

A Case of Eruptive Xanthoma in Mycosis Fungoides

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Xanthomas have been shown to occur in association with underlying lymphoproliferative disease, and sometimes are the result of lipid deposition in damaged or altered skin. Here in, we describe a case of eruptive xanthomas which developed in a patient suffering from mycosis fungoides. A 45-year-old Korean man presented for the evaluation of patches on the glans of his penis and on pretibial areas, which had persisted for a period of 3 years. Three months before the patient's admission, erythematous papules had developed on his trunk and extremities. Biopsies of lesions which had manifested as patches on the patient's pretibial areas and as papules on his right arm showed dermal infiltration of atypical lymphocytes, with epidermotropism and a diffuse infiltration of lipid-laden foamy cells. The histological findings were determined to be consistent with both mycosis fungoides and xanthoma. (*Ann Dermatol (Seoul)* 18(2) 82~85, 2006)

Key Words: Eruptive xanthoma, Mycosis fungoides

INTRODUCTION

Cutaneous xanthomas and lymphoproliferative diseases are only associated infrequently. Xanthomas have been noted to occur in patients suffering from multiple myeloma¹, Waldenstrom's macroglobulinemia², paraproteinemias³, leukemia/lymphoma^{1,4} and have also been observed in isolated cases of mycosis fungoides^{5,6}.

Mycosis fungoides (MF) is a cutaneous T-cell lymphoma, which is associated with a wide variety of clinical presentations, and tends to manifest an unpredictable course.

Xanthomatosis has been reported to occur in MF patients. Most episodes of xanthomatosis have been reported to be dystrophic, and tend to occur in tumor masses which are undergoing degeneration or regression.

Histologically, lipid-laden macrophages have been described in degenerated tumor masses which exhibit either only a little malignant T-cell infiltration, or none at all.

Here in, we describe a case of eruptive xanthoma in a patient suffering from mycosis fungoides. We suggest the mechanism underlying the development of eruptive xanthoma in cases of MF.

CASE REPORT

A 45-year-old Korean man presented at our institution for an evaluation of patches which had emerged on the glans of the his penis and in the pretibial areas over a 3 year period. The patient also required an evaluation of a series of papules which had emerged on his trunk and both extremities in the 3 months prior to presentation. The patient had a 1-year history of hyperlipoproteinemia without treatment, but his family had no specific medical history. The patient's lesions manifested as dusky-red to violaceous colored, sharply - demarcated scaly patches, located on both shins and the glans (Fig. 1), and multiple, yellowish papules on the trunk and extremities (Fig. 2). Laboratory examinations, in-

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Fig. 1. Dusky red to violaceous colored, sharply demarcated scaly patches on both shins (A) and glans penis (B).

cluding chest PA, CBC, and LFT were within normal limits, but the patient's urinary analysis revealed protein (1+) and glucose (1+). The patient's lipid profile indicated some elevated values: 5110 mg/dl of total lipids, 3496 mg/dl of triglycerides, 199 mg/dl of LDL-cholesterol, and 781 mg/dl of total cholesterol. Lipoprotein electrophoresis showed increased levels of pre- β 22%, beta 61% and chylomicron 6.7%, mandating a diagnosis of type 5 hyperlipoproteinemia. In order to evaluate the staging and metastasis of mycosis fungoides (MF), we performed a bone marrow biopsy and computer tomography on the patient's head, neck, chest, and abdomen. The patient was designated as stage 1A MF without metastasis. Our histopathological examination of the skin lesions on the right shin (Fig. 1A) revealed dense, atypical lymphocyte infiltration in the dermis and also showed epidermotrophism (Fig. 3A). Immunohistochemical studies demonstrated that the infil-

