A Case of Systemic Sclerosis with Sarcoidosis

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Sarcoidosis is a Th1-mediated multisystem granulomatous disorder characterized by lymphadenopathy, internal organ involvement, and a variety of skin lesions. Systemic sclerosis (SSc) is a multisystem autoimmune disorder characterized by vascular injuries and fibrosis of the skin and various internal organs. Th2 polarized immune responses have been shown in the early and active stage of SSc (1). We report here a case of rare overlap of SSc with sarcoidosis, occurring in a female patient with lupus pernio, sarcoid myopathy and interstitial lung disease (ILD).

CASE REPORT

A 59-year-old woman was referred to our hospital for further examination of sclerodactyly and muscle weakness. One year previously, Raynaud's phenomenon had developed on all fingers of both hands. Two months prior to presentation, sclerodactyly had developed. Muscle weakness was also seen. The patient's medical history revealed a radical operation for colon cancer when she was 52 years old. No cytotoxic drugs were administered after the surgery.

Physical examination revealed sclerosis and swelling of all fingers (Fig. 1a) and a shiny, up to egg-sized, sclerotic plaque on the right buttock (Fig. 1b). The patient also had indurated chilblain-like erythema on the palms (Fig. 1c). Raynaud's phenomenon and nailfold bleeding were seen. The strength of bilateral deltoid and triceps muscles was grade 4 (normal: 5) on manual muscle testing. Laboratory tests revealed positive serum anti-nuclear antibody (×320, speckled) and an elevated serum anti-U1 RNP antibody level of 131.1 Index (normal 0–21 Index). Anti-Sm, anti-topoisomerase I, anti-centromere, and anti-Jo-1 antibodies were all negative. The patient had an elevated level of C-reactive protein (CRP) 1.11 mg/dl (0–0.3 mg/dl), elevated creatinine phosphokinase (CK) 300 IU/l (0–50 IU/l), elevated aldolase 9.8 U/l (2.5–6.2 U/l), and elevated KL-6 571 U/ml (0–500 U/ml). Serum surfactant protein-D and calcium levels, and liver and kidney functions were all within normal ranges. Pulmonary function tests revealed that the percentage of predicted vital capacity was 92%, forced expiratory volume1.0/forced vital capacity 83%, and the percentage of predicted diffusing lung capacity for carbon monoxide 80%.

A skin biopsy was taken from the buttock sclerosis. Histopathology revealed thickened collagen bundles throughout the reticular dermis, especially in the deep dermis (Fig. 2a). According to the classification criteria proposed by LeRoy et al. (2), we diagnosed the patient with limited cutaneous SSc. Due to the clinical features of muscle weakness and elevated muscle enzymes, we suspected that she also had polymyositis. Magnetic resonance imaging showed inflammation in the left deltoid muscle. Histopathological examination of the left deltoid muscle showed non-caseating granulomas with Langhans' giant cells between muscle fibres (Fig. 2b and c). Lymphocytic infiltration and slight degeneration of muscle fibres were also seen, but not to a degree that could be labelled polymyositis. Based on these findings, we diagnosed her muscle involvement as sarcoid myopathy. Serum lysozyme was elevated to 11.0 μg/ml (normal 5.0–10.2 μg/ml), while angiotensin-converting enzyme was normal. Tuberculin skin test showed negative reaction. Computed tomography of the chest showed mediastinal and bilateral hilar lymphadenopathy, and ground-glass opacity in the basal segment of both lungs. We also took a skin biopsy from the indurated erythema on the right palm. Non-caseating granulomas were seen in the dermis and adipose tissue (Fig. 2d). Extensive studies failed to reveal other organ involvements, including ocular lesions, neurosarcoidosis, and myocardial sarcoidosis. Oral prednisone was started at a dose of 30 mg/day. Serum CK and CRP levels were normalized after 8 days. Skin lesions including buttock sclerosis, ILD, and hilar lymphadenopathy also responded to the treatment. Prednisone was tapered gradually to 17.5 mg/day with no relapse of sarcoidosis-associated symptoms during the 9-month follow-up period.

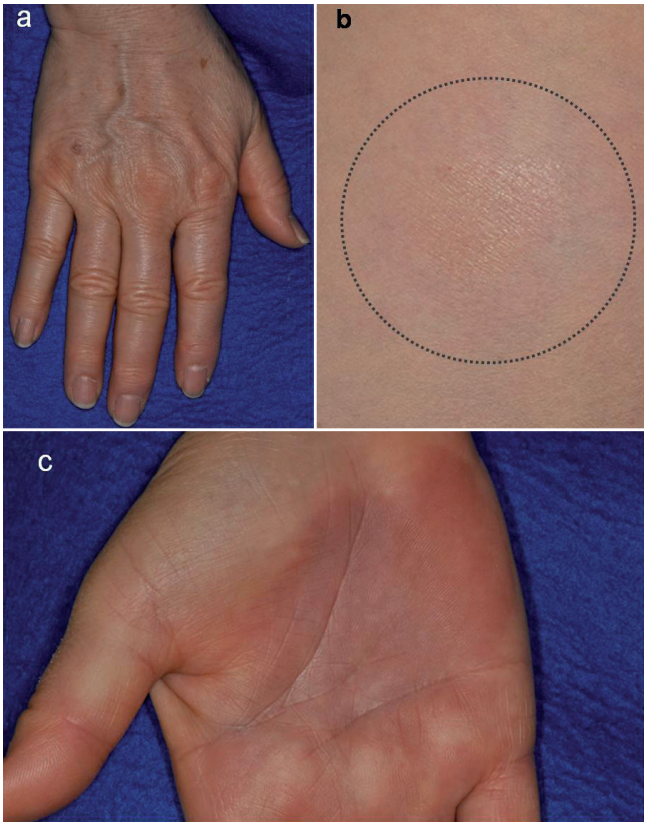

Fig. 1. (a) Sclerosis and swelling of all fingers. (b) A shiny and up to egg-sized sclerotic plaque on the right buttock. (c) Indurated chilblain-like erythema on the palm.

