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Intralymphatic Histiocytosis with Massive Interstitial Granulomatous Foci in a Patient with Rheumatoid Arthritis

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Dear Editor:

Intralymphatic histiocytosis (ILH) is a rare cutaneous manifestation of rheumatoid arthtritis (RA) which is characterized by the presence of histiocytes in dilated dermal lymphatic vessels[1]. We describe here a case of ILH with massive interstitial granulomatous foci mimicking interstitial granulomatous dermatitis (IGD)[2] in a patient with RA.

A 56-year-old Japanese man with RA for 2 years who had been treated with prednisolone, methotrexate and adalimumab was referred to our department in December 2014 for evaluation of his skin lesion. Physical examination revealed slightly tender erythematous nodules on the right knee which was slightly swollen (Fig. 1A). The skin lesions had first appeared 2 years ago and disappeared spontaneously in a couple of days. They had recurred several times and gradually become refractory. Laboratory finding disclosed an elevated level of matrix metalloproteinase-3 (199.7 ng/ml, normal 36.9～121.0 ng/ml). The skin biopsy specimen showed several irregularly dilated vessels which contained numerous mononuclear cells in the upper dermis (Fig. 1B, C). Immunohistochemically, these mononuclear cells stained positively for CD68 (Fig. 1D) and endothelial cells lining the vessels were positive for D2-40 (Fig. 1E). In addition, there was a dense interstitial histiocytic infiltrate admixed with a few interspersed neutrophils which surrounded the degenerative collagen bundles (Fig. 1B, F). Neither vasculitis nor thrombosis was present. The histological diagnosis of ILH with massive interstitial granulomatous foci was made. He was treated with a topical application of a very strong class of corticosteroid with remarkable effect and no recurrence.

Clinically, the lesions of ILH were located predominantly on the limbs, and they consisted of erythematous plaques and livedo reticularis-like lesions[3]. The dominant manifestation of IGD was erythematous papules and plaques on the trunk and proximal limbs[4]. An inflammatory response of variable intensity was also present in the adjacent dermis of ILH. This inflammatory infiltrate was composed mostly of small mature lymphocytes and a variable number of histiocytes[3]. The denser interstitial histiocytic infiltrate mimicking IGD seems to be a characteristic feature of our case compared with previous reports of ILH. Interstitial granuloma annulare (IGA) may be difficult to distinguish from IGD histologically. Generally, in IGA the histological changes are focal, not diffuse as in IGD[4].

Although the cause of ILH remains unknown, the clinical finding that ILH develops at inflamed juxtra-articular sites indicates that chronic inflammation could be the cause of lymphostasis with subsequent development of lymphangiectases[5]. Lymph stasis may lead to poor clearance of antigen, localized immune dysfunction, and persistent inflammation which may stimulate histiocytes to proliferate and aggregate in the lymphatic vessels[3]. Although the mechanism of ILH with massive interstitial granulomatous foci remains unclear, chronic inflammation induced by RA may cause this condition. One possible explanation is that as a result of strong activation of histiocytes due to

