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CASE REPORT

Cutaneous Sarcoidosis Clinically Mimicking Necrobiosis Lipoidica in a Patient with Systemic Sarcoidosis

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A 70-year-old woman with an 8-year history of systemic sarcoidosis developed round, red-brown eruptions, with central atrophic lesions on her lower legs. The features of the biopsy specimen resembled those of necrobiosis lipoidica (NL), but although necrobiosis was present there were well-formed non-necrotizing granulomas in the dermis. The histological diagnosis was cutaneous sarcoidosis. Systemic sarcoidosis presenting with NL has rarely been reported. The histological features of cutaneous sarcoidosis sometimes mimic those of other granulomatous diseases, including NL and granuloma annulare, which are difficult to distinguish. We discuss the novel association between sarcoidosis and other granulomatous diseases. **(Ann Dermatol 24(1) 74～76, 2012)**

-Keywords-
Granuloma, Necrobiosis lipoidica, Sarcoidosis

INTRODUCTION

Necrobiosis lipoidica (NL) is a granulomatous skin disease strongly associated with diabetes mellitus (DM)[1]. Sarcoidosis, which is also a multisystem granulomatous disorder, has sometimes been complicated by other granulomatous diseases such as NL, granuloma annulare (GA), and rheumatoid nodules[2]. Several cases of concomitant NL and sarcoidosis in the same patient have been reported[3-5]. This report describes a case of systemic sarcoidosis in which lesions on the skin of the leg had features of NL. We discuss the clinical presentations and pathological findings of this case in comparison with those in previous reports.

CASE REPORT

A 64-year-old woman presented to a dermatologist with a 3-year history (from 2000) of erythematous plaques on both lower legs. The erythematous plaques had nearly disappeared in response to treatment with topical corticosteroid ointment. In 2003, the patient was referred to our university with a chief complaint of breathlessness and blurred vision. An ophthalmological examination revealed mild binocular uveitis and vitreous opacity. A chest X-ray demonstrated bilateral hilar lymphadenopathy, and a computed tomography scan revealed diffuse small nodular shadows. Investigations into respiratory function revealed a restrictive lung disease pattern (%vital capacity was 67.4% of predicted, and forced expiratory volume in 1 second was 84.6% of predicted). The CD4/CD8 ratio in bronchoalveolar lavage fluid was 22.9. Serum examinations revealed elevated levels of angiotensin-converting enzyme (34.7 U/L; normal range: 6.0～22.0 U/L) and lysozyme (13.6 μg/ml; normal range: 5.0～10.2 μg/ml). The tuberculin reaction was negative. Based on these findings and the diagnostic criteria of the Japanese Ministry of Health, the patient was diagnosed clinically with systemic sarcoidosis. She was treated with corticosteroid

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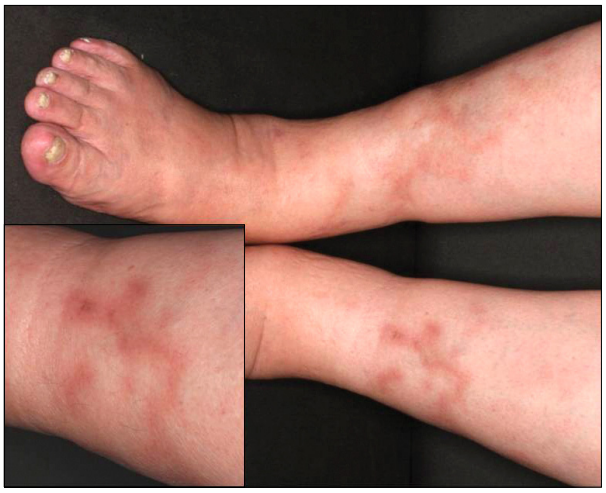

Fig. 1. Necrobiosis lipoidica-like skin lesions on both shins.

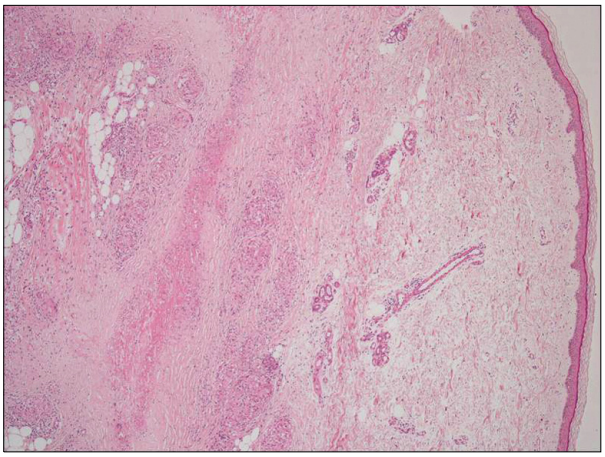

Fig. 2. Histopathology of the left shin skin lesion biopsy showed degeneration of collagen fibers in the dermis surrounded by inflammatory cells (H&E, ×40).

eye drops for the uveitis.

In 2009, the patient was referred to our dermatology department with a different skin eruption on the legs that had persisted for more than 2 years. A physical examination revealed multiple round and red-brown plaques, with atrophic lesions in the centers (Fig. 1). The clinical features appeared to be those of NL. Random blood-sugar testing and hemoglobin A1c analysis were within normal limits. The patient's systemic sarcoidosis was under control without the need for internal medication.

