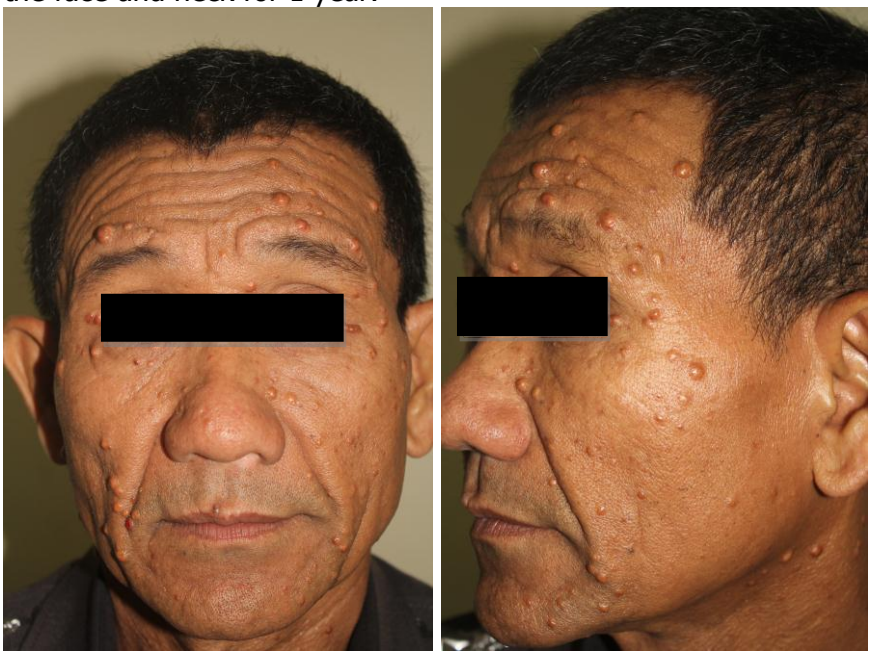
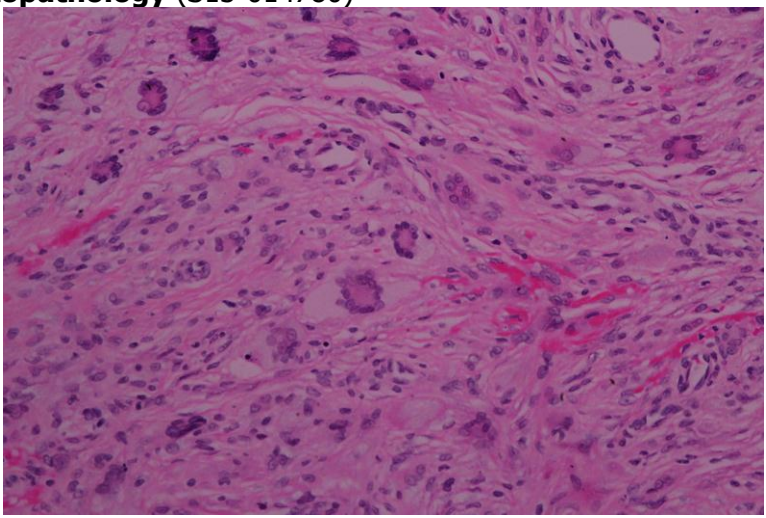
Case 1
A 57-year-old Thai male from Bangkok.
Chief complaint: Multiple asymptomatic papules and nodules on the face and neck for 1 year.



Present illness: He presented with a 1-year history of asymptomatic papulonodular eruption initially his face and neck. The lesions had slowly increased in size and number. None of the lesions had spontaneously resolved. He went to a private clinic and received laser treatment on some lesions. The treated lesions resolved without recurrence. But new lesions slowly developed and are cosmetically unacceptable to the patient. He was otherwise healthy and had no other constitutional symptoms.
Past history
He has intermittently been taking sildenafil (Viagra®) for 2-3 years.

Family history : Nil.
Physical examination
VS: T 37 ^{0}C, RR 20/min, BP 112/67 mm Hg, HR 80/min
GA: good consciousness, not pale, no jaundice
Abdomen: no hepatosplenomegaly
LN: not palpable
Ophthalmologic examination were normal
Skin examination
Multiple discrete erythematous to yellowish firm dome-shaped papules and nodules on the face and neck with a few scattered papules on his upper extremities.

Investigation: CBC: Hb 13.4 g/dL, Hct 39.9% WBC 10,180/mm^3 (N 62%, L 28%, M 9%, E 1%) Platelets 203,000/mm^3
Fasting blood sugar 88 mg/dl
Chol 198 mg/dL ,Trig 57 mg/dL
HDL 48 mg/dL, LDL 125 mg/dL
BUN 16 mg/dL, Cr 1.23 mg/dL
Histopathology (S13-014780)



• Diffuse inflammatory-cell infiltrate in the upper dermis.
• Inflammatory-cell infiltrate composed of histiocytes, foam cell, foreign body and Touton, giant cells intermingled with spindle cells dispersed throughout the lesion.
• The histiocytes are positive for CD8 but negative for S100.