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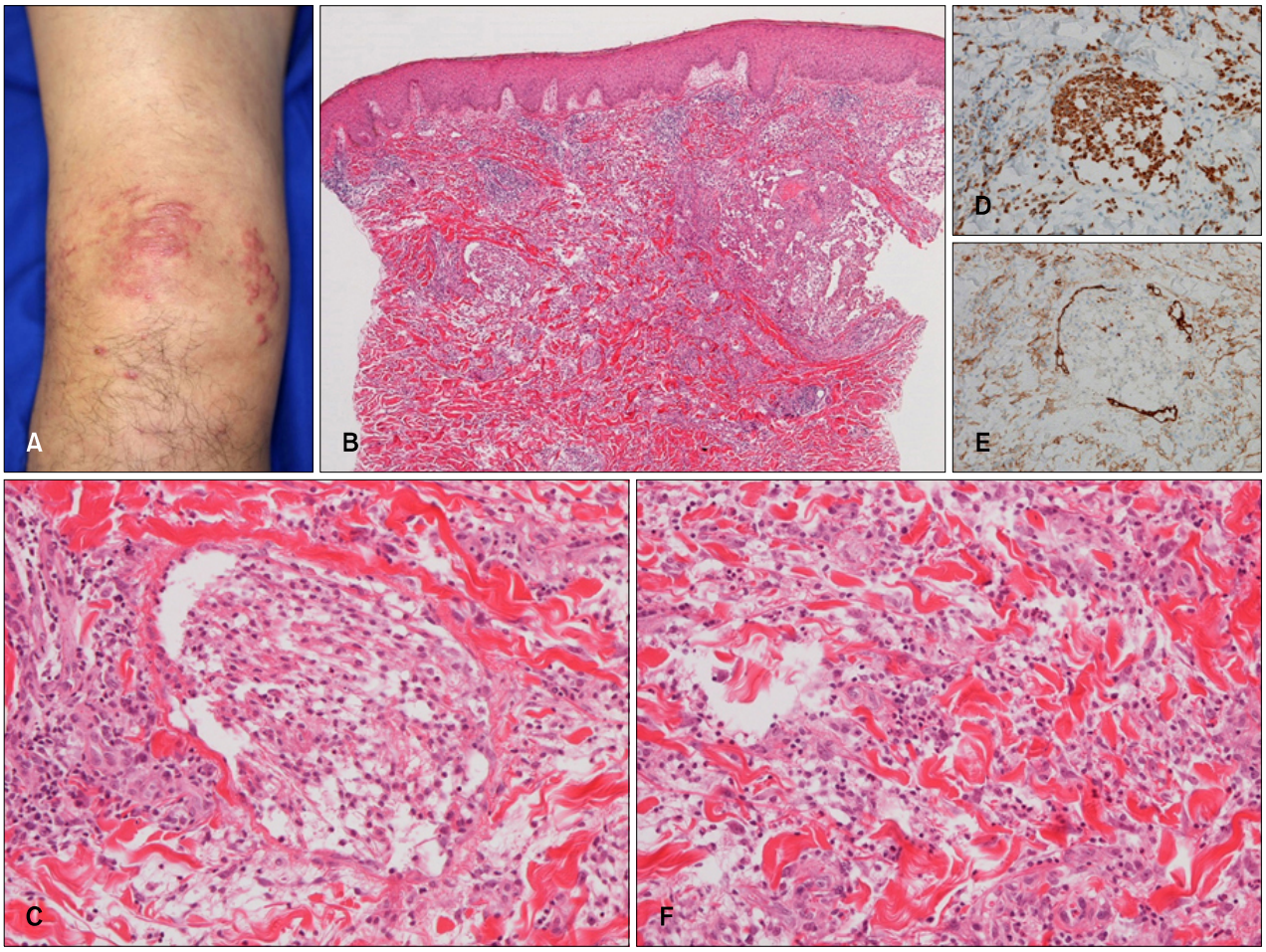

Fig. 1. (A) Slightly tender erythematous nodules on the right knee which was slightly swollen. (B) The skin biopsy showed several irregularly dilated vessels which contained numerous mononuclear cells and interstitial histiocytic infiltrates in the upper dermis (H&E, ×40). (C) A dilated vessel which contained mononuclear cells (H&E, ×200). (D) Mononuclear cells stained positively for CD68 (anti CD68, ×200). (E) Endothelial cells lining the vessels were positive for D2-40 (anti D2-40, ×200). (F) A dense interstitial histiocytic infiltrate admixed with a few interspersed neutrophils which surrounded the degenerative collagen bundles (H&E, ×200).

RA, proliferated histiocytes in the lymphatic vessels leak out to the dermis, which may partially contribute to the formation of a dense interstitial histiocytic infiltrate. Because there are some reports of IGD induced by tumor necrosis factor-α inhibitors, the possibility remains that adalimumab had something to do with IGD like changes in our case.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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