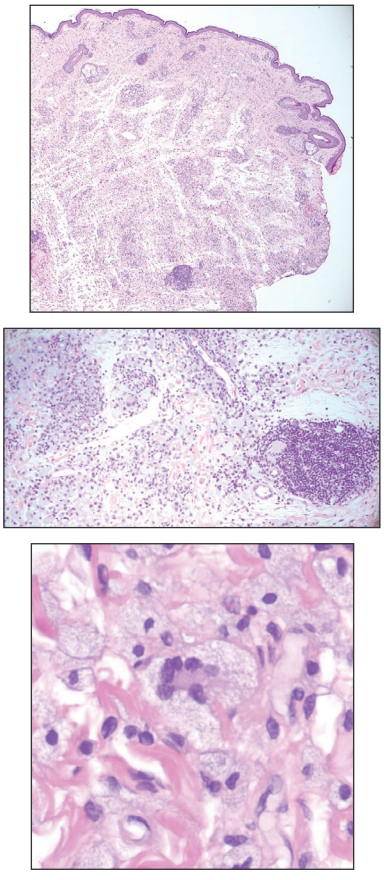
Thick Yellow Plaques on the Eyelids

Sarah Rigali, MD; Albert E. Zhou, MD, PhD; Ekaterina Korytnikova, MD; Medina Falcone, MD; Katalin Ferenczi, MD

Eligible for 1 MOC SA Credit From the ABD

This Dermatopathology Diagnosis in our print edition is eligible for 1 self-assessment credit for Maintenance of Certification from the American Board of Dermatology (ABD). After completing this activity, diplomates can visit the ABD website (http://www.abderm.org) to self-report the credits under the activity title "*Cutis* Dermatopathology Diagnosis." You may report the credit after each activity is completed or after accumulating multiple credits.



H&E, original magnifications ×10 (top), ×100 (middle), and ×400 (bottom).

A 54-year-old man presented to the dermatology department for evaluation of enlarging lesions on the eyelids of 18 months' duration causing tearing, dryness, and heaviness. The patient's medical history was positive for hyperlipidemia, chronic rhinosinusitis, and mild asthma diagnosed in adulthood. A review of systems was negative for bone pain, polyuria, polydipsia, dysuria, hematuria, decreased coordination, chest pain, palpitations, abdominal pain, easy bruising, and jaundice. Laboratory testing revealed elevated IgG4 levels and a slight increase in gamma globulins on serum protein electrophoresis, with no evidence of paraproteinemia. Liver and kidney function test results were within normal limits. Magnetic resonance imaging of the orbits revealed bilateral superolateral intraorbital masses within the extraconal fat that were displacing the superior and lateral rectus muscles. No intraconal masses were identified. Due to bilateral eyelid ptosis, the patient underwent debulking by oculoplastic surgery, and the tissue was submitted for histologic examination.

THE BEST **DIAGNOSIS IS:**

a. adult-onset asthma with periocular xanthogranuloma
b. juvenile xanthogranuloma
c. necrobiotic xanthogranuloma
d. reticulohistiocytoma
e. xanthelasma

PLEASE TURN TO PAGE 88 FOR THE DIAGNOSIS

Dr. Rigali is from the Rosalind Franklin University of Medicine and Science, Chicago Medical School, Illinois. Drs. Zhou, Korytnikova, Falcone, and Ferenczi are from the University of Connecticut, Farmington. Drs. Zhou, Korytnikova, and Ferenczi are from the Department of Dermatology, and Dr. Falcone is from the Department of Ophthalmology.

The authors have no financial disclosures to report.

Correspondence: Katalin Ferenczi, MD, Department of Dermatology, University of Connecticut, 21 South Rd, Farmington, CT 06032 (ferenczi@uchc.edu).

