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A Case of Generalized Morphea with a High Titer of Anti-*Borrelia burgdorferi* Antibodies

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Abstract

A 69-year-old male had noticed pruritus on the back for the previous 3–4 years and cutaneous sclerosis with swelling of the dorsum of the neck had developed in the last one and a half years. However, he had never complained of Raynaud's phenomenon of the fingers, dry mouth, or dry eyes. At this first visit to our hospital, he complained of erythematous cutaneous sclerosis with swelling of the dorsum of the neck. Histopathological findings biopsed from the neck showed epidermal hyperplasia with elongation of rete ridges and homogeneous and fibromatous changes of the dermis with dense perivascular cell infiltration consisting of mononuclear cells or lymphocytes with several nests of incontinentia pigmenti. However, there were no sclerotic changes in blood vessels in the upper dermis biopsied from the forearm skin, although slightly homogeneous and fibromatous changes of the dermis were seen. In the clinical course, the cutaneous sclerotic change enlarged to extend to the bottom of the cheek, forearm, and lower legs. These clinical features and histopathological findings led to the diagnosis of generalized morphea. Hematologic examination showed positive anti-*Borrelia burgdorferi* IgM antibodies, although there were no positive anti-*Borrelia burgdorferi* IgG antibodies. These results revealed that there can be a close association of localized scleroderma with *Borrelia burgdorferi* and that generalized morphea may also represent a *Borrelia* infection.

Key words: generalized morphea; anti-*Borrelia burgdorferi* antibodies

Introduction

Recently, the possible association of *Borrelia burgdorferi* with localized scleroderma as well as other diseases such as lichen sclerosus et atrophicus (1), acrodermatitis chronica atrophicans (2), progressive facial hemiatrophy, benign lymphocytic infiltrate, and Shulman syndrome (3) has been a focus of clinical research and discussion, because these diseases include similar histopathological findings, including diffuse dermal fibrosis (4). We report a male case of generalized morphea with a high titer of anti-*Borrelia burgdorferi* antibodies and compare our data with those of other investigators (4–8).

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Case Report

A 69-year-old male visited the Department of Dermatology of Kumiai Hospital, Takayama City on January 4, 1996, because of a swelling with erythema on the dorsum of the neck for the past 3 to 4 months. He had never complained of Raynaud's phenomenon of the fingers, dry mouth, or dry eyes. He has worked in a chemical factory treating sulfuric acid gas for more than eight years. However, he neither complained of pruritus nor pain and seemed to be in good general health. He is taking cerebral metabolic agents because of a 15-year history of brain thrombosis. There was no relevant family history. At the first visit, physical examination disclosed a swelling and cutaneous sclerosis with erythema and pigmentation of the dorsum of the neck and back and lateral side of the abdomen (Fig. 1A, B & C); there were no pitting scars of the fingertips, pulmonary fibrosis, diffuse pigmentation of the

