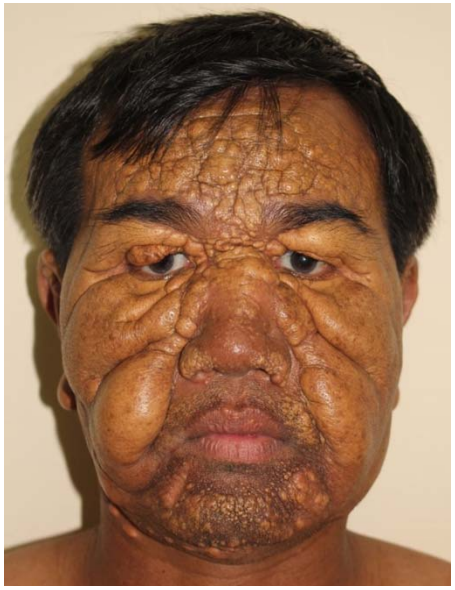
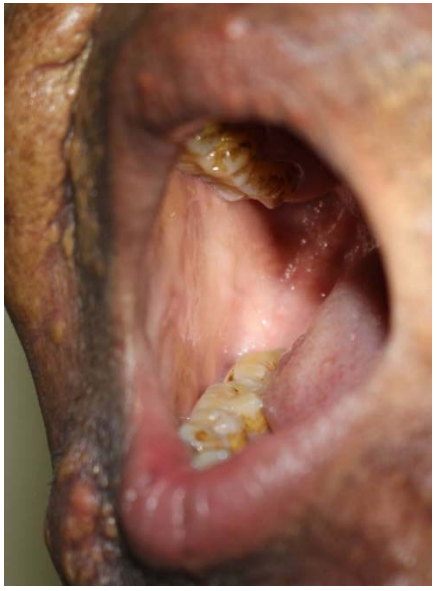
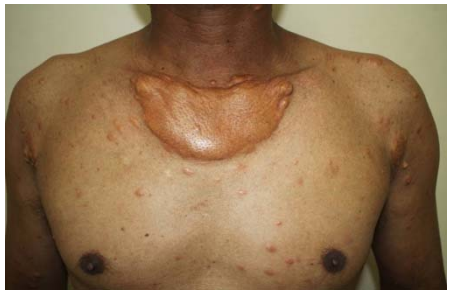
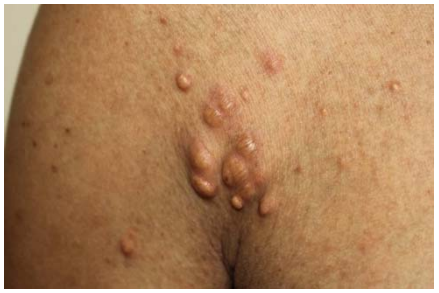
Case 4.1
A 43-year-old Thai man from Bangkok

Chief complaint: progressive yellowish eruptions on face, trunk and upper extremities for 4 years

(Fig. 4.1.1)

Present illness: This patient developed multiple yellow-brown papules and nodules on face, trunk and proximal upper extremities for 4 years. By the time of presentation, the increased in number and size into plaques most prominently on his cheeks, periorbital and upper chest. These lesions were non-pruritic and not painful. He was otherwise in good health.

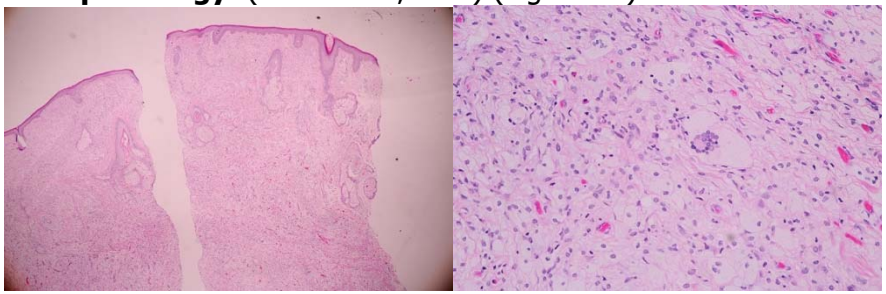
Past history:
Hypertriglyceridemia controlled with fenofibrate 300 mg/day

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

Dermatological examination: (Fig 4.1.1)
Multiple yellowish-brownish papules, nodules and plaques on face resembling "leonine facies", trunk and upper extremities with mucosal involvement

Physical examination: Physical examination other than skin revealed no abnormalities.