Skin biopsies from the edges of the atrophic lesions revealed areas of collagen degeneration, enclosed by inflammatory cells in the dermis (Fig. 2). Well-formed non-necrotizing epithelioid granulomas were evident around the degenerated collagen (Fig. 3), and plasma cells were present in places. The degenerated collagen

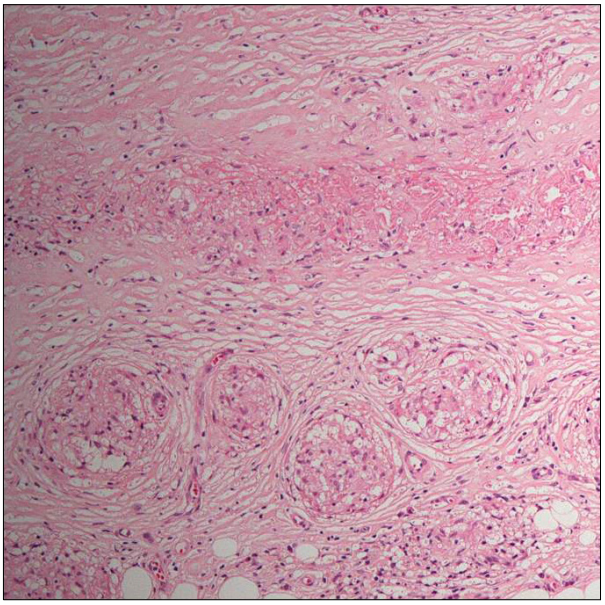

Fig. 3. High-power image shows epithelioid-cell granuloma formation around the dermal collagen degeneration (H&E, ×200).

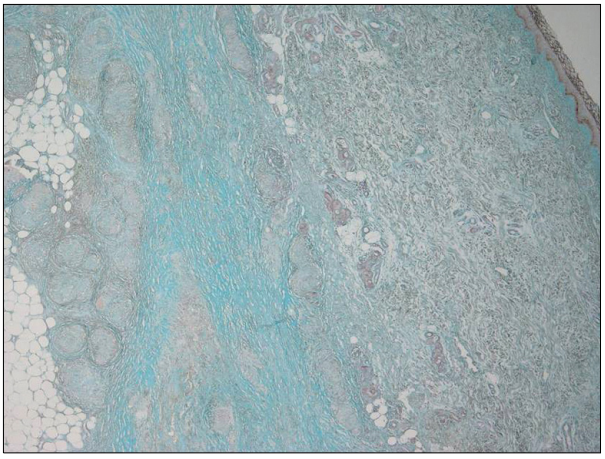

Fig. 4. Alcian blue staining reveals mucin deposits within the area of collagen degeneration (×40).

stained positively with alcian blue (Fig. 4). These histological findings were those of cutaneous sarcoidosis. Although the patient was treated with topical corticosteroid and tacrolimus ointment for several months, the necrobiotic lesions have remained unchanged.

DISCUSSION

Coexistence of NL and sarcoidosis in the same patient has been reported in several studies[3-5]. Interestingly, these cases shared a couple of features. All patients were females aged 35～62 years, and none of the patients

showed evidence of DM or glucose intolerance. Additionally, the rashes in all cases developed on the legs, which histopathologically showed epithelioid granulomas in the dermis. In the past, it was considered that NL developed as a result of diabetic microangiopathy, and this was supported by a report that the vessel walls in NL lesions become thickened with periodic acid-Schiff- positive materials and immunoglobulin[6]. However, a substantial number of patients with NL have neither DM nor thickening of vascular walls[1].

The patients reported in these studies had NL-like lesions and systemic sarcoidosis.

Although the skin eruptions were compatible with a diagnosis of NL based on the clinical and histological examinations, whether the occurrence of sarcoidosis and NL in the same patient was coincidental or due to an association of these two disorders was unclear. Sarcoidosis is a multisystem granulomatous disorder of unknown etiology. Complications of sarcoidosis by other granulomatous diseases such as GA[2], nodular rheumatoid arthritis[7], or Crohn's disease[8] have been described in several cases. For this reason, it is expected that sarcoidosis and other granulomatous diseases may be directly related and that the cellular signal mechanisms in these two diseases are similar. Furthermore, Macaron et al.[9] have demonstrated that granulomatous lesions, including cutaneous sarcoidosis, NL, and GA, highly express glioma- associated oncogene homolog (*gli*)-1. *Gli*-1 is a member of one of the zinc finger transcription factor families; these factors regulate the expression of genes involved in many important cellular signaling processes such as embryonic development and cellular differentiation. This finding suggests that the mechanism of granuloma formation overlaps among the various cutaneous granulomatous disorders.

Typical NL can usually be easily distinguished from classical cutaneous sarcoidosis. NL is characterized by lesions containing necrobiotic collagen fibers surrounded by palisading histiocytes in the dermis. The necrobiotic foci sometimes contain mucin. NL can also be of the tuberculoid type, in which case granulomatous lesions may develop. In contrast, sarcoidosis is defined by well-formed epithelioid cell granulomas; however, necrobiotic changes can occur within the lesions in some patients with sarcoidosis[10]. In such cases, making a distinction between NL and sarcoidosis becomes a challenge. Our patient had systemic sarcoidosis with NL-like lesions, but the histological features were similar to those of skin sarcoidosis, with uniform accumulation of epithelioid cells forming separate non-caseating granulomas around the necrotic foci. Ball et al.[11] showed that the histological features of some patients with known systemic sarcoidosis resemble those of other granulomatous diseases, such as tuberculoid leprosy, rosacea, NL, GA, and lichenoid inflammations caused by syphilis. Their findings suggest that the histological changes in cutaneous sarcoidosis are more diverse than were previously recognized. According to this alternative viewpoint, the NL-like lesions in this patient might be a form of histological change in cutaneous sarcoidosis. Thus, we scsuggest that the possibility of associated sarcoidosis should always be considered and investigated in an appropriate manner in patients with NL, particularly without DM.

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