Cutis. 2026 March;117(3):83, 88-89. doi:10.12788/cutis.1354

THE **DIAGNOSIS:** Adult-Onset Asthma With Periocular Xanthogranuloma

In the context of pre-existing sinonasal disease and features consistent with adult-onset asthma, the constellation of clinical findings including linear periorbital yellow-orange plaques, imaging demonstrating extension of xanthogranulomatous lesions into the orbital fat, histopathologic features, and serologic abnormalities including elevated IgG4 levels supported a diagnosis of adult-onset asthma with periocular xanthogranuloma (AAPOX).

Adult-onset xanthogranuloma is a non–Langerhans cell histiocytosis (historically classified as type II) within the group of adult orbital xanthogranulomatous diseases resulting from infiltration and proliferation of histiocytes in the orbital and ocular adnexal structures and eyelids. Adult orbital xanthogranulomatous diseases are classified as 4 distinct conditions: adult-onset xanthogranuloma, AAPOX, Erdheim-Chester disease, and necrobiotic xanthogranuloma (NXG). Erdheim-Chester disease is the most severe among this group and often is fatal due to infiltration of the xanthogranulomas into multiple organ systems and tissues, including the long bones, heart, lungs, and retroperitoneum. Neurologic symptoms such as incoordination can occur. Adult-onset xanthogranuloma manifests as an isolated cutaneous lesion without systemic involvement. This entity often is self-limited and does not require aggressive treatment. Adult-onset asthma with periocular xanthogranuloma affects more males than females.[1] Clinically, it manifests as bilateral yellow-orange, thickened, indurated eyelid plaques that can extend to the extraocular muscles or lacrimal glands. As the name suggests, this entity is associated with adult-onset asthma or rhinosinusitis as well as lymphadenopathy and extension into the orbital fat.[1]

When patients present with periorbital lesions and optic symptoms such as visual disturbances, tearing, and/or a foreign body sensation in the eyes, a work-up should be performed to rule out infiltration of orbital adnexal structures and other organ systems, as AAPOX can be associated with IgG4-related disease. Histologically, adult xanthogranulomatous diseases are characterized by sheets of foamy histiocytes accompanied by variable numbers of lymphoid aggregates, plasma cells, and Touton giant cells. These infiltrating xanthoma cells appear as a garland or wreathlike nuclei surrounded by foamy cytoplasm. Oil-red O staining of frozen sections confirms the lipid content of the xanthoma cells.[2] Immunohistochemically, the foamy histiocytes are strongly positive for CD68, CD163, and factor XIIIa but usually are negative for S100, CD1a and Birbeck granules.[3] More distinctively, AAPOX is associated with prominent lymphoid aggregates containing reactive germinal centers.[1]

Given that AAPOX is a systemic multiorgan disease, local therapies such as surgical debulking or intralesional corticosteroids generally are insufficient to address the underlying pathology and therefore necessitate systemic, often multimodal, treatment within a multidisciplinary framework.[1,4] Systemic corticosteroids remain first-line therapy, with steroid-sparing agents (eg, methotrexate, azathioprine, cyclophosphamide) used in refractory cases or to reduce steroid dependence.[4,5] Rituximab has demonstrated efficacy in AAPOX, further highlighting the association between AAPOX and IgG4-related disease.[5] Inebilizumab, a B-cell–depleting monoclonal antibody targeting CD19 and approved for the treatment of IgG4-related disease, represents a theoretically promising therapeutic option; however, additional studies are needed to establish its efficacy and safety in AAPOX.[5]

Necrobiotic xanthogranuloma is another xanthogranulomatous disorder that manifests as yellow-orange papules or nodules that gradually form infiltrative plaques. Scarring and ulceration can occur in 40% to 50% of patients.[6] The most common site of involvement is the periorbital area, affecting 80% of cases, often resulting in ophthalmologic complications.[6] Necrobiotic xanthogranuloma lesions also can involve the trunk, arms, and legs. Extracutaneous sites include the lungs, myocardium, larynx, pharynx, skeletal muscles, kidneys, ovaries, and intestines. The prognosis of NXG is poor due to associated hematologic malignancies such as multiple myeloma and lymphoma. About 80% of patients have a serum monoclonal gammopathy.[6] Histologically, NXG shows features overlapping with other xanthogranulomatous disorders, such as foamy histiocytes, multinucleated giant cells, Touton giant cells, and nodular lymphocytic aggregates[6,7]; however, broad zones of necrobiosis are a distinct histologic finding in NXG that helps differentiate it from other xanthogranulomatous disorders (Figure 1).[6]

