish nonulcerative papules and nodules on her eyelids. On histopathological examination of a nodule, plenty of foamy histiocytes admixed with lymphocytes and few giant cells in the deep dermis which showed positive for specific histiocytic marker CD163. There was no apparent necrobiosis of collagen fibres. She had clinical symptoms of asthma and bilateral hilar lymphadenopathy, but no laboratory signs of paraproteinemia.Hence a diagnosis of adult-onset asthma with periocular xanthogranuloma (AAPOX) was made and patient was started with oral steroid and methotrexate following which there is reduction of swelling and symptoms. Dermatologists should be aware of these rare granulomatous conditions with ocular/orbital location.

Case Summary

A 48-year-old female presented with bilateral periorbital swelling which progressed over 1 year. The swelling temporarily regressed with courses of oral steroids, but always recurred when treatment was discontinued. Gradually she developed persistent brownish-yellow swelling more marked over lower eyelids. She also reported history of recent onset asthma for which she was being treated with oral and inhalation steroids by a pulmonary medicine specialist. Dermatological examination revealed persistent brownish-yellow swelling with multiple yellowish papules and nodules studded more over lower eyelids [Figures 1 and 2]. Other body parts revealed no abnormality or no skin lesion. Laboratory investigation showed normal blood count Urinalysis, liver and kidney biochemistry, serum lipid profile and thyroid hormones were normal. Antithyroid autoantibodies were negative. Rheumatoid factor, antinuclear antibodies and antineutrophil cytoplasmic antibodies were negative. Immunological tests for immunoglobulins and serum protein electrophoresis did not reveal any

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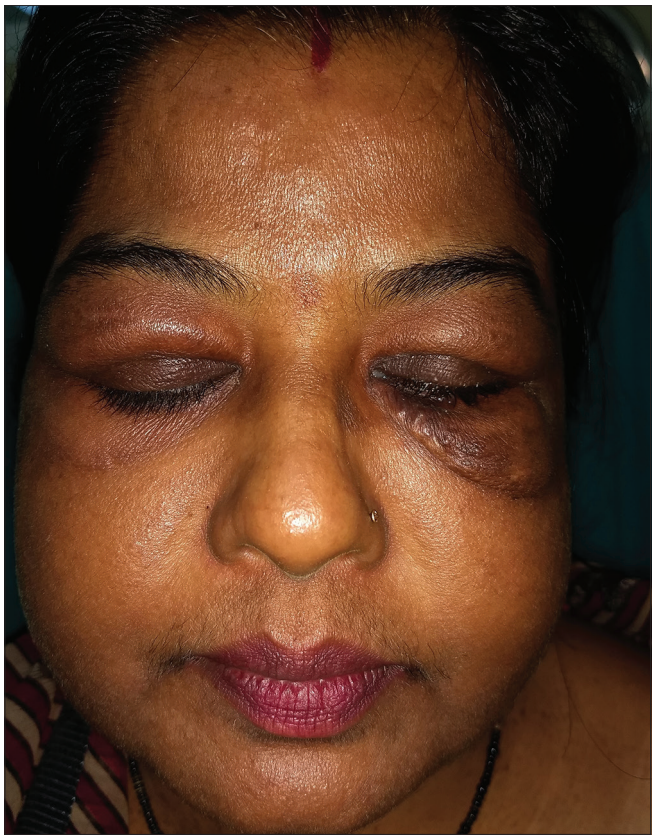

Figure 1: Brownish-yellow periorbital swelling

evidence of a monoclonal protein. Serum complement levels (C3 and C4) were normal. CT orbit showed periorbital swelling with enhancement of rectus muscles [Figure 3]. Computed tomography (CT) of the lungs showed small interstitial nodules and hilar lymph node enlargement [Figure 4]. Abdominal CT was unremarkable. Pulmonary function tests were normal. Clinical differential diagnosis included xanthelasma, amyloidosis, sarcoidosis, allergic granulomatosis, non-Langerhans histiocytosis (juvenile xanthogranuloma, papular xanthoma, xanthoma disseminatum), periocular xanthogranuloma with adult-onset asthma (PXAOA), necrobiotic xanthogranuloma (NXG), and Erdheim–Chester disease (ECd). Skin biopsy of the right lower eyelid showed large areas of histiocytic and lymphocytic infiltration throughout the reticular dermis along with few giant cells [Figure 5a-c]. There was no evidence of necrobiosis. Immunohistochemistry showed that the histiocytes were CD163 positive [Figure 6]. Considering that the patient suffered from an infiltrative non-malignant non-Langerhans histiocytic disorder that was limited to facial structures and was associated with asthma, a diagnosis of AAPOX was proposed. The patient was started on oral methyl prednisolone 16 mg daily and methotrexate 10 mg weekly and following 2 months of treatment there was improvement of swelling and other symptoms [Figure 7].

