

The half-yellow man

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Introduction

Diffuse normolipaemic plane xanthoma is a rare form of xanthoma usually associated with an underlying haematological or inflammatory condition, and may present many years prior to the onset of systemic illness. We present a case of this uncommon condition occurring in association with a monoclonal gammopathy of unknown significance.



Figure 1: Xanthomata, featuring extensive involvement of the chest, upper limbs and face

Case study

A 74-year-old Caucasian male presented with diffuse yellow-orange skin discolouration, which had progressed over the preceding few months. There was no medical history of note, and he was not taking any medication. There was no family history of dyslipidaemia or premature cardiovascular disease. On examination, the patient was found to be clinically well, but had diffuse mildly raised yellow-orange skin discolouration of his face, neck, arms, chest and back (Figure 1). *Arcus cornealis* was not visible, and there was no palpable tendon xanthomata.

Initial laboratory tests, which included renal and liver function, calcium, phosphate and urate, thyroid function and glucose levels, as well as a complete blood count, were within normal limits. The fasting lipid profile showed only mild hyperlipidaemia, with a total serum cholesterol level of 5.4 mmol/l, triglycerides of 1.2 mmol/l, high-density lipoprotein (HDL) cholesterol of 1.3 mmol/l and calculated low-density lipoprotein (LDL) cholesterol of 1.3 mmol/l. A skin biopsy indicated groups of lipid-laden foamy histiocytes in the dermis and perivascular areas, with no

evidence of necrobiosis or Touton cells, in keeping with diffuse normolipaemic planar xanthomatosis (DNPX) (Figure 2). The erythrocyte sedimentation rate was 76 mm/hour and an immunoglobulin G kappa monoclonal band was demonstrated on serum protein electrophoresis. The urine was negative using the Bence-Jones protein test. Both the chest radiograph and an

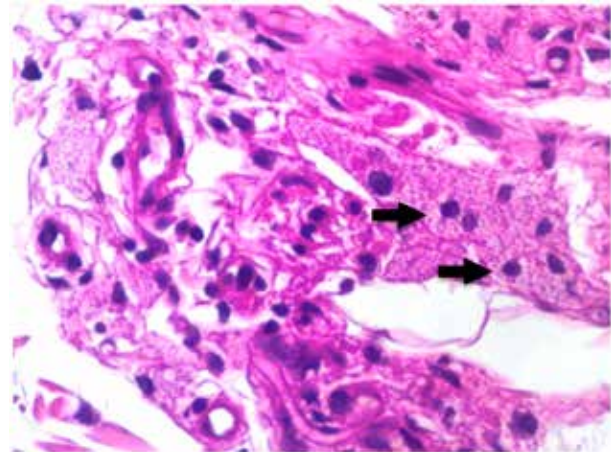


Figure 2: The haematoxylin and eosin findings; a skin biopsy demonstrating intradermal and perivascular infiltration by foamy histiocytes (arrows) (magnification × 200)

abdominal ultrasound were unremarkable. The electrocardiogram showed a normal tracing. A bone marrow aspirate and trephine biopsy demonstrated a variably cellular bone marrow with < 10% plasma cells, suggestive of a monoclonal gammopathy of unknown significance (MGUS).

These findings are consistent with a diagnosis of DNPX, associated with MGUS. The patient was started on atorvastatin 20 mg daily for his mild hyperlipidaemia, and did not require specific therapy for the skin lesions. There was some resolution of the skin lesions on statin therapy, and he continues to follow-up routinely at our facility.

Discussion

Also called generalised planar xanthomatosis, DNPX is a rare form of xanthoma which occurs as a macular yellow-orange or yellow-brown skin discolouration, and is most commonly seen in a symmetrical distribution over the upper torso and neck, though rarely as extensively as in our patient. These xanthomata were originally thought to occur idiosyncratically because of

their association with normal serum lipid levels. However, many of these patients subsequently developed paraproteinaemia or dysglobulinaemia.¹ In addition to MGUS, multiple myeloma, leukaemia, adult T-cell lymphoma, cryoglobulinaemia, rheumatoid arthritis, Takayasu's arteritis and eosinophilic granulomatosis have all been described as being associated with the condition.^{1,2} The skin lesions may precede the haematological or systemic disorder by many years. The cause of the xanthomatous deposition within the skin is not well understood, but a number of theories have been proposed. According to the most plausible theory, the monoclonal immunoglobulin binds with apolipoprotein B-100 on the LDL particles at a site remote from the LDL receptor-binding site. This does not result in a change in affinity for the LDL receptor, but in an increased affinity for the acetyl LDL receptor, enhancing macrophage uptake and esterification, and resulting in cutaneous xanthomata with normolipidaemia.^{3,4}

Conclusion

This case illustrates the occurrence of DNPX in association with a monoclonal gammopathy of unknown significance. Although a rare form of xanthomatosis, this condition often heralds an

underlying haematological or systemic condition, and highlights the need to search for such conditions.

References

1. Cruz PD, East C, Bergstresser PR. Dermal, subcutaneous, and tendon xanthomas: diagnostic markers for specific lipoprotein disorders. *J Am Acad Dermatol.* 1988;19:95–111.
2. Miyagawa F, Fukumoto T, Kobayashi N, et al. Successful treatment of diffuse normolipemic plane xanthoma with probucol. *Case Rep Dermatol.* 2013 May–Aug;5(2):148–51.
3. Feingold KR, Castro GR, Ishikawa Y, et al. Cutaneous xanthoma in association with paraproteinemia in the absence of hyperlipidemia. *J Clin Invest.* 1989 Mar;83(3):796–802.
4. Szalat R, Arnulf B, Karlin L, et al. Pathogenesis and treatment of xanthomatosis associated with monoclonal gammopathy. *Blood.* 2011 Oct;118(14):3777–84.

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