

4. Collamer AN, Battafarano DF. Psoriatic skin lesions induced by tumor necrosis factor antagonist therapy: clinical features and possible immunopathogenesis. *Semin Arthritis Rheum.* 2010;40(3):233-240.
5. Gerdes S, Franke J, Domm S, Mrowietz U. Ustekinumab in the treatment of palmoplantar pustulosis. *Br J Dermatol.* 2010;163(5):1116-1118.

A Case of Adult-Onset Asthma With Periocular Xanthogranulomas

We report a case of adult-onset asthma with periocular xanthogranuloma (AAPOX), a rare syndrome that falls into the general clinical category of periocular adult xanthogranulomatous diseases such as necrobiotic xanthogranuloma and Erdheim-Chester disease. Adult-onset asthma with periocular xanthogranuloma is a distinct entity within this group, which, to our knowledge, has not been previously described in the dermatology literature and may be an underrecognized entity.

Report of a Case. A 55-year-old African American man presented with a 35-year history of indurated periorbital nodules associated with mild periocular pruritus. One year after the onset of periorbital induration, he developed asthma, which was confirmed by the results of pulmonary function testing and was well controlled with inhalers. He denied a history of chronic rhinosinusitis.

Physical examination showed bilateral, nontender, indurated periocular nodules infiltrating both upper and lower eyelids, with normal extraocular movement (**Figure 1**). The findings of laboratory evaluation were notable for polyclonal hypergammaglobulinemia without paraproteinemia and a normal complete blood cell count and chemistry profile. Radiography of the chest revealed no abnormalities.

The patient underwent bilateral periocular excisions for diagnosis and therapeutic debulking. Histologic sections demonstrated prominent follicular lymphoid hyperplasia and a diffuse, sheetlike xanthogranulomatous infiltrate consisting of foamy histiocytes, lymphocytes, and multinucleated giant cells, many of them of Touton type (**Figure 2**). Cholesterol clefts were notably absent. There was no evidence of lymphedema.

Comment. The clinical and histologic findings in this case are consistent with the diagnosis of AAPOX. First described in 1993, the entity has primarily appeared in the ophthalmology and pathology literature.¹⁻³ Similar to other adult orbital xanthogranulomatous diseases, AAPOX presents histologically with Touton giant cells and lipid-laden histiocytes. However, it also characteristically shows large lymphoid aggregates with germinal centers, a finding that distinguishes it from necrobiotic xanthogranuloma and Erdheim-Chester disease.¹⁻⁴ Necrobiotic xanthogranuloma is clinically characterized by ulcerative plaques and nodules, is commonly associated with a monoclonal gammopathy, and may be complicated by hematologic disorders, including cancer. Erdheim-Chester disease is differentiated from AAPOX by increased fibrosclerosis and has a poor prognosis because of xanthogranulomatous infiltration and fibrosis involving internal organs.^{2,5} Conversely, AAPOX is considered a more benign entity than Erdheim-Chester disease and necrobiotic xanthogranuloma. Most reported cases have either no gammopathy or a polyclonal gammopathy without underlying malignancy. A monoclonal gammopathy has been reported in up to 35% of patients with AAPOX (5 of 14 cases) based on 1 case series and review; therefore, yearly monitoring with serum protein electrophoresis is suggested.^{1,3}

The pathogenesis of AAPOX is not understood. The presence of asthma or rhinosinusitis, gammopathy,