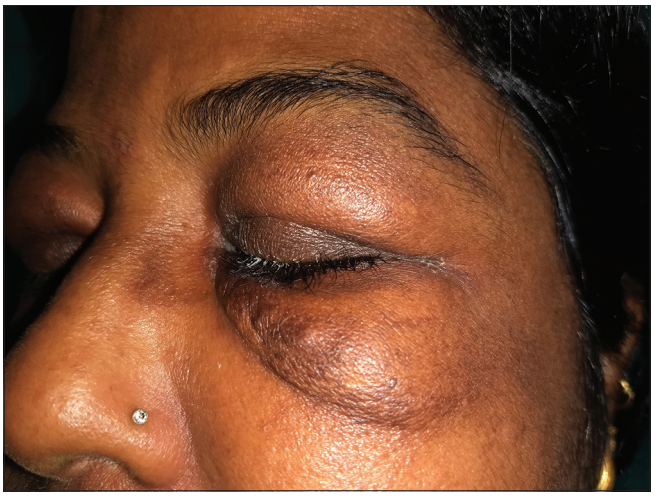

Figure 2: Yellowish papules and nodules studded over lower eyelids

Discussion

Orbital xanthogranulomatous disease in adults is a rare, non-Langerhans (type II) histiocytosis, categorized into four syndromes: Adult onset xanthogranuloma (AOX), AAPOX, ECD, and necrobiotic xanthogranuloma (NBX). AAPOX is a systemic disorder characterized by adult-onset asthma, lymphadenopathy, and periocular xanthogranulomatous disease. AAPOX was first described by Jakobiec *et al*. as patients with eyelid and orbital lesions.[1] APOX remains an uncommon entity and till now fewer than 50 cases reported in the English literature.[2-6] AAPOX is characterized clinically by periocular swelling with yellowish nodules and asthma. Patients generally have systemic lymphadenopathy, salivary gland enlargement, preseptal, and anterior orbital involvement, immune dysfunction, paraproteinemia and elevated IgG serum levels.[7,8] AAPOX may be associated with IgG4-related disease.[7] It should be differentiated from its closest mimickers both clinically and histopathologically [Table 1]. Necrobiotic xanthogranuloma typically presents with ulcerated nodules and histopathologically characterized by the presence of necrobiosis surrounded by palisaded epithelioid histiocytes, more numerous Touton giant cells and cholesterol clefts than AAPOX.[9] It is commonly associated with paraproteinemia and multiple myeloma.[2] Similarly, Erdheim–Chester disease involves progressive fibrosclerosis of the orbit resulting impairment of visual acuity and fibrotic involvement of internal organs.[10] Adult-onset orbital xanthogranuloma presents with isolated orbital involvement without accompanying immune dysfunction, asthma or paraproteinemia.[11] Patients with AAPOX lack the typical systemic associations of ECD, but have the onset of differing degrees of adult-onset asthma near the time that their periocular lesions appear.

Our patient presented with gradual periorbital swelling along with yellowish-brown papules and plaques on both eyelids. CT-scan of orbit demonstrated periorbital