Xanthelasma manifests as yellow plaques on the medial upper and lower eyelids and lateral canthi resulting from accumulation of cholesterol-rich material in the skin, soft tissue, and sometimes the tendons. Fifty percent of patients have a primary or secondary lipid disorder

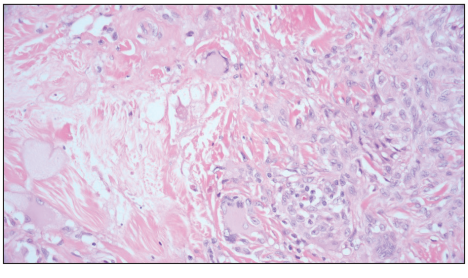


FIGURE 1. Necrobiotic xanthogranuloma. Multinucleated giant cells, histiocytes, lymphocytes, and altered collagen (necrobiosis) are present (H&E, original magnification ×400).

such as familial dyslipidemia, thyroid disease, diabetes mellitus, or primary biliary cholangitis.[8] Histologically, xanthelasmas demonstrate lipid-laden foamy histiocytes in the superficial dermis (Figure 2).[8] Despite some clinical overlap in our case, the depth of orbital involvement and supportive systemic and histopathologic findings (including Touton giant cells) supported the diagnosis of AAPOX rather than xanthelasma.

Juvenile xanthogranuloma manifests as solitary to multiple firm, yellow-orange papules or nodules on the face, neck, and upper torso. The lesions develop in early childhood, with 75% of lesions appearing in the first year of life, but rarely it may develop in adulthood.[9] The most common extracutaneous manifestation involves ocular structures, most frequently the iris, followed by the lungs. Cutaneous lesions usually are asymptomatic and involute over the span of a few years. Ocular lesions can result in blindness, and juvenile xanthogranuloma also has been associated with neurofibromatosis type 1 and juvenile chronic myelogenous leukemia.[9] The histopathology of juvenile xanthogranuloma often will show a dense histiocytic infiltrate in the dermis with blunting of the overlying rete ridges admixed with lymphocytes, plasma cells, and eosinophils. In the more mature phase, foam cells, foreign body giant cells, and Touton giant cells predominate. Touton giant cells have a garlandlike appearance (Figure 3).[9]

Reticulohistiocytoma (or solitary epithelioid histiocytoma) and multicentric reticulohistiocytosis are rare histiocytic proliferations. Multicentric reticulohistiocytosis refers to a systemic disease with arthropathy and multiple cutaneous histiocytic lesions located on acral sites and the face. Solitary reticulohistiocytoma manifests as papules or nodules found in many body locations, such as the trunk, arms, and legs. The lesions are uncommon on the face, which almost always is involved in multicentric reticulohistiocytosis. Solitary reticulohistiocytomas tend not to recur once excised and do not demonstrate systemic involvement. Histologically, the lesions demonstrate large eosinophilic epithelioid histiocytes with abundant glassy cytoplasm (Figure 4). Some of the epithelioid histiocytes are multinucleated, and immunophenotyping will show positivity for lysozyme, CD68, and CD163.[10]

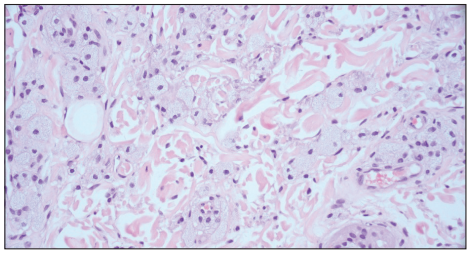


FIGURE 2. Xanthelasma. Lipid-laden foamy histiocytes are seen (H&E, original magnification ×400).