DISCUSSION

To our knowledge, 21 overlap cases of sarcoidosis with SSc have been reported in the English literature

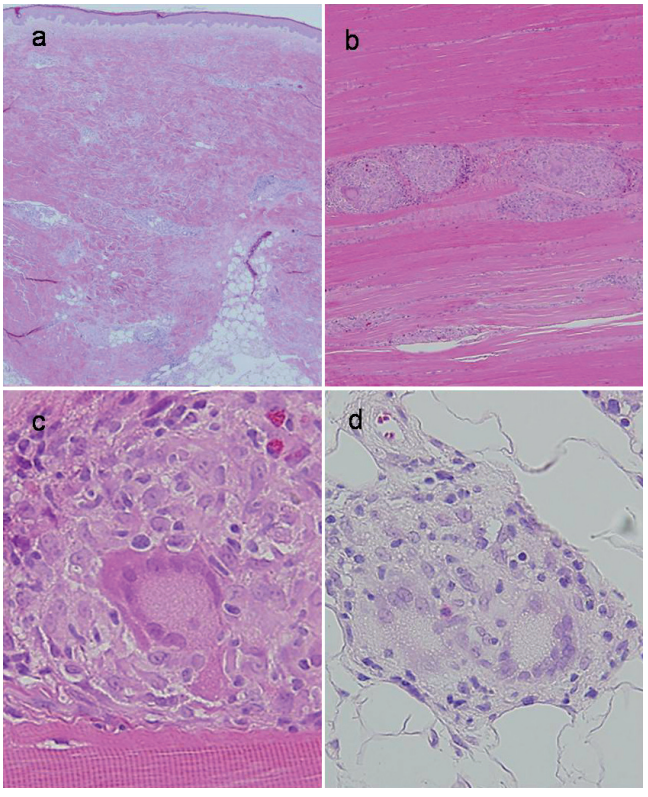

Fig. 2. (a) In the right buttock sclerosis, collagen fibres were increased and swollen throughout the reticular dermis, especially in the deep dermis (haematoxylin-eosin stain, original magnification ×40). (b) Non-caseating granulomas between muscle fibres, slight lymphocytes infiltration, and degeneration of muscle fibres were seen (×100). (c) Langhans' giant cells were seen (×400). (d) Non-caseating granulomas with Langhans' granuloma cells were also seen in the palmar chilblain-like erythema (×400).

(3–11). The incidence of the overlap cases appears to be lower than expected, given the incidence of sarcoidosis (50–400/million/year) and the incidence of SSc (20/million/year) (12, 13). The Th1/Th2 paradigm provides one possible explanation for this. For example, sarcoidosis has been reported to be associated with a low incidence of atopy and allergic diseases characterized by Th2 immune responses (14). On the other hand, atopy improves the disease activities and the clinical courses of several Th1-mediated diseases, such as rheumatoid arthritis, multiple sclerosis, and sarcoidosis (15). Given that Th2 immune responses are predominant in the early and/or active stage of SSc (1), the overlap of Th1-mediated sarcoidosis with early and/or active SSc should theoretically be rare.

When assessing the clinical relevance of SSc with sarcoidosis, it is important to focus on the cases in which SSc precedes sarcoidosis, or in which the two diseases develop simultaneously, because sarcoidosis may be self-limiting. Therefore, we scrutinized the previously reported 9 cases meeting this criterion (3, 4). Although ILD existed in most of the cases, exacerbation of ILD that was probably due to sarcoidosis was not reported. Given that ILD is progressive and life-threatening in a certain subset of sarcoidosis, these previous observations suggest that the clinical course of sarcoidosis associated with SSc is milder than others, supporting the conventional Th1/Th2 paradigm, as described above. Importantly, this was also the case in our patient. She developed SSc and sarcoidosis simultaneously and she had ILD and myopathy associated with sarcoidosis. However, both of these involvements were mild, and fairly responsive to corticosteroid. Thus, the co-existence of SSc with sarcoidosis may serve as a useful clinical clue to predict a milder disease course of sarcoidosis.

Sarcoidosis in SSc is probably often misdiagnosed because organ involvements in sarcoidosis are quite similar to those of many other collagen diseases. Lupus pernio is clinically similar to chilblain erythema and can be misdiagnosed in association with impaired peripheral circulation, such as SSc. ILD frequently occurs in both sarcoidosis and SSc. Furthermore, myositis occasionally coexists with SSc, and it is indistinguishable from sarcoid myopathy without muscle biopsy, especially in cases in which muscle weakness is prominent in the proximal extremity muscle groups. Biopsy of the skin and/or muscle may be useful to determine the origin of ILD in cases with overlapping SSc and sarcoidosis.

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