Case Report

**A middle-aged man with multiple yellowish papules all over the body**

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A 47-year-old man presented with progressive eruption of papules over bilateral upper limbs and lower limbs for one year. The lesions were non-itchy, non-tender and there was no discharge. He was a smoker and non drinker. He had no known history of hypertension, diabetes mellitus or ischaemic heart disease. He had a history of acute pancreatitis at the age of 37, otherwise he enjoyed good past health.

Physical examination demonstrated multiple brownish, yellowish papules over bilateral upper limbs and lower limbs especially over the extensor surface (Figure 1a). Similar lesions were also noted over the knuckles of fingers (Figure 1b) and toes as well as the chin. There was no mucosal lesion noted.

Differential diagnoses included eruptive xanthoma, xanthogranuloma and lichen amyloidosis.
Investigations including blood tests for complete blood picture, renal and liver function were normal except for a mildly elevated alkaline phosphatase (198 IU/L). The fasting glucose was 6.1 mmol/L. The fasting lipid profile revealed an elevated total cholesterol (18.3 mmol/L) and triglyceride (51.7 mmol/L) level.

Skin biopsy showed large aggregates of foamy histiocytes, histiocytic cells and mononuclear inflammatory cells with mild fibrosis (Figures 2a & 2b). The histopathological and clinical findings were consistent with eruptive xanthoma.

This patient was referred to the medical unit for management of hyperlipidaemia. He was put on gemfibrozil. The papular lesions gradually flattened within weeks after initiation of gemfibrozil (Figures 3a & 3b). The triglyceride level dropped to 15.6 mmol/L four months after initiation of lipid. Cholestyramine was then added to achieve a better control of the triglyceride level.

**Discussion**

Xanthomas are lesions characterised by accumulations of lipid-laden macrophages. Xanthomas can occur as a result of general metabolic disease (e.g. altered lipid metabolism), generalised histiocytosis or local fat phagocytosing storage process. Xanthomas are common manifestation of lipid metabolism disorders. The condition can occur in any age and its prevalence in male and female is the same. Cutaneous xanthomas are mostly cosmetic disorder but their presence might suggest an underlying disorder of lipid metabolism. The morbidity and mortality are related to atherosclerosis and pancreatitis. A family history of xanthomas may be encountered in hereditary hyperlipoproteinaemia. There may be a prior history of myocardial infarction as well as pancreatitis. The cutaneous manifestation may precede a diagnosis of hyperlipidaemia.1

Cutaneous xanthomas can be clinically subdivided into: xanthelasma palpebrarum, tuberous xanthomas, tendinous xanthomas, eruptive xanthomas, xanthoma striatum palmare, generalised plane xanthomas. Xanthelasma palpebrarum, the most common form of the xanthomas, is an asymptomatic, usually bilateral and symmetrical condition. Soft, velvety, yellow

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**Figure 1.** Multiple yellowish papules over the extensor surface of fingers and forearm.
Multiple yellowish papules

Figure 2. (a) Low power view shows aggregations of histiocytes and mononuclear inflammatory cells in dermis. (b) High power view shows multiple foamy histiocytes present in the dermal aggregate.

Figure 3. Four months after treatment with gemfibrozil, most of the lesions flattened with post-inflammatory hyperpigmentation left.
polygonal papules are found around the eyelids. Around 50% of the patients with xanthelasma are normolipaemic. Tuberous xanthomas are firm, painless, red-yellow nodules which may coalesce to form multilobulated tumours. They usually develop in pressure areas such as the extensor surface of knees, elbows and buttocks. They are particularly associated with increased low-density lipoprotein and may be associated with familial dysbetalipoproteinaemia and familial hypercholesterolaemia. Tendinous xanthomas present as slowly enlarging subcutaneous nodules related to the tendons or the ligaments. They are commonly located on the Achilles tendon, and extensor tendons of hands and feet. The lesions are related to trauma and are associated with severe hypercholesterolaemia. Eruptive xanthomas often arise over the buttock, elbows and knees. Rarely, the oral mucosa and face may be affected. They appear as crops of small, red-yellow papules on an erythematous base, and may be pruritic or tender. They are associated with hypertriglyceridaemia. Xanthoma striatum palmare is a subtle lesion. The palmar creases appear yellow. It is the characteristic skin lesion of type III dysbetalipoproteinaemia. Generalised plane xanthomas present as diffuse orange-yellow pigmentation and slight elevation of skin with a recognisable border. They may cover large areas of the face, neck, thorax and flexural areas. The patients are usually normolipaemic. This condition may be idiopathic or associated with monoclonal gammopathy, leukaemia or lymphoma.

Although xanthomas can usually be diagnosed clinically, histological examination provides confirmation. The histological finding is characterised by the presence of vacuolated macrophages. The macrophages are filled with lipid droplets. Eruptive xanthomas may contain infiltrates of lymphocytes and typically contain extracellular lipid. The main investigation for cutaneous xanthomas is the blood lipid profile to search for any disorder of lipid metabolism.

Treatment options include medical treatment, surgery or locally destructive treatment. While the effectiveness of the lipid lowering agents such as statin and fibrates are well documented, only a few studies mentioned the efficacy of these drugs for resolving xanthoma. Eruptive xanthomas usually resolve within weeks of initiating systemic treatment, tuberous xanthomas usually resolve within months and tendinous xanthomas may take years to resolve or even persist indefinitely. Topical application of trichloroacetic acid (TCAA) to xanthelasma is an acceptable treatment option. However, the major complication is hypopigmentation. Other locally destructive therapies e.g. electrodessication and laser therapy have been tried with variable success. Surgical excision can be considered for large periocular xanthelasma but recurrences do occur.

In conclusion, cutaneous xanthoma is mostly a cosmetic disorder, but its presence might suggest an underlying lipid metabolism disorder. It can be subdivided into different types according to morphology, distribution and the associated type of lipid disorder.

References