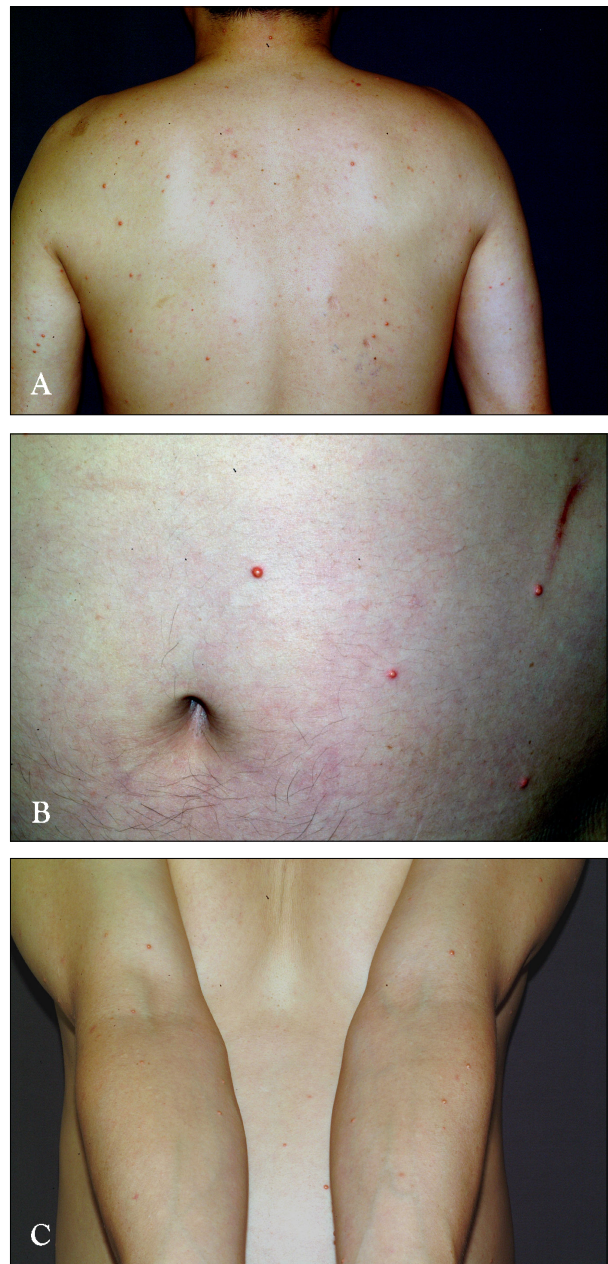


Fig. 2. Multiple yellowish papules on the trunk (A), close up view (B) and extremities (C).

trates were composed of T cells which expressed the pan-T-cell antigen CD3 (Fig. 3B), but not the pan- β -cell antigen, CD40 and the histiocyte marker, CD68. In the xanthoma lesions on the patient's abdomen (Fig. 2B), our histopathological examination revealed an infiltration of lipid laden foamy cells with small nuclei (Fig. 4A), and our immunohistochemical studies indicated CD3 expression (Fig. 4B).

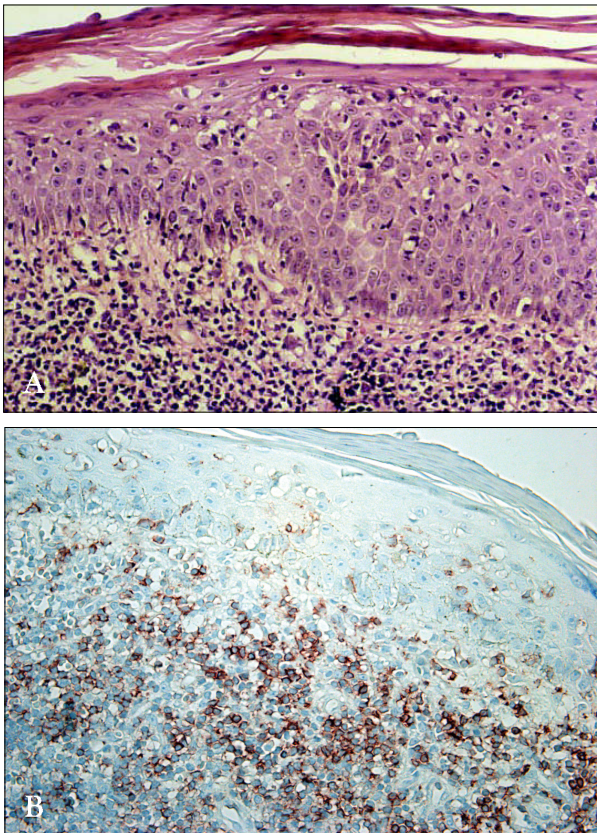


Fig. 3. (A) Dense atypical lymphocyte infiltration in dermis and epidermotropism (H & E, $\times 100$). (B) Atypical lymphocytes are positive for CD3.

We diagnosed this case as eruptive xanthoma with mycosis fungoides. This patient was then treated with PUVA therapy for MF and with a lipid lowering agent for the management of his hyperlipoproteinemia.

DISCUSSION

Xanthomatosis, which refers to the accumulation of lipid-rich foam cells in abnormal skin, has been previously reported in some MF patients and also in conjunction with a number of other inflammatory skin disorders, including mosquito bites, chronic photosensitivity, herpes zoster, fresh vaccination scars, thrombophlebitis, and leukemia^{7,8}. The forms of xanthomatosis which are associated with MF include dystrophic, papular and plane xanthomatosis⁹⁻¹¹. Fatty changes have been observed in both normolipidemic and hyperlipidemic patients^{5,9}.

