Case Report

Unveiling the Uncommon: A Case Study on Adult-Onset Asthma Coexisting with Periorbital Xanthogranuloma

PJO – Official Journal of Ophthalmological Society of Pakistan

Asna Tahir[1], Ansa Anam[2], Jawad Humayun[3]
[1-3]MTI Khyber Teaching Hospital, Peshawar

ABSTRACT

Eyelid and orbital lesions with asthma are the hallmarks of adult-onset asthma and periocular Xanthogranuloma (AAPOX). We present a rare case of an adult female diagnosed with AAPOX proven by biopsy with an elevated IgG4 serum level, showing a possible association between the two diseases. A 60-year-old female presented to the out-patient department of Khyber Teaching Hospital with the chief complaint of bilateral yellow, painless, upper eyelid swellings for the past 5 years. She had been treated for tuberculosis 15 years ago and was diagnosed with asthma 15 years ago, when she was 45 years old. She had history of chronic sinusitis. The patient had an elevated serum human IgG4 level of 874 mg/L. Anterior orbitotomy was performed. Based on histopathology, the diagnosis of adult-onset asthma and periocular Xanthogranuloma was confirmed. AAPOX, though rare, is a significant cause of orbital lesions.

Keywords: Adult-onset asthma and periorbital Xanthogranuloma, anterior orbitotomy, IgG4, Orbit, Eyelids.

How to Cite this Article: Tahir A, Anam A, Humayun J. Unveiling the Uncommon: A Case Study on Adult-Onset Asthma Coexisting with Periorbital Xanthogranuloma. 2025;41(4):447-450. **Doi:10.36351/pjo.v41i4.2063**

Correspondence: Jawad Humayun
MTI Khyber Teaching Hospital, Peshawar
Email: jawadhumayun462@yahoo.com

Received: March 22, 2025
Revised: September 5, 2025
Accepted: September 21, 2025

INTRODUCTION

In 1993, Jakobiec et al, in his study described a rare disease of the orbit, characterized by periorbital swelling with a specific pattern of granulomatous inflammation which was identified as adult-onset asthma with periorbital Xanthogranuloma (AAPOX) syndrome.[1] Xanthogranulomatous inflammatory disease is a non-Langerhans cell form of histiocytosis. Among adults Erdheim-Chester disease (ECD), adult-onset Xanthogranuloma (AOX), AAPOX, and necrobiotic Xanthogranuloma (NBX) make up Xanthogranulomatous diseases.[2] Eyelid and orbital lesions and asthma are the hallmark of AAPOX.[1] An addition to the list of diseases is IgG4-related disease (IgG4-RD), which has specific histological features and elevated serum IgG4 levels.[3] A characteristic feature shared by both AAPOX and IgG4-RD is the benign hyperplasia with plasma cell infiltration. Any organ in the body can be affected by IgG4-RD.[4]

We present a case of an adult female diagnosed with AAPOX proven by biopsy with an elevated IgG4 serum level, showing a possible association between the two diseases.

CASE REPORT

A 60-year-old female presented to the out-patient department of Khyber Teaching Hospital with the chief complaint of bilateral yellow, painless, upper eyelid swellings for the past 5 years(Figure-1).

A detailed history revealed that the swellings were gradually increasing in size which was associated with itching and drooping of eyelids bilaterally. There were no redness, watering, diplopia and photophobia. According to the past medical history of the patient she had been treated for tuberculosis 15 years back and was diagnosed with asthma 15 years ago when she was 45 years old. She had been using inhalers and had chronic sinusitis. Past Ocular and surgical histories were insignificant. Rest of the history was

unremarkable for any findings. On ocular examination, her visual acuity (VA) at the time of first visit was counting fingers (CF) in the right eye (OD) and 6/36 in the left eye (OS) whereas her best corrected visual acuity (BCVA) was CF in OD and 6/18 in OS. Extraocular movements (EOM) were restricted superiorly. On slit lamp examination, she had bilateral cataract. The pupils were regular in size, round and reactive to light in both eyes. Regurgitation test was negative. Intraocular pressure (IOP) was 18 in both eyes. Anterior segment and fundus examination were unremarkable. These periorbital swellings were previously diagnosed as idiopathic orbital inflammation without any biopsy or radiological tests in some other hospital. The patient used steroids to which the periorbital swellings responded well but then the inflammation recurred after she stopped using steroids.