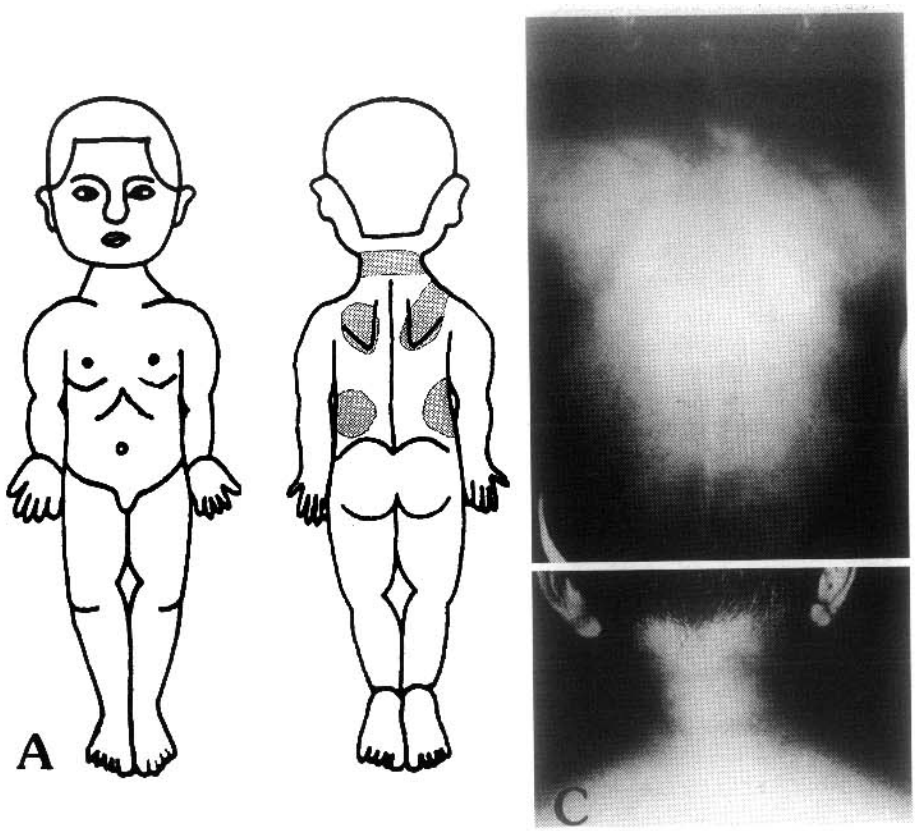

Fig. 1. Distribution of the eruptions (A) and the clinical features of the back (B) and the dorsum of the neck (C)

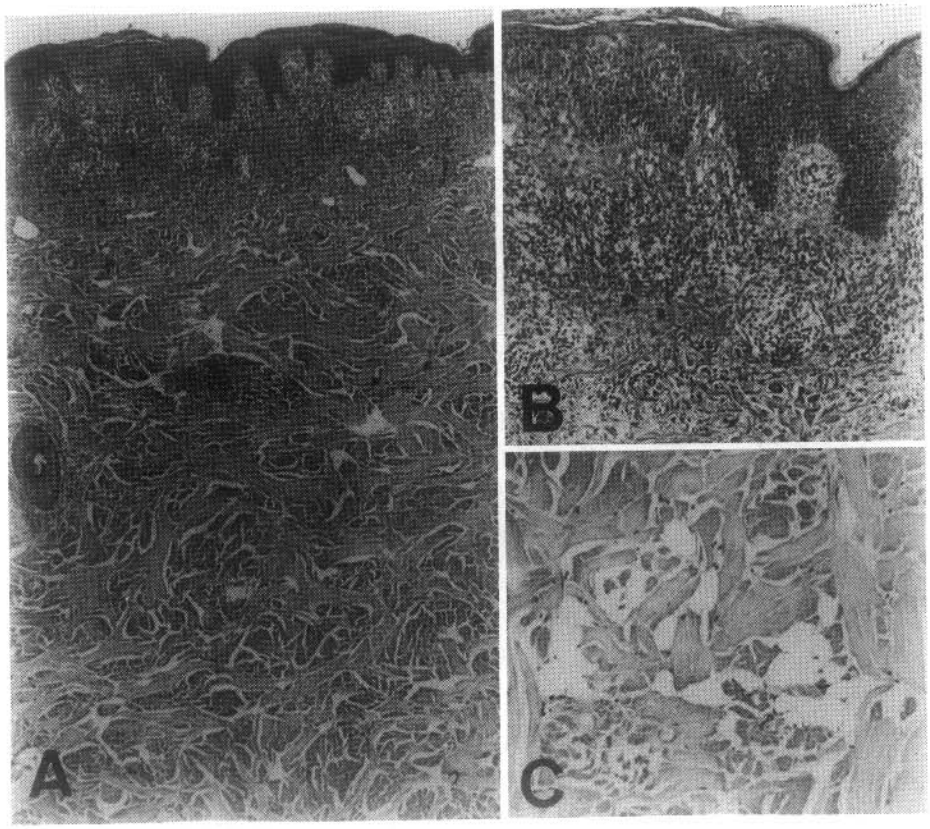

Fig. 2. Histopathological features of the dorsum of the neck (A, B and C)