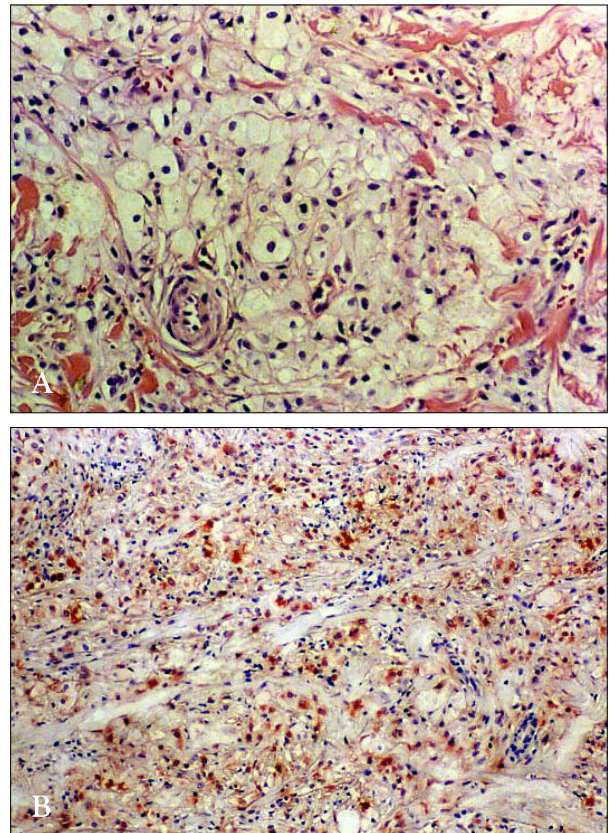


Fig. 4. (A) Infiltration of lipid laden foamy cells small nucleus (H & E, $\times 400$). (B) Infiltrated cells are positive for CD3.

The pathogenesis of xanthomatosis in MF remains a subject of some controversy. However, in the previous cases, we can muster some hypotheses. In cases of dystrophic xanthomatosis, inflammation must have some function in the development of the xanthoma^{11,12}. The author suggests that MF may develop in local tissues, which have been altered by processes such as inflammation and may result in reticular endothelial cell hyperplasia. Also lipoprotein has been shown to leak through the dermal vessels, and therefore normocholesteromic xanthoma may tend to develop as the result of reticuloendothelial cell hyperplasia and secondary histiocyte or macrophage lipidization^{9,12}. Another hypothesis involves the association of xanthoma with lymphoproliferative disease. In cases of lymphoproliferative disease, activated T-cells secrete chemotactic factors which can then activate local endothelial cells. This phenomenon is coupled with the aggregation of circulating monocytes, but

otherwise progresses in a manner concordant with the first hypothesis. Also, activated T-cells may secrete lymphokines, which then induce macrophage activation, and directly accelerate lipid phagocytosis. This indicates that xanthoma may be associated with multiple myeloma, leukemia/lymphoma, MF, and Waldenstrom's macroglobulinemia. We see our case as being akin to the case in which xanthomatosis developed into MF in a hyperlipoproteinemic patient. In previous cases of xanthomatosis, the foam cells have been described as both histiocytes and xanthoma, sites overlapping with MF lesions. However, in our case, lipid-laden cells with atypical nuclei were determined to be neoplastic T-cells. This demonstration of lipid-laden neoplastic T-cells is unique and is also fundamentally different from the lipidized histiocytes referenced in the previously reported cases. Immunohistochemical studies have demonstrated that many of the detected lipid-laden cells were, in fact, phenotypically consistent with helper T-cells. Interactions occurring between lipoproteins and T-cells have recently been subjected to closer scrutiny¹². Some studies have also shown that T-cell-macrophage interactions are instrumental to the formation of atherosclerotic fatty plaques^{13,14}. It has been explained that lymphokines secreted by the activated T-cells are able to activate macrophages and regulate the uptake of lipoproteins. T-cells are known to express membrane-bound LDL receptors, and activated T-cells have been shown to express an increased number of these receptors¹⁵. The presence of lipids within these MF cells might be attributable to an increase in the number of LDL receptors on increasingly "activated" cells, and this might serve to further increase the number of lipid-laden T-cells¹⁵. These cells have been shown to induce macrophage phagocytosis, followed by the formation of foamy cells and the development of the characteristic xanthoma lesions.

In conclusion, the LDL receptors on the T-cells are increased as the result of T-cell activation, and T-cells are directly involved in the processing of lipoproteins, as well as the formation of lipid-laden T-cells. The immunohistochemical staining of xanthoma lesions reveals a large quantity of T-cell marker-positive cells. This finding supports our hypothesis. Our patient represents a unique case of eruptive xanthomatosis with MF.

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