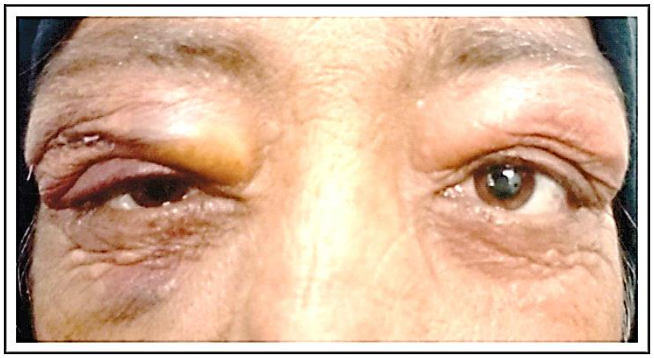

Figure-1: Showing bilateral, yellow, painless upper eyelid swellings.

Hematological investigations showed mildly elevated serum human IgG4 level of 874mg/L (Normal Range 39.20 mg/L – 864.00 mg/L). Alkaline phosphatase was high (147U/L). Triglycerides and cholesterol were also raised (208 mg/dL and 214 mg/dL respectively). Her complete blood count (CBC), renal function tests (RFTs), glycosylated hemoglobin (HbA1c), random blood sugar (RBS), Fasting blood sugar (FBS), thyroid function tests (TFTs) and platelet count were normal. Electrocardiogram (ECG) was unremarkable, and Echocardiography (Echo) showed 63% ejection fraction (EF). Chest X-Ray showed left lung fibrosis with pulmonary function tests showing severe restriction. Computerized tomography (CT) scan of the brain and orbit (axial and coronal view) were conducted which showed bulky heterogenous bilateral superior extra ocular muscles. The Superior Rectus and Levator Palpebrae Superioris showed exaggerated fats in the upper eyelids. Signs of sinusitis were also present.

The patient underwent anterior orbitotomy under local anesthesia and excision biopsy was conducted which revealed ducts with surrounding inflammation comprising of lymphocytes, histiocytes, plasma cells and fibrofatty tissue. Tuton type giant cells were also seen. No granuloma was seen and there was no evidence of malignancy. The diagnosis of AAPOX was confirmed (Figure-2).

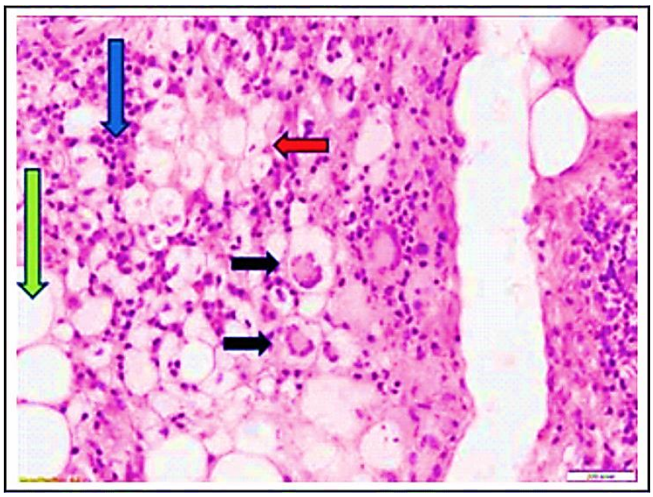

Figure-2: Showing Tuton type giant cells (Black Arrows) with nuclei in the periphery and central lightly stained cytoplasm, Foamy histiocytes (Red Arrow), Lymphocytes (Blue Arrow), Mature adipocytes (Green Arrow).

The patient was started on oral methotrexate 10 mg once weekly and folic acid 5mg once weekly after consultation with a rheumatologist. Follow up was done after every two weeks and the swelling resolved gradually overtime (Figure-3).

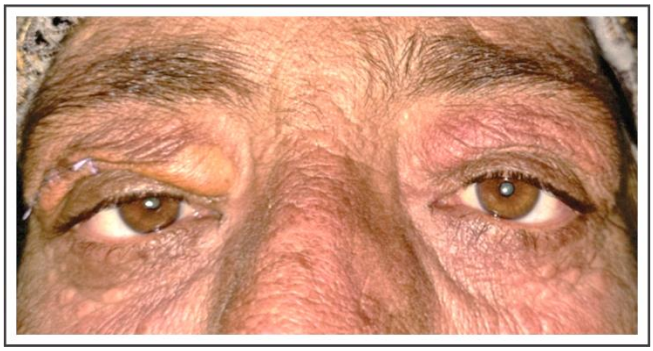

Figure-3: Resolution of bilateral eyelid swellings after surgery and medical therapy.