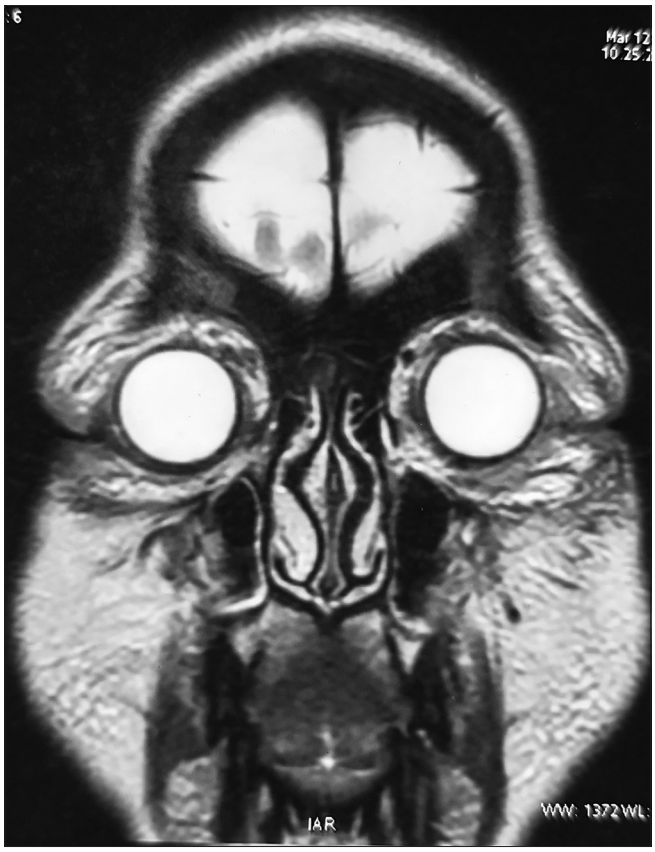

Figure 3: CT orbit showing asymmetric periorbital swelling with rectus muscle enhancement

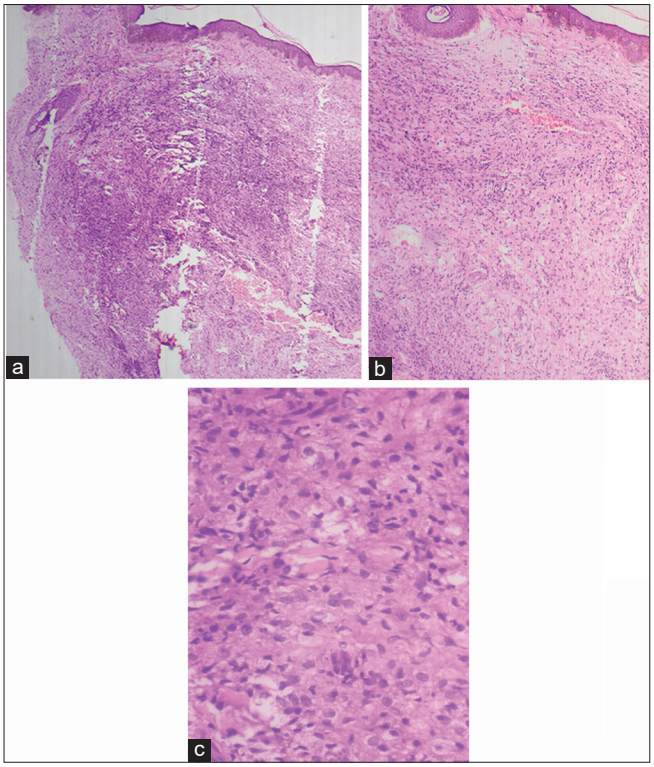

Figure 5: (a) Infiltrates in mid and lower dermis (H & E × 40). (b) Histiocytic and lymphocytic infiltration throughout the reticular dermis (H & E × 100). (c) Foamy histiocytes in dermis (H & E × 400)