Histopathology: (S17-19554, Chin) (Fig. 4.1.2)



(Fig 4.1.2)

- Diffuse inflammatory cell infiltration of foamy histiocytes intermingled with some lymphocytes, eosinophils, plasma cells and few Touton giant cells in the entire dermis

Immunohistochemistry:

- Positive CD68 staining
- Negative CD1a, S100 and factor XIIIa staining

Laboratory investigations:

- CBC: Hct 41%, WBC 9,000 cells/µL (N 61%, L 33%, Mono 5%, Eo 1%), Platelets 349,000 cells/µL
- BUN 15 mg/dL, Cr 0.87 mg/dL
- LFT: ALP 54 U/L, GGT 67 U/L, AST 18 U/L, ALT 67 U/L, TP 52 g/L Alb 28 g/L, TB 0.6 mg/dL, DB 0.2 mg/dL
- Electrolytes: Na 140 mEq/dL, K 4.21 mEq/dL, Cl 107 mEq/dL, HCO3 25 mEq/dL
- Lipid profiles: Chol 213, TG 119, HDL 46, LDL 157
- Serum protein electrophoresis: Normal
- Serum kappa: 22.5 mg/dL (3.30-19.40), Lambda level: 17.20 mg/dL (5.71-26.30)
- Cryoglobulin: Negative

Imaging study: Pending for CT Chest and whole abdomen

Diagnosis: Xanthoma disseminatum

Management:

- Ophthalmology consult showed no abnormal findings
- ENT consult revealed three yellowish nodules 1x1 mm in size in the nasopharynx
- Simvastatin 20 mg/day
- Pioglitazone 30 mg/day
- Fenofibrate 500 mg/day

Presenter: Phatcharawat Chirasuthat, MD

Consultant: Pamela Chayavichitsilp, MD

Discussion:

Xanthoma disseminatum(XD) is a rare normolipidemic mucocutaneous xanthomatosis that arises from the proliferation of non-Langerhans cell histiocytes.[1,2] XD was first described as a distinct entity by Montgomery and Osterberg[3] in 1938. Age at onset ranges from as early as 8 months[4] to 85 years[5] with an average age of over 40 years. [6] The male to female ratio is 2.4:1[7]. The classical symptom triad consists of cutaneous xanthoma, xanthomas of the mucous membranes, and diabetes insipidus. Metabolic derangements is the most likely pathogenesis, more specifically, a primary proliferation of histiocytic elements with a secondary accumulation of lipids (cholesterol).[8] Three clinical variants have been described: a common persistent form, a less common progressive form with systemic involvement, and a rare self-healing form with spontaneous resolution[6].

Cutaneous manifestations in XD is characterized by multiple

symmetric red-brown to yellow papules and nodules on the trunk, face, and proximal extremities, including the flexural folds, such as the neck, axillae, antecubital fossa, groin, and perianal regions. [7] Involvement of the mucous membrane is observed in 30–50% of patients and most frequently affects the mouth, pharynx, larynx, conjunctiva and cornea which can cause significant morbidity.[6] For instance, localized mucous lesions in the oropharynx, larynx, and cornea can lead to dysphagia, dyspnea, and obstructive blindness respectively. XD may also manifest in the bone marrow, the hepatobiliary, musculoskeletal, respiratory and gastrointestinal tracts and the central nervous system.[9]

Diabetes insipidus (DI) occurs in about 40% of patients with XD which is a result of xanthomatoid cell infiltration in the hypothalamic-posterior pituitary axis.[6, 7, 10] CNS involvement other than pituitary/region also has been reported but is extremely rare.[11]

There have also been reports of rare associations of XD with multiple myeloma, Waldenström's macroglobulinemia, hypothyroidism, and hyperthyroidism.[5, 6, 12, 13]

Histopathologically, in early stages of XD, scalloped macrophages predominate with few foamy cells. In more-developed lesions, xanthomatized cells appear. Fully developed lesions contain a mixture of scalloped cells, foam cells and inflammatory cells as well as Touton and foreign body giant cells.[14] Immunohistochemical staining of lesional macrophages is typically positive for CD68 and factor XIIIa, but negative for CD1a, CD34, and S-100 protein.[2, 14] Our case atypical immunohistochemically because Factor XIIIa which uniquely stains dermal dendrocytes was negative. From review of the literature, Patel *et al*[15] and Sueki *et al*[16] also reported cases of XD with negative Factor XIIIa. This was explained by antigenic heterogenicity of dermal dendrocytes or that the immunocytochemistry and electron microscopy favor macrophages rather than the dermal dendrocytes as the cell of origin.[16, 17]

There is no standard treatment for XD. Options including diet,[7,18] surgical excision,[6, 7, 19-21] electrocoagulation,[21] cryotherapy[18], radiation,[7, 22, 23] glucocorticoids,[9, 21, 24-27] anti-metabolites,[9,28] anti-cancer drugs,[6, 18, 27, 29] lipid-lowering agents[6, 30-32] or a combination of these therapies[6, 9, 18, 27] have been tried.

In our patient, we plan to start a lipid-lowering agent since many reports showed moderate to high efficacy with a more favorable side-effect profile.

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