**Case 4.2**
A 48-year-old Thai woman from Bangkok

**Chief complaint**: Bilateral periorbital swelling for 4 years


(Fig. 4.2.1)

**Present illness**: The patient developed asymptomatic progressive periorbital swelling with yellowish discoloration on both eyes for 4 years. She was otherwise in good health.

**Past history**: None

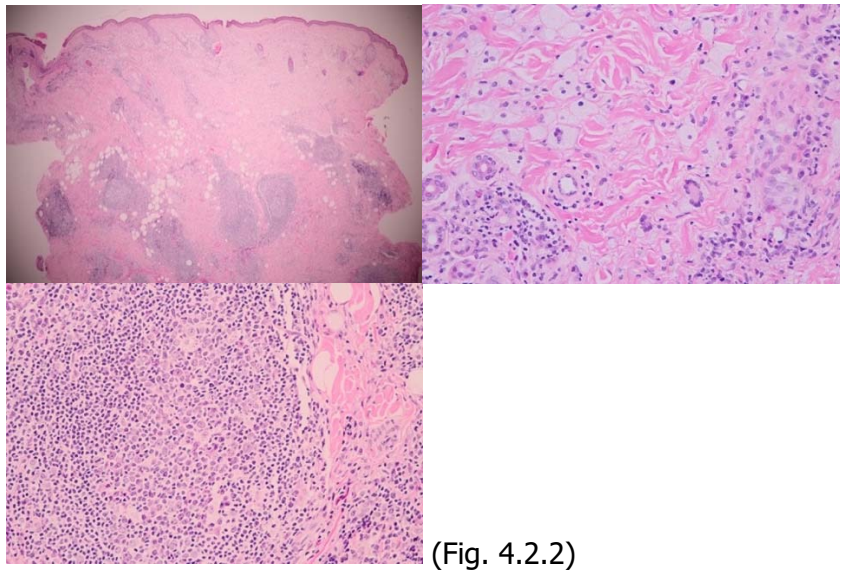
**Family history:** No family history of similar cutaneous lesions, dyslipidemia or malignancies

**Dermatological examination:** (Fig. 4.2.1)

Bilateral symmetrical ill-defined yellow indurated plaques on upper and lower eyelids

**Physical examination**: Physical examination other than skin revealed no abnormality.

**Histopathology:** (S17-014936, Right periorbital area) (Fig 4.2.2)


(Fig. 4.2.2)

- Diffuse inflammatory cell infiltrate of mainly foamy histiocytes intermingled with some lymphocytes and a few Touton giant cells in the upper to mid dermis
- Dense nodular infiltrate of lymphocytes with lymphoid follicles in the lower dermis to subcutaneous tissue

**Immunohistochemistry**:
- Positive CD68, factor XIIIa staining
- Negative CD1a and S100 staining

**Laboratory investigations:**
- CBC: Hct 42.7%, WBC 12,540 cells/µL (N 70%, L 21%, Mono 6%, Eo 2%, B 1%), Platelets 454,000 cells/µL
- BUN 9 mg/dL, Cr 0.42 mg/dL
- LFT: ALP 60 U/L, GGT 19 U/L, AST 21 U/L, ALT 19 U/L, TP 79.5 g/L Alb 41.8 g/L, TB 0.2 mg/dL, DB 0.1 mg/dL
- Lipid profiles: Chol 234 mg/dL, TG 124 mg/dL, HDL 38 mg/dL, LDL 174 mg/dL
- ANA: Negative, Anti-DNA: Negative
- Thyroid function test: FT3 2.89 pg/mL (1.71-3.71), FT4 1.13 ng/dL (0.70-1.48), TSH 0.63 IU/mL (0.35-4.94)
- SPEP: Normal
- Serum free light chain: Kappa 12.8 mg/dL (3.3-19.4), Lambda 11.8 mg/dL (5.71-26.3)
- Cryoglobulin: Negative

**Diagnosis:** Adult-onset periorbital xanthogranuloma

**Treatment:**
- Observe the patient clinically and start systemic corticosteroid if necessary
- Close follow-up for clinical asthma and hematologic malignancy

**Presenter:** Phatcharawat Chirasuthat, MD

**Consultant:** Pamela Chayavichitsilp, MD

**Discussion:**

Adult-onset periorbital xanthogranuloma belongs to the heterogeneous group of class II non-langerhans histiocytic proliferations, called "adult orbital xanthogranulomatous disease" It is classified into 4 subtypes: adult-onset periorbital xanthogranuloma, necrobiotic xanthogranuloma (NXG), Erdheim–Chester disease (ECD) and adult-onset asthma and periocular xanthogranuloma (AAPOX). Histopathologically, each of these entities is characterized by infiltration of "hallmark cells," especially foamy histiocytes and Touton-type giant cells, both of which are often negative for S100 and CD1a.[1, 2]

The pathogenesis of this entity is still unknown, but is thought to be secondary to a reactive proliferation of the free tissue macrophages following triggers such as cytomegalovirus infection-induced process, [3] and paraproteinemia in NXG.[4]

Adult-onset periorbital xanthogranuloma (AOX) is an isolated xanthogranulomatous proliferation without significant systemic involvement. It is the least common among AOXGDs, with barely 10 case reports in the literature.[2] AOX has been reported in patients aged 38 to 79 years, with no sex preference.[2] It usually presents as unilateral, solitary, yellow to orange, elevated xanthomatous lesions that are more indurated and deeper than xanthoma palpebarum.

Adult-onset periorbital xanthogranuloma (AOX) may be confused with juvenile xanthogranuloma (JXG) in adults due to similar clinical presentations. However, the difference lies in the histopathology and associated conditions. Juvenile xanthogranuloma in adults typically presents with noninfiltrative, well-demarcated lesions in comparision to lesions in AOX with more infiltrate and larger size.[5] There are also often reports extracutaneous manifestations in

JXG, most commonly the eye, followed by the lungs and liver,[6] while AOX has reported associations of extraocular muscle involvement.[7] In adult-onset JXG associated conditions include neurofibromatosis and leukemia, most commonly juvenile chronic myelogenous leukemia,[6] while AOX has no reported systemic involvements. Histopathologically, AOX shows lymphoid follicles in deep dermis while adult-onset JXG lacks this feature.[8]

Treatment of adult orbital xanthogranulomatous disease is based on 3 aspects: control of the disease of the orbit, control of hematologic conditions (when present) and control of systemic manifestations. To control the disease of orbit, systemic corticosteroid is the most common approach which showed moderate improvement.[9]In cases refractory to systemic corticosteroids, methotrexate has shown promising results. It has also been used in corticosteroid-dependent AOX to reduce to reduce the necessary dose of corticosteroid and thus avoid adverse effects in the long term.[10] Other options include intralesional corticosteroids,[11] surgery,[2, 9] radiotherapies combined with systemic corticosteroids,[13] intravenous immunoglobulins and extracorporeal photophoresis.[11]

Our patient presented with bilateral yellow indurated plaques on upper and lower eyelids (anterior orbit) with histopathology that was compatible with xanthogranuloma group and multiple lymphoid follicles. AOX and AAPOX are the most likely diagnoses. Given that asthma may develop months to years following the onset of eyelid lesions, we cannot rule out AAPOX and further follow-up of the patient is necessary for a final diagnosis. Due to the self-limiting nature of this condition, we elected to observe the patient clinically and start systemic corticosteroid if necessary.

**References:**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