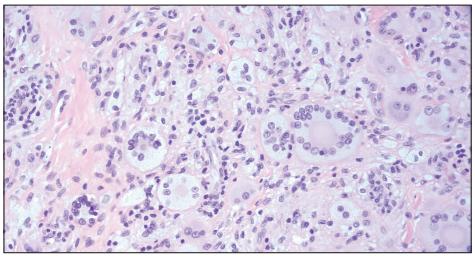


FIGURE 3. Juvenile xanthogranuloma. Touton giant cells, lymphocytes, and histiocytes are present (H&E, original magnification ×400).

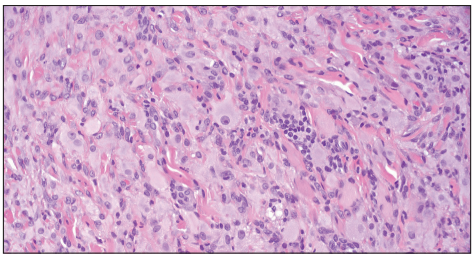


FIGURE 4. Reticulohistiocytoma. Large epithelioid histiocytes with glassy cytoplasm (H&E, original magnification ×400).

REFERENCES

1. Kerstetter J, Wang J. Adult orbital xanthogranulomatous disease: a review with emphasis on etiology, systemic associations, diagnostic tools, and treatment. *Dermatol Clin.* 2015;33:457-463. doi:10.1016/j.det.2015.03.010
2. MandićJJ, Bakula M, Šklebar LK, et al. Histiocytosis and adult-onset orbital xanthogranuloma in 2023: a review of the literature and mini case series. *Int Ophthalmol.* 2024;44:301. doi:10.1007/s10792-024-03181-y
3. Campochiaro C, Tomelleri A, Cavalli G, et al. Erdheim-Chester disease. *Eur J Intern Med*. 2015;26:223-229. doi: 10.1016/j.ejim.2015.03.004
4. Detiger SE, Hötte GJ, Verdijk RM, et al. Adult orbital xanthogranuloma: long-term follow-up of treated cases. *Eye (Lond)*. 2023;37:2475-2481. doi: 10.1038/s41433-022-02357-z
5. Stone JH, Khosroshahi A, Zhang W, et al. Inebilizumab for treatment of IgG4-related disease. *N Engl J Med*. 2025;392:1168-1177. doi:10.1056/NEJMoa2409712
6. Wood AJ, Wagner MVU, Abbott JJ, et al. Necrobiotic xanthogranuloma: a review of 17 cases with emphasis on clinical and pathologic correlation. *Arch Dermatol*. 2009;145:279–284. doi:10.1001/archdermatol.2008.583
7. Schadt C, Jacobsen E. *Necrobiotic xanthogranuloma*. In: Connor RF, ed. UpToDate. Wolters Kluwer.
8. Al Aboud AM, Shah SS, Blair K, et al. Xanthelasma palpebrarum. StatPearls [Internet]. StatPearls Publishing; 2024. Updated March 1, 2024. Accessed February 10, 2026. https://www.ncbi.nlm.nih.gov/books/NBK531501/
9. Collie JS, Harper CD, Fillman EP. Juvenile xanthogranuloma. StatPearls [Internet]. StatPearls Publishing; 2024. Updated August 8, 2023. Accessed February 10, 2026. https://www.ncbi.nlm.nih.gov/books/NBK526103/
10. Miettinen M, Fetsch JF. Reticulohistiocytoma (solitary epithelioid histiocytoma): a clinicopathologic and immunohistochemical study of 44 cases. *Am J Surg Pathol*. 2006;30:521-528. doi:10.1097/00000478-200604000-00014