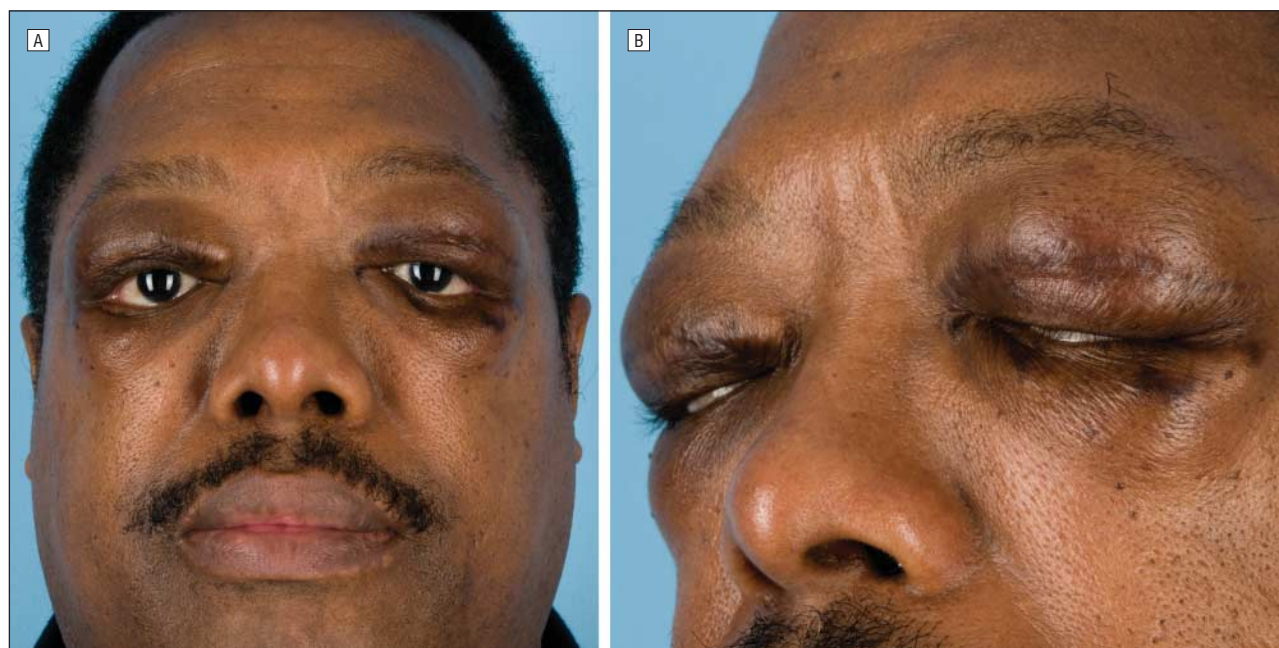


Figure 1. A, Frontal view of the indurated, hyperpigmented periocular nodules infiltrating the bilateral upper and lower eyelids. B, Lateral close-up view of the infiltrative nodular plaques.