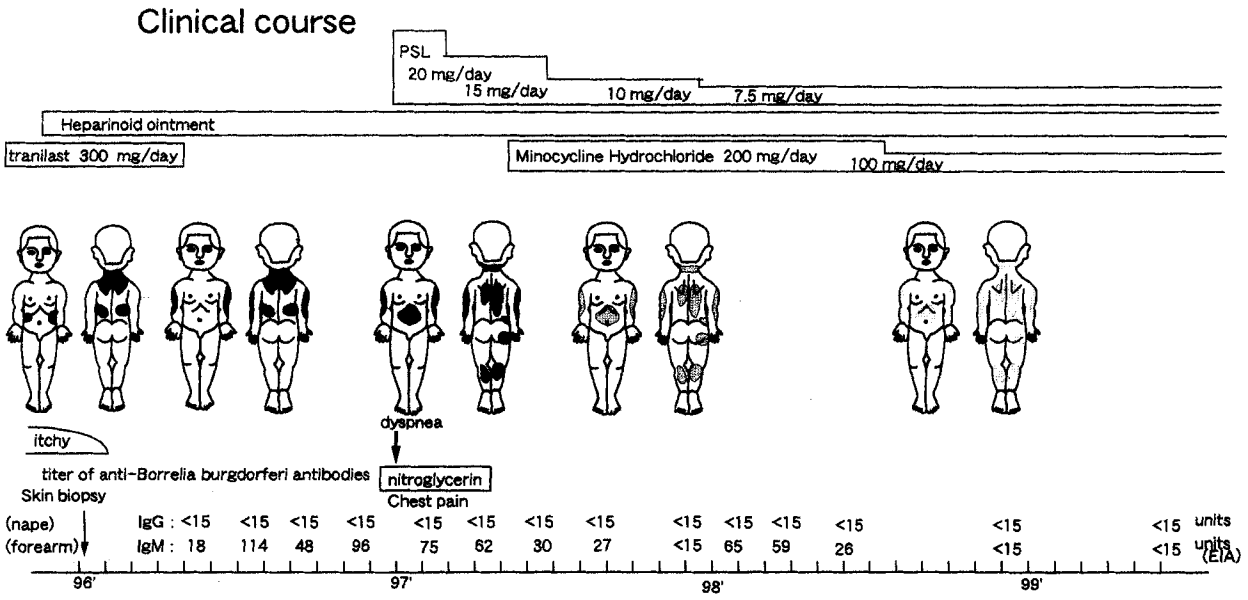

Fig. 3. Clinical course and treatment

whole body, or finger contracture. Results of routine laboratory investigations including blood counts and blood sedimentation rate (BSR) were elevated slightly (17 mm/a hour, 44 mm/two hours), although C-reactive protein (CRP), rheumatoid factor, and TPHA were negative. Hematologic examination showed hypergammaglobulinemia A (746 mg per dL), hypogammaglobulinemia M (76.6 mg per dL), and hypocomplementemia of C_4 (15.1 mg/dL) and CH_{50} (26.3 mg/dL). LE test, anti-nuclear antibodies (ANA), anti-ss-DNA, anti-SSA/B, anti-Scl-70 and anti-RNA antibodies were negative, and there was no hyperglycemia. Mantoux reaction was positive (20 × 18 mm). Electrocardiograph, cardiac echograph and respiratory function including %DLco were within normal limits. No fibrotic changes were detected in the chest CT film. Barium examination of the esophagus revealed no dilatation changes. Ophthalmologically, Schirmer's test was positive (right; 3 mm/left; 0 mm), but the fluorescein test was negative. Sialography of the parotid gland has not been done.

Histopathological examination of the neck skin, taken from a sclerotic area, revealed epidermal hyperplasia (approximately three times thicker) with elongation of rete ridges, thick and packed bundles of collagen in the lobular adipose connective tissue, and partial hyalinization of collagen bundles (Fig. 2a, b & c). In the upper dermis, there were several nests of incontinentia pigmenti, as shown in Figure 2b. At a higher magnification, there were perivascular mononuclear cells or lymphocytes and small blood vessels showed thickening and hyalinization. These clinical features and histopathological findings led to the diagnosis of generalized morphea.

Combined medication with perioral corticosteroid (PSL; 20 mg per day) and anti-allergic drugs for 4 months led to improvement of not only the pruritus but also the erythema and cutaneous sclerosis on the dorsum of his neck; however, similar, newly formed lesions gradually occurred in the upper arms six months after the first visit, and, one year later, an attack of anterior chest pain and slight dyspnea preceeded by 2 weeks the appearance of cutaneous sclerosis in the chest and lower abdomen. Perioral corticosteroid therapy (predonisolone; 20 mg per day) was started but had no good effect on the lesion. On the contrary, newly formed cutaneous sclerosis appeared on his bilateral cheeks, buttocks, and the flexor sides of his lower extremities. Then a four-week-trial of an anti-bacterial drug (tetracycline; 100 mg per day) produced good improvement of the cutaneous sclerosis. The

eruptions improved within 4–5 months after starting the tetracycline, and there has been no recurrence during the most recent six months (Fig. 3). The titer of anti-*Borrelia burgdorferi* IgM antibodies was significantly high during the clinical course. This was clearly not non-specific because a specific band was detected by the double immunodiffusion method. This result has been reconfirmed periodically. Additionally, the titer of anti-*Borrelia burgdorferi* IgM antibodies has gradually fallen with the oral administration of tetracycline. The titer finally normalized 9 months after the start of tetracycline.