Diagnosis: Multiple adult xanthogranulomas
Treatment: Isotretinoin 20 mg/day
Carbon dioxide laser

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Discussion

Xanthogranulomas (XG) are the most frequent form of non-Langerhans cell histiocytoses. There are benign, usually asymptomatic, self-healing, red, yellow, or brown papules, nodules composed of histiocytic cells, usually present at birth or within the first several months of life (40–70% before 1 year); thus is named juvenile xanthogranuloma (JXG).[1]

An adult form of xanthogranulomas was first described by Gartmann and Tritsch in 1963.[2] The skin lesions develop in adults and are histologically indistinguishable from those of juvenile xanthogranuloma. The etiology of adult xanthogranulomas is not clear. Certain authors insist that xanthogranuloma is a reactive granulomatous response of histiocytes to infection, mechanical or unknown stimuli.[3-4] Adult xanthogranuloma (AXG) is typically a solitary lesion and multiple xanthogranulomas in adults are rare. There have been about 22 reported cases of multiple adult xanthogranulomas including our case.

Solitary AXG is the commonest presentation of AXG (70–89% of cases). In solitary AXG, the sex ratio is 0.9 (male/female), with a mean age at diagnosis of 35. The lesions are most frequent

on the face (73%), trunk (13%) and limbs (13%).[5-6]

Multiple adult xanthogranulomas (MAXG) is defined by the presence of more than 5 XG lesions.[5] In adults, multiple XG lesions are observed in 11–30% of cases versus 12-47% in JXG.[5] A literature review of 16 MAXG cases[6] shows that MAXG is more common in men (1.6 male/1 female). The mean age at diagnosis was 46.7 years old (median = 43). The lesions mainly involve the trunk (92%), head and neck (69%), and the limbs (38%) in contrast to MJXG, which affect the head and neck (50–70%), the trunk (20–30%), and the limbs (10–20%). In our patient, he is a middle-aged man, but his lesions are predominantly on face and neck, but spare the trunk. Extracutaneous manifestation (oral and conjunctival) was reported in only 1 case of MAXG.[7]

The association of AXG with non-insulin-dependent diabetes mellitus appears significant (23% of AXG cases versus 5% in the general population), whereas the incidence of hypercholesterolemia and hypertriglyceridemia in AXG patients is equivalent to the general population. A review by Saad et al[6] highlights the benign natural history of adult-onset XG. However more recent studies report eight AXG cases developing in the context of a hematologic malignancy.[8] The hematologic conditions associated with adult XG include; leukemias (3 cases : 2 cases of chronic lymphocytic leukaemia[9-10] and 1 case of B-cell acute lymphoblastic leukemia[11]), lymphomas (3 cases: large B-cell lymphoma[11], Adult T-cell leukaemia/lymphoma[12], follicular lymphoma[8]),monoclonal gammopathy (1 case[10])and essential thrombocytosis(1 case[13]). The XG may develop before, concomitantly with, or after diagnosis of the hematologic malignancy. In XG cases developing before, the malignancy has been reported to appear as long as 9 years. [11]

Histologic examination is indistinguishable from those of JXG. It initially reveals histiocytic proliferation without xanthomatous cells, associated with a moderate infiltrate (lymphoid cells and eosinophils). In a second phase, histiocytes become

foamy, the inflammatory infiltrate increases and giant multinucleated cells (Touton) appear in 95% of cases. Histiocytic markers such as CD68, HAM56, and factor XIIIa show strong reactivity indicating the macrophagocytic lineage of these cells. Langerhans cell markers such as S-100 and CD1a are characteristically absent.

In adult with multiple cutaneous lesions, spontaneous regression was observed in 54% of the cases with a duration ranging from 9-180 months(median 22 months).[6] Usually, no treatment is necessary for cutaneous xanthogranuloma but extensive cutaneous involvement in adult like our case may require some treatment to hasten improvement. There are no clear guidelines for treatment of adult onset xanthogranuloma. Surgical excision is the mainstay of treatment for inflamed or cosmetically distressing lesions. Other treatments have been described in the literature, including the use of topical, intralesional steroids, cryotherapy and radiotherapy. For systemic involvement of the lesions, systemic steroid, chemotherapy, cyclosporin has been used.[14] One report shows successful treatment after 2 months oral isotretinoin 20 mg once daily, in which most of the lesions had flattened with yellowish and hyperpigmented macules.[15] Due to our patient's extensive skin involvement, we decided to treat him with systemic isotretinoin 20 mg/day, and carbon dioxide laser on selected lesions to improve cosmetic appearance.

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