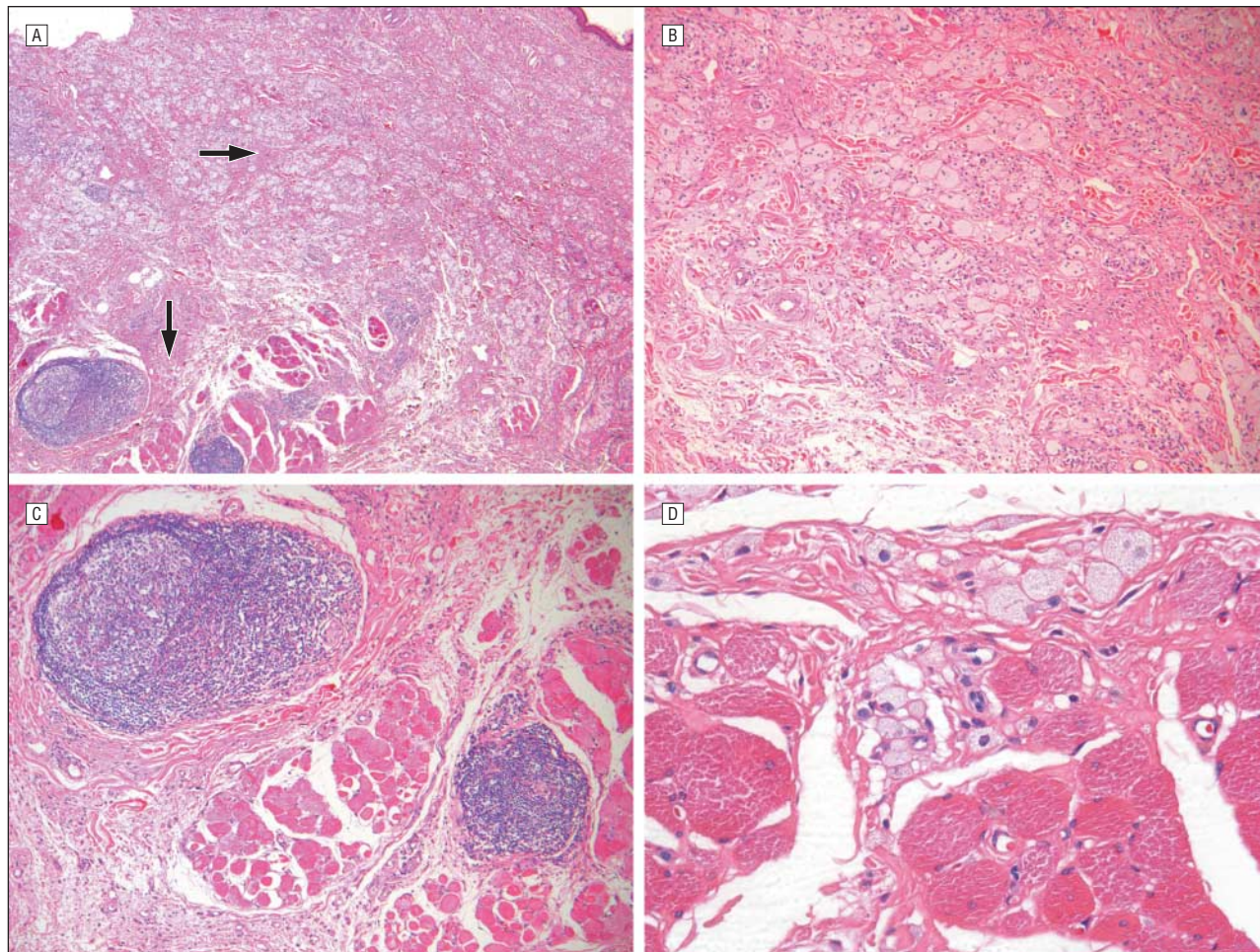


Figure 2. Hematoxylin-eosin-stained histologic sections. A, Low-power view showing diffuse infiltrating sheets of foamy histiocytes with Touton-type giant cells in the superficial and middle dermis (arrows) and prominent lymphoid follicles (original magnification $\times 4$). Higher-power view of areas in A denoted by arrows showing infiltrating foamy histiocytes in the dermis (B, original magnification $\times 10$) and lymphoid follicle formation with well-formed germinal centers in the deep dermis and involving orbicularis oculi muscle (C, original magnification $\times 10$). D, Infiltrating foamy macrophages extend into the subcutis and involve the orbicularis oculi muscle (original magnification $\times 40$).

and large lymphoid aggregates with germinal centers suggests an underlying B-cell disorder.³ Various immunomodulatory agents, including prednisone, cyclosporine, cyclophosphamide, and methotrexate, have shown some success in treating AAPOX.²⁻⁴ Surgery alone is not advocated because of a high rate of recurrence.² Our patient was started on methotrexate therapy and has noted softening of the indurated nodules after 3 months of treatment.

Given the potential for significant complications of periocular xanthogranulomatous diseases, differentiating these entities is important. Adult-onset asthma with periocular xanthogranuloma is a rare disorder with unique histologic features that should be included in the differential diagnosis when patients with periorbital infiltrated nodules are being evaluated.

Crystal U. Agi, BA
Michael D. Gober, MD, PhD
Katalin Ferenczi, MD
Patricia Takach, MD
Ralph C. Eagle, MD
Misha Rosenbach, MD

Author Affiliations: University of Pennsylvania School of Medicine (Ms Agi), Departments of Dermatology (Drs Gober, Ferenczi, and Rosenbach) and Allergy and Immunology (Dr Takach), Hospital of the University of Pennsylvania, Wills Eye Institute (Dr Eagle), and Department of Pathology, Thomas Jefferson University (Dr Eagle), Philadelphia, Pennsylvania.

Correspondence: Dr Rosenbach, Department of Dermatology, University of Pennsylvania, 2 Maloney Bldg, 3600 Spruce St, Philadelphia, PA 19104-4208 (misha.rosenbach@uphs.upenn.edu).

Financial Disclosure: None reported.

1. Jakobiec FA, Mills MD, Hidayat AA, et al. Periocular xanthogranulomas associated with severe adult-onset asthma. *Trans Am Ophthalmol Soc.* 1993; 91:99-129.
2. Guo J, Wang J. Adult orbital xanthogranulomatous disease: review of the literature. *Arch Pathol Lab Med.* 2009;133(12):1994-1997.
3. Sivak-Callcott JA, Rootman J, Rasmussen SL, 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.
4. Cavallazzi R, Hirani A, Vasu TS, et al. Clinical manifestations and treatment of adult-onset asthma and periocular xanthogranuloma. *Can Respir J.* 2009; 16(5):159-162.
5. Lau WW, Chan E, Chan CW. Orbital involvement in Erdheim-Chester disease. *Hong Kong Med J.* 2007;13(3):238-240.