DISCUSSION

With only 21 reported cases, a rare entity, adult-onset asthma and periocular Xanthogranuloma, have the characteristic presentation of bilateral indurated orbital masses and xanthomatous eyelids which are elevated and yellow.[5] AAPOX affects individuals of 22 to 74 years of age with a higher affinity for males.[5] Although the mechanism of AAPOX is yet to be completely understood, it points towards a derangement in the systemic immunology.[6] According to the comprehensive clinical diagnostic criteria for IgG4-RD the serum levels of IgG4 should be 135 mg/dL (1350 mg/L).[7]Our patient had an elevated serum IgG4 level of 87.4 mg/dL (874 mg/L) which was not high enough to be diagnosed as probable IgG4-RD but due to an elevated value it might indicate an association between the two diseases.

Although, for AOX, surgical excision was the promising treatment option, however for other subtypes like ECD, NBX and AAPOX a combination of surgical and systemic treatments was beneficial, as described by Detiger et al.[8] There is a need for multidisciplinary approach based on the patient characteristics and the subtype of the disease.

Due to the existence of limited literature on the prevalence of adult-onset asthma and periocular Xanthogranuloma, particularly in the South Asian region, there is a dire need of focused research in this area specifically to have a better understanding about the clinical presentation and importance of the disease.[5]

CONCLUSION

AAPOX, although rare, is a significant cause of orbital lesions. The co-existence of AAPOX and a mildly elevated serum IgG4 level may also indicate some association between the two diseases. Therefore, there is a need for vigilant diagnosis and multidisciplinary management whenever a patient presents with AAPOX. However, to treat and understand these complex conditions further research is needed.

Funding: This study was not funded by any organization.

Patient's Consent: Researchers followed the guide lines set forth in the Declaration of Helsinki.

Conflict of Interest: Authors declared no conflict of interest.

REFERENCES

1. **Jakobiec FA, Mills MD, Hidayat AA, Dallow RL, Townsend DJ, Brinker EA, et al.** Periocular Xanthogranuloma associated with severe adult-onset asthma. Trans Am Ophthalmol Soc. 1993;**91:**99-125. Discussion 125-9. PMID: 8140711; PMCID: PMC1298462.
2. **Sivak-Callcott JA, Rootman J, Rasmussen SL, Nugent RA, White VA, Paridaens D, et al.** Adult Xanthogranulomatous disease of the orbit and ocular adnexa: new immunohistochemical findings and clinical review. Br J Ophthalmol. 2006;**90(5):**602-608. Doi:10.1136/bjo.2005.085894
3. **Masaki Y, Dong L, Kurose N, Kitagawa K, Morikawa Y, Yamamoto M, et al.** Proposal for a new clinical entity, IgG4-positive multiorgan lymphoproliferative syndrome: analysis of 64 cases of IgG4-related disorders. Ann Rheum Dis. 2009;**68(8):**1310-1315.Doi:10.1136/ard.2008.089144
4. **Burris CKH, Rodriguez ME, Raven ML, Burkat CN, Albert DM.** Adult-onset asthma and periocular Xanthogranuloma associated with systemic IgG4-related disease. Am J Ophthalmol Case Rep. 2016;**1:**34-37. Doi:10.1016/j.ajoc.2016.04.002
5. **Manzoor A, Taimur F, Saad M, Ahmad S, Tahir F, Khan S.** Frequency and unusual clinical manifestation of orbital Xanthogranuloma: an overview. J Rawalpindi Med Coll. 2024 Sep 27;**28(3)**. Doi: 10.37939/jrmc.v28i3.2516
6. **Davies MJ, Whitehead K, Quagliotto G, Wood D, Patheja RS, Sullivan TJ.** Adult Orbital and Adnexal Xanthogranulomatous Disease. Asia Pac J Ophthalmol (Phila). 2017;**6(5):**435-443. Doi: 10.22608/APO.2017246.
7. **Umehara H, Okazaki K, Masaki Y, Kawano M, Yamamoto M, Saeki T, et al.** Comprehensive diagnostic criteria for IgG4-related disease (IgG4-RD), 2011.Mod Rheumatol. 2012;**22(1):**21-30. Doi: 10.1007/s10165-011-0571-z
8. **Detiger SE, Hötte GJ, Verdijk RM, de Keizer ROB, van Hagen PM, van Laar JAM, et al.** Adult orbital Xanthogranuloma: long-term follow-up of treated cases. Eye (Lond). 2023;**37(12):**2475-2481. Doi:10.1038/s41433-022-02357-z

Authors Designation and Contribution

Asna Tahir; Resident: *Concepts, Design, Literature Search, Data Acquisition, Manuscript Preparation, Manuscript Editing, Manuscript Review.*

Ansa Anam; Resident: *Concepts, Design, Literature Search, Data Acquisition, Manuscript Preparation, Manuscript Editing, Manuscript Review.*

Jawad Humayum; ER: *Concepts, Design, Literature Search, Data Acquisition, Manuscript Preparation, Manuscript Editing, Manuscript Review.*