Case report

Diffuse normolipemic plane xanthoma with underlying photosensitive dermatoses

Mudita Gupta,¹ Rajni Sharma,¹ Anchana Gulati,² Archit Gupta ³¹Dermatology, Indira Gandhi Medical College, Shimla, Himachal Pradesh, India²Pathology, Indira Gandhi Medical College, Shimla, Himachal Pradesh, India³Surgery, Indira Gandhi Medical College, Shimla, Himachal Pradesh, India**Correspondence to**Dr Archit Gupta;
archit9th@gmail.com

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SUMMARY

Diffuse plane xanthomatosis is a normolipemic non-Langerhan cell histiocytosis. Clinically, patient presents as asymptomatic yellowish plaques involving eyelids, neck, upper trunk and flexures. Usually, there is an associated haematological or lymphoproliferative malignancy which may precede or follow dermatological manifestations by many years. Rarely inflammatory dermatosis like atopic eczema, photosensitive dermatosis, erythroderma, previous scars and lymphoedema have been found to be associated with these xanthomas. We are reporting a 46-year-old male patient who had a history of photosensitivity for the last 15 years and subsequently developed diffuse plane normolipemic xanthomas.

BACKGROUND

Diffuse normolipemic plane xanthoma (DNPX) is a rare and non-inherited form of xanthomatosis. It was first described by Altman and Winkelmann in 1962.¹ Clinically, patient presents with xanthelasma palpebrarum-like lesions followed by appearance of symmetric, yellowish-orange plaques that favour the neck, upper trunk and flexural folds. DNPX is most commonly associated with malignant haematological (especially multiple myeloma) or lymphoproliferative disorders.² There are a few case reports of DNPX associated with inflammatory disorders while other cases have been labelled as idiopathic.^{3,4} We present a case of 46-year-old man with history of photosensitivity with no other systemic disease presenting with plane xanthomatous lesions on face and neck.

CASE PRESENTATION

A 46-year-old man presented with extensive yellow-orange raised lesions over face, neck and trunk for the last 8 years. The lesions started on the upper eyelid gradually increased in size, then progressed to other sites. These lesions were asymptomatic. There was no history of any weight loss, easy fatigability or bone pains. There was a history of itchy eruptions off and on on sun-exposed sites. There was no history of intake of any drug. There was no history of any other cutaneous lesion. On examination, there was no pallor, icterus or lymphadenopathy. The general physical examination was non-contributory. Cutaneous examination showed multiple yellow-orange plaques with wide base and flat surface present around the eyes, on the forehead, both sides of the neck and upper trunk (figures 1 and 2). The lesions were distributed

Figure 1 Xanthelasma palpebrarum and xanthoma plaques on forehead. Few lichenoid plaques on forehead.

symmetrically. There were multiple lichenoid plaques on the forehead (figure 1). There were no mucosal lesions. There was no organomegaly.

INVESTIGATIONS

Haemoglobin was 110 g/L; white blood cell count was 7600/mm³; platelet count 1.2 lacs/mm³; erythrocyte sedimentation rate was 12 mm/hour. There was no hypoalbuminaemia, renal and liver function tests, fasting blood sugar and thyroid function tests were within normal limits. Serum electrolytes were not deranged. Tests for C reactive protein, rheumatoid factor, C3, C4, CH50, antinuclear antibodies, anti-double-stranded were negative. No abnormality in fasting lipid panel or serum protein electrophoresis were detected. Urine electrophoresis

Figure 2 Symmetrical plane xanthoma plaques on sides of neck and trunk.

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Figure 3 (H&E 40×) Histopathology showing normal epidermis with subepidermal aggregates of foamy histiocytes.

showed no globulins and albumin was <5 mg/dL (within normal range) and serum electrophoresis showed albumin was 4.5 g/dL (normal 3.5–5 g/dL) and globulin 2.5 g/dL (normal 2.3–3.4 g/dL). Urine examination showed no proteinuria or haematuria. Bone marrow aspiration and biopsy did not show any pathological change. Patch test and photopatch test were negative. HLA-DR 4 was done to differentiate idiopathic polymorphic light eruption from actinic prurigo which was negative. Monochromator is not available at our institute so we did a biopsy from the lichenoid lesion. Histopathological examination from plaque on neck showed stratified squamous epithelium with subepithelial aggregates of foamy histiocytes/xanthoma cells (figures 3 and 4). No giant cells (Touton or epithelioid), cholesterol clefts or areas of necrosis were seen. Histopathology from the lichenoid plaque showed epidermal spongiosis, an interface dermatitis, papillary dermal oedema and perivascular lymphocytic infiltrate suggesting polymorphous light eruption.