Discussion

PSS is characterized by sclerodactylia, finger-contracture, pulmonary fibrosis, diffuse pigmentation, shortening of the tongue frenulum, and pitting scars of the fingertips, as described by Ishikawa (9). On the other hand, morphea (localized cutaneous scleroderma) is not usually associated with clinical signs other than cutaneous sclerosis, one of the most important clinical signs needed for the diagnosis. However, its etiology remains unclear, although Yamakage and Ishikawa reported that generalized morphea-like scleroderma, occurred in people exposed to organic solvents (10).

Recently, a possible association of *Borrelia burgdorferi* with not only morphea but also with lichen sclerosus et atrophicus and acrodermatitis chronica atrophicans has been the focus of clinical research by several authors (1–8), although the reliability of various *in vitro* techniques for identifying *Borrelia burgdorferi* infection is still unsatisfactory. These diseases have been thought to be chronic forms of borreliosis, because their histopathological findings such as fibrosis in the dermis were quite similar (4). Such observations have led several investigators to consider the possibility of *Borrelia burgdorferi* as a common etiologic factor among all of these diseases, because infection due to *Borrelia burgdorferi* is thought to play an important role in the development of sclerosis in the dermis (8). In our case, we have no further evidence that *Borrelia burgdorferi* infection can cause a disease such as generalized morphea other than the elevated titer of anti-*Borrelia burgdorferi* antibodies. However, we measured the titer of anti-*Borrelia burgdorferi* antibody eight times during the clinical course of one year and found that the improvement in the cutaneous sclerosis paralleled the reduction of anti-*Borrelia burgdorferi* antibody titer after the administration of tetracycline, another evidence of *Borrelia burgdorferi* infection. Our experience with this case may help resolve the pathogenesis of not only morphea but also of similar diseases such as lichen sclerosus et atrophicus and acrodermatitis chronica atrophicans in the future.

References

1) Fujiwara H, Fujiwara K, Hashimoto K, et al: Detection of *Borrelia burgdorferi* DNA (*B garinii or B afzelii*) in morphea and lichen sclerosus et atrophicus tissues of German and Japanese but not of US patients, *Arch Dermatol,* **133**: 41–44, 1997.
2) Aberer E, Stanek G, Ertl M, Neumann R: Evidence for spirochetal origin of circumscribed scleroderma (morphea), *Acta Derm Venereol,* **67**: 225–231, 1987.
3) Abele DC, Anders KH: The many faces and phases of borreliosis II, *J Am Acad Dermatol,* **23**: 401–410, 1990.
4) DeVito JR, Merogi AJ, Vo T, et al: Role of *Borrelia burgdorferi* in the pathogenesis of morphea/scleroderma and lichen sclerosus et atrophicus: A PCR study of thirty-five cases, *J Cutan Pathol,* **23**: 350–358, 1996.
5) Buechner SA, Lautenschlager S, Itin P, Bircher A, Erb P: Lymphoproliferative responses to *Borrelia burgdorferi* in patients with erythema migrans, acrodermatitis chronica atrophicans, lymphadenosis benigna cutis, and morphea, *Arch Dermatol,* **131**: 673–677, 1995.
6) Halkier-Smgensen L, Kragballe K, Hansen K: Antibodies to the *Borrelia burgdorferi flagellum* in patients with scleroderma, granuloma annulare and porphyria cutanea tarda, *Acta Derm Venereol,* **69**: 116–119, 1989.
7) Schempp C, Bocklage H, Lange R, Kolmel HW, Orfanos CE, Gollnick H: Further evidence for *Borrelia burgdorferi* infection in morphea and lichen sclerosus et atrophicus confirmed by DNA amplification, *J Invest Dermatol,* **100**: 717–720, 1993.
8) Aberer E, Klade H: Cutaneous manifestations of Lyme borreliosis, *Infection,* **19**: 284–286, 1991.
9) Ishikawa H: Revised diagnostic criteria for progressive systemic sclerosis, *Ryumachi,* **24**: 198–203, 1984.
10) Yamakage A, Ishikawa H: Generalized morphea-like scleroderma occuring in people exposed to organic solvents, *Dermatologica,* **165**: 186–193, 1982.