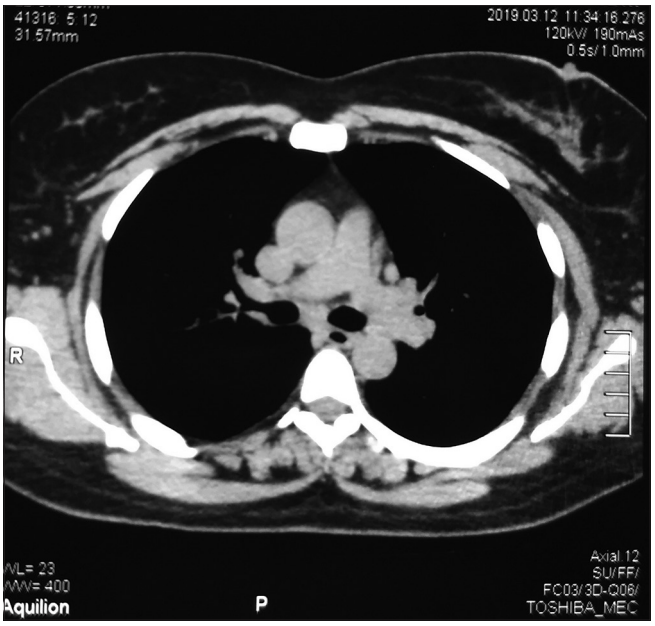

Figure 4: CECT thorax showing bilateral hilar lymphadenopathy

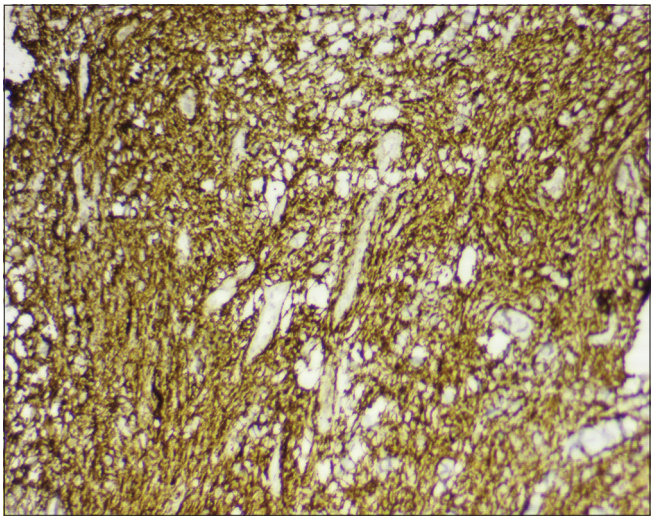

Figure 6: Immunohistochemistry showing CD163 positive (sensitive marker for histiocytes)

swelling without anterior chamber involvement. She had also developed asthma symptoms within one year of his periocular process and having bilateral hilar lymphadenopathy on CECT of chest. We could not find association of paraproteinemia. Histopathology showed lymphoid aggregates with scattered foamy histiocytes and giant cells in mid and lower dermis with immunohistochemistry showing immunopositivity for CD 163 which is a specific marker for histiocytes.[12] All the above findings favor the diagnosis of AAPOX.

Several treatment modalities have been used in adult orbital xanthogranulomatous disease with varying success and include surgery, intralesional corticosteroid injections, systemic corticosteroids, chemotherapeutic agents and/or radiation.[2,9,10] Our patient was started with

Table 1: Adult orbital xanthogranulomatous disease (AOXGD) subtypes

Adult orbital xanthogranulomatous disease (AOXGD)	Adult-onset xanthogranuloma	Adult-onset asthma with periocular xanthogranuloma	Erdheim-Chester Disease	Necrobiotic xanthogranuloma
Dermatological findings	Bilateral periorbital yellowish plaque	Bilateral periorbital yellowish plaque	Periorbital fibrosclerosis of orbit	Yellowish-red subcutaneous nodules with ulceration in periorbital area
Histopathological examination	Xanthomatous histiocytes, lymphocytes and tauton giant cells	Aggregates of lymphoid follicles with reactive germinal centre	Prominent fibrosis	Necrobiosis surrounded by palisading histiocytes, tauton giant cells and cholesterol cleft
Systemic association	None	Asthma, lymphadenopathy and paraproteinemia	Multisystem involvement like bones, heart, lung, retroperitoneum	Paraproteinemia, multiple myeloma, lymphoma, other haematological malignancy
Prognosis	Favourable	Favourable	Poor	Poor

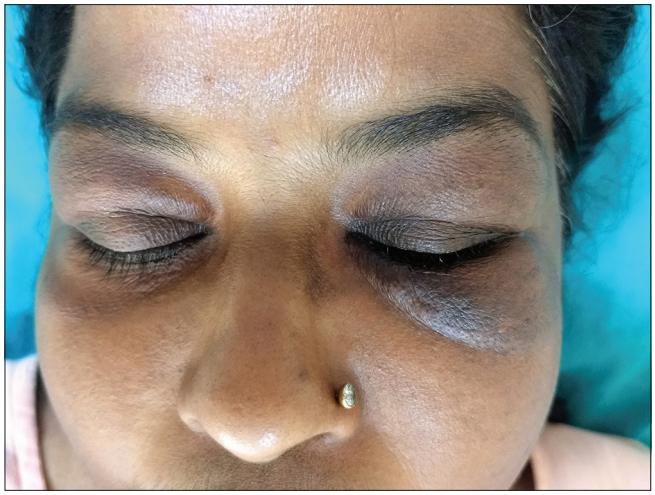

Figure 7: Improvement 2 month after treatment

methylprednisolone 16 mg along with 10 mg methotrexate weekly. There was significant improvement of symptoms and swelling at the end of 2 months and patient is now follow-up. Ocular symptoms should also be addressed, emphasizing the importance of co-operation between the dermatologist and the ophthalmologist.

In conclusion, AOXGD is a heterogeneous entity that should prompt a thorough evaluation for potential systemic associations. Clinico-pathological correlation is important for the diagnosis and sub-classification of this rare condition.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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