DIFFERENTIAL DIAGNOSIS

Necrobiotic xanthogranulomas (NXGs) may also be normolipemic but more commonly presents as nodules, ulcerative lesions with eye involvement. Also histopathologically, there are sheets

Figure 4 (H&E 100×) Histopathology showing foamy histiocytes.

of histiocytes, with presence of multiple Touton giant cells and areas of necrosis seen in NXG. In our patient, there was a presence of aggregates of foamy histiocytes only. Like DNPX Montgomery syndrome or xanthoma disseminatum may also present with papular and patchy xanthomas on flexures or eyelids but these are associated with mucosal involvement and hypothalamic/hypophyseal compromise leading to diabetes insipidus.⁵ A final diagnosis of DNPX with idiopathic photosensitive dermatosis was made.

TREATMENT

Patient was advised excision of the xanthomas by erbium Yag laser but patient refused as the lesions were only causing cosmetic disfigurement but were otherwise asymptomatic.

OUTCOME AND FOLLOW-UP

Patient was advised regular follow-up. After 6 months of follow-up, there was no significant change in the haematological and biochemical parameters.

DISCUSSION

Xanthomas are disorders of altered lipid metabolism characterised by the deposition of yellowish cholesterol-rich material in histiocytes accumulating in the skin and the tendons. They are broadly divided into hyperlipemic and normolipemic xanthoma, and NXG. Normolipemic xanthomas can be seen in xanthogranuloma, xanthelasma palpebrarum, disseminated xanthomatosis, diffuse plane, verruciform and localised type. Diffuse plane xanthomas are usually normolipemic but may be occasionally hyperlipemic.⁶ DNPX is a uncommon non-inherited subtype of non-Langerhans histiocytosis. According to Parker's classification, normocholesterolemic xanthomatosis can be grouped into three categories: in type I patients have an altered lipoprotein content or structure, type II is associated with underlying lymphoproliferative disorders and in type III local tissue alterations (local tissue lipid synthesis, trauma and inflammation of the skin) leads to xanthoma formation.⁷

Altman and Winkelmann described the features characteristic of DNPX as a benign entity presenting with (1) xanthelasma palpebrarum; (2) diffuse xanthoma planum of the head, neck, trunk and extremities; and (3) normal plasma lipid levels.¹ In 1966, Lynch and Winkelmann found that DNPX is commonly associated with disorders of the reticuloendothelial system.⁸ In addition to multiple myeloma and monoclonal gammopathy, DNPX can be associated with other malignant haematological or lymphoproliferative disorders.³ All these cases belong to Parker's type II category. DNPX developing at sites of inflammatory dermatosis, for example, photosensitivity, actinic reticuloid, atopic dermatitis and so on, have been rarely described and these type of lesions are of Parker's type III category.⁴ Rarely, DNPX is idiopathic.³

The precise pathogenesis of DNPX remains largely uncertain. In gammopathy-associated DNPX, paraproteins having antilipoprotein activity form complexes with lipoprotein and are deposited around dermal vessels.⁹ In type III DNPX, altered vascular and lymphatic permeability may lead to accumulation of lipids.^{10 11} James *et al* proposed that in inflammatory dermatosis there are increased number of macrophages with overproduction of lipid material that leads to formation of xanthoma.⁴ The association of photosensitive eczema, actinic reticuloid and development of normolipemic xanthoma has been reported in various other case reports.^{12 13} There is a scavenger receptor-mediated control of cholesterol uptake on

the skin macrophages. Breakdown of the inhibitory feedback mechanism leads to accumulation of intracellular cholesterol and cholesteryl ester rich in oleic acid leading to formation of xanthomas

Clinically, the disorder is characterised by appearance of yellow to yellow-brown flat patches or slightly elevated plaques that vary greatly in size and may be sharply demarcated from the surrounding skin or may have rather indistinct borders.³ Usually, deposits in periorbital area are first to appear, but in few cases it may appear later. Lateral sides of the neck, the upper trunk (plane xanthoma) and extremities are the other common sites involved. Xanthomas may also get localised at previous injuries or scars.

Histopathologically, foam cells, that is macrophages that have engulfed lipid droplets, variable numbers of Touton giant cells, lymphocytes and foamy histiocytes can be seen. These xanthomas are cosmetically unacceptable and cauterisation or surgical excision may be done if feasible. Other physical therapies like chemabrasion, dermabrasion and ablative laser therapy (erbium YAG) can be used.¹⁴ Cladribine has been used for treatment of various histiocytosis.¹⁵

Careful follow-up and periodic laboratory examinations are recommended even for patients who seems to have no underlying disease as DPNX can precede the appearance of its associated disorders by several years.³ Presently, our patient is free from any underlying associated malignancy and is still under follow-up. Moreover, this case shows that although dermatological lesions can be the first manifestation of important haematological diseases; however, rarely some inflammatory dermatosis

which may occasionally be thought to be unrelated may lead to formation of DNPX.

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ORCID iD

Archit Gupta <http://orcid.org/0000-0002-9476-2000>

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Learning points

- Diffuse normolipemic plane xanthomatosis is a type of non-Langerhan cell histiocytosis.
- Haematological and lymphoproliferative disorders are the most common associations seen.
- Inflammatory dermatoses may lead to development of plane xanthoma.
- Alteration in vascular, lymphatic permeability and increased macrophages may predispose to development of xanthoma in inflammatory dermatosis.

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