CASE REPORT

Venous Leg Ulcer in a Sarcoidosis Patient: A Case Report

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Venous leg ulcers, the most common form of leg ulcers, are relevant to the pathogenicity of pericapillary fibrin cuff. Sarcoidosis, a multiorgan granulomatous disease, causes fibrin deposition in tissues. We report a case of a 50-year-old man with venous leg ulcers coexisting with sarcoidosis. On the basis of the histologic findings, we propose the hypothesis that sarcoidosis patients are prone to the development of venous leg ulcers. (*Ann Dermatol* 27(6) 744~747, 2015)

-Keywords-

Capillaries, D-dimer, Fibrin, Sarcoidosis, Venous leg ulcer

INTRODUCTION

The risk factors for venous leg ulcers include old age, obesity, varicose veins, a history of significant leg injury, phlebitis, and heart disease¹. Here, we describe an aged Korean male patient with venous leg ulcers and hyperpigmentation on both lower legs, who was consequently found to have sarcoidosis. We consider that this patient may provide a basis for an association between venous leg ulcers and sarcoidosis.

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CASE REPORT

A 50-year-old man presented with painful ulcers and hyperpigmentation on both lower legs (Fig. 1A). He also showed extensive annular pigmentary skin lesions on the chest and upper back. The lesions began to develop several years ago and had deteriorated recently, within the last year. Ulcers were found on both ankles, as well as the lower third part of both lower legs, with yellowish material, accompanied by mild lower-leg pitting edema. In addition, he complained of multiple erythematous macules with ulcer and crust on the torso, accompanied by pruritus (Fig. 1B).

The pulse of the dorsalis pedis artery was well palpable on physical examination, and the ankle-brachial index was measured as 1.18, which is within the reference range. There was no specific finding in the laboratory examinations, except for an elevated plasma fibrinogen level of up to 516 (reference range, 170~350). To exclude pulmonary vein thrombosis and deep vein thrombosis, chest computed tomography and leg magnetic resonance imaging were performed. They showed multiple bronchial lymph node enlargements instead of deep vein thrombosis and atherosclerosis. Skin biopsies were performed in the lower leg (Fig. 2) and chest (Fig. 3). In the histopathologic examination of the leg specimen, fibrin material overlying the epidermis, dermal fibrosis, perivascular lymphocytic infiltration, and extravasation of red blood cells were observed. In the histopathologic examination of the chest specimen, no specific finding other than inflammatory skin reactions, like perivascular lymphocytic infiltration without evidence of granulomatous inflammation, was noted. A lymph node biopsy was obtained through endobronchial ultrasound-guided transbronchial needle aspiration, which showed chronic granulomatous inflammation with multinucleated giant cells. The result of the interferon-gamma release assay was negative. There was a de-

Fig. 1. (A) Painful ulcers with yellowish material and hyperpigmentation on both lower legs, especially on both ankles. (B) Multiple erythematous macules with ulcer and crust on the torso.

Fig. 2. (A) Thick eosinophilic material layer overlying the spongiotic epidermis. (B) Dermal fibrosis and perivascular lymphocytic infiltration. (C) Extravasation of red blood cells with lymphocytes in the dermis. A~C: H&E.

creased diffusing capacity of the lungs for carbon monoxide of 68%, representing a restrictive pattern in the lung function test.

On the basis of these findings, sarcoidosis was diagnosed. He was referred to the department of rheumatology and prescribed with 4 mg methylprednisolone every other day for the treatment of sarcoidosis. His cutaneous lesions on the torso and lower legs were diagnosed as nonspecific lesions of cutaneous sarcoidosis and venous leg ulcers, respectively. Pentoxifylline (400 mg) and folic acid (1 mg)

were administered on a daily basis, in addition to methylprednisolone. After 5 weeks, the lower-leg ulcers were healed, leaving hyperpigmentation. Moreover, the skin lesions on the torso were much improved, with decreased associated symptoms such as pruritus.

DISCUSSION

Venous leg ulcers account for more than half of all chronic leg ulcers². It is known that there are several risk factors

Fig. 3. (A) Focal parakeratosis with acanthosis. (B) Perivascular lymphohistiocytic infiltration in the dermis. A, B: H&E.

Fig. 4. Pathophysiologic hypothesis: accelerated venous leg ulcer formation in a sarcoidosis patient.

for venous leg ulcers¹. However, the present patient did have not any of the risk factors for venous leg ulcers, such as obesity, old age, smoking, deep venous thrombosis, history of significant leg injury, diabetes, hypertension, and hypercholesterolemia. The diagnosis of sarcoidosis was the only specific factor.

To date, it is known that chronic venous insufficiency is responsible for the development of venous ulceration. However, there is no agreement on the pathogenic mechanism. Burnand et al.³ and Pardes et al.⁴ suggested a hypothesis that pericapillary fibrin cuff impedes oxygen and nutrient diffusion, which leads to a dermal microenvironmental change that induces cell damage and delayed wound healing. In addition, chronic venous insufficiency causes distension of the vessel wall and hemoconcentration in the capillary⁵, which makes the vascular structure more permeable. Consequently, macromolecules, such as fibrinogen, leak into the extravascular space, forming pericapillary fibrin cuffs.

Falanga et al.⁶ and Falanga⁷ found increased plasma total fibrin-related antigen and D-dimer level in patients with venous disease, reflecting elevated fibrin formation in the body. In addition, it was observed that fibrin cuff encircles

the dermal capillary of the venous ulcer lesion on direct immunofluorescence.

Sarcoidosis is a multiorgan granulomatous disease with unknown etiology and with variable skin manifestations^{8,9}. Especially, leg swelling has been described as a non-specific symptom of sarcoidosis¹⁰, which means that a patient with sarcoidosis would have chronic venous insufficiency. An immunopathological study has revealed that a fibrin network was observed within the granulomas¹¹. D-dimer, a fibrin degradation product, is elevated in the bronchoalveolar lavage fluid and plasma in patients with pulmonary sarcoidosis¹². Moreover, its level is associated with disease activity¹³.

Overall, both venous leg ulcers and sarcoidosis have common histologic manifestations and biochemical findings, with respect to fibrin deposition in the tissue and elevated D-dimer level in plasma. Furthermore, they share some pathophysiologic processes in terms of chronic venous insufficiency.

On the basis of these findings, it may be hypothesized that sarcoidosis could manifest as chronic venous insufficiency, which causes venous leg ulcer. Moreover, the greater the severity of sarcoidosis, which indicates a high-

er level of fibrin in plasma, the more accelerated the formation of fibrin cuffs and venous leg ulcers will be (Fig. 4). To the best of our knowledge, the association between sarcoidosis and venous leg ulcers has never been previously reported. In this report, we present the hypothesis that sarcoidosis patients are at a higher risk to develop venous leg ulcers, on the basis of the clinical manifestation and the common pathology between the two different diseases. To determine this correlation, further molecular and epidemiologic studies with a large population are needed.

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