Diffuse plane xanthoma in an otherwise healthy woman

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Summary

We report a case of diffuse plane xanthoma in a 40-year-old otherwise healthy woman. Her disease began 18 years ago as xanthelasma and progressed to involve large areas of her face, neck and trunk. No associated diseases were detected on repeated laboratory testing.

Report

A 32-year-old woman, presented in September 1991 with a 9-year history of bilateral orange–yellow plaques at the inner canthi. She had also developed more recent well-demarcated reddish-brown patches around the eyes, on the forehead, temples, and neck. Yellow plaques were seen in some areas. Histology showed dermal histiocytes with vacuolated foamy cytoplasms and Touton giant cells with an admixture of inflammatory cells, predominantly lymphocytes. The findings were consistent with diffuse plane xanthoma. Investigations for underlying pathology, including complete blood count, erythrocyte sedimentation rate, liver function tests, triglyceride and cholesterol levels, high and low density lipoprotein cholesterol, lipoprotein electrophoresis, immunoelectrophoresis, urinary Bence–John’s protein, chest X-ray and skull radiograph were all normal. There was no relevant family history.

Repeated examination 7 years later showed more extensive, but similar, skin plaques on the anterior portion of the scalp, ears, retroauricular areas, much of the neck, chest, and proximal extremities. (Fig. 1) Again no other physical abnormalities were noted and all of the previous investigations were again negative. Further normal tests included thyroid function tests, uric acid, protein electrophoresis, albumin, globulin, C-reactive protein, rheumatoid factor, C3, C4, CH50, anti-nuclear antibodies, anti-double stranded DNA antibodies, abdominal and pelvic sonography. Bone marrow aspiration was normal and bone marrow biopsy showed reactive changes. Skin biopsy findings were unchanged. (Fig. 2) S100 and Perl stains were negative. Bone marrow examination was also normal in July 2000.

Altman and Winkelmann first recognized ‘diffuse normolipemic plane xanthoma’ in 1962 after reviewing the literature and describing five new cases. The features of the disease were: (i) xanthelasma palpebrarum; (ii) diffuse xanthoma planum of the head, neck, trunk, and extremities; and (iii) normal plasma lipid levels. They considered the condition to be benign and unassociated with internal diseases.1,2 Four years later, Lynch and Winkelmann detected a strong association of diffuse plane xanthomata (DPX) with disorders of the reticuloendothelial system.3 Since then, most reported cases of DPX have been associated with an underlying disease, particularly multiple myeloma and monoclonal gammopathy.4–6 However many other lymphoproliferative disorders have been associated, including chronic myeloid leukaemia, acute monoblastic leukaemia (M5), chronic lymphatic leukaemia, chronic myelomonocytic leukaemia, lymphoma, Sezary syndrome, Castleman’s disease, Waldenstrom’s macroglobulinaemia, cryoglobulinaemia, and histiocytosis X.3,5 According to some authors, only a minority of cases can be regarded as idiopathic. However, the frequency of reports describing an underlying disease may be explained on the basis of authors tending to report only those patients with a significant association. On the other hand, patients without an underlying disorder may be under-reported. In a recent series by Marcovel et al.5 only three of the eight patients had a reticuloendothelial disease. These three had disseminated skin lesions involving the trunk and extremities, suggesting that extensive...
cutaneous involvement may indicate the presence of an associated systemic illness. They concluded that the incidence of underlying disease associated with DPX seems to be lower than expected.

The xanthomatous lesions in DPX appear as yellow to yellow–brown flat patches or slightly elevated plaques. The lesions vary greatly in size and may appear sharply demarcated from the surrounding skin or may have rather indistinct borders. The face, particularly the periorbital areas, lateral sides of the neck and the upper trunk are the sites of predilection. They are usually distributed symmetrically. They may appear on any part of the body. Most of the patients with DPX have xanthelasma palpebrarum present as a prominent part of their cutaneous disease and may have had the lesions on the eyelid for years before the other lesions appear. The sites of old scars are involved occasionally. Xanthomas may precede the appearance of other manifestations of systemic disease by several years.

The histological appearance of DPX is characterized by the presence of foam cells. Oil Red O and scarlet red stains confirmed the presence of neutral fat. In some cases the cells are sparse, but in others large sheets and clusters scattered diffusely throughout the dermis are seen. There may be an admixture of histiocytes and lymphocytes. Touton giant cells as well as focal necrobiosis have been observed in DPX, and progression of DPX into necrobiotic xanthogranuloma has also been reported, suggesting that DPX and necrobiotic xanthogranuloma are two conditions associated with paraproteinaemia that could represent a disease spectrum.

There is no single pathogenic mechanism that could explain all cases of DPX. In cases associated with gammopathy it is postulated that paraprotein–lipoprotein complexes (IgG–LDL) may be recognized as modified LDL by scavenger receptors on macrophages, resulting in development of cutaneous xanthomas. On the other hand, other authors consider that DPX is a histiocytosis-derived xanthomatosis in the spectrum of non-X histiocytosis. Vail, Adler and Rothenberg suggested that the cells in the skin lesions represent direct cutaneous infiltration by the same leukaemic cells found in other organs in one patient with chronic myelomonocytic leukaemia. Probably all of these hypotheses are valid for selected cases. Although most patients with DPX and paraproteinaemia are normolipidemic, some are hyperlipidemic or hypolipidemic.

Although the reddish patches seen in our case were
unusual, the presence of xanthelasma for several years, the appearance of xanthomatous plaques, the absence of atrophy, nodules, ulceration and ophthalmic involvement were suggestive of DPX rather than necrobiotic xanthogranuloma. In addition, neither granuloma nor necrobiosis was seen in repeated biopsies. Nevertheless the concept of a disease spectrum cannot be overlooked.

Patients with DPX must be clinically followed because it can precede the occurrence of an associated condition. In our case, the 18-year history of DPX without any associated illness despite extensive work-up is remarkable. Nevertheless, we still recommend careful follow-up and periodic laboratory examinations to detect any possible associated disease.

References