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LETTER TO THE EDITOR

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Localized cutaneous nodular amyloidosis in a patient with primary Sjögren syndrome: A revisit of autoimmunity-modifying clinicopathology through an updated literature review

Dear Editor,

Localized cutaneous nodular amyloidosis (LCNA) is a rare clinical form of cutaneous amyloidosis characterized by deposition of AL amyloid fibrils from immunoglobulin light chain in the dermis. Reports suggest an association with hematopoietic or autoimmune disorders, particularly Sjögren syndrome (SS),[1] although knowledge regarding the clinicopathological modification of LCNA with or without SS is limited. We describe a representative case of LCNA with primary SS and comprehensively reviewed to update the clinical characteristics of this complication.

An 88-year-old Japanese woman presented a 6-month history of elastic hard, multiple cutaneous nodules distributing on the back and chest (Figure 1A,B, respectively). Abnormal laboratory data showed a higher serum immunoglobulin G (2552 mg/dL; ref. <1700 mg/dL) with increased kappa and lambda free light chains (77.8 mg/L; ref. <19.4 mg/L and 54.6 mg/L; ref. <26.3 mg/L, respectively), although the serum kappa/lambda ratio was normal. She was positive for antinuclear antibodies (17.9; ref. <1.0 relative ratio), and anti-SS-A and anti-SS-B antibodies (>240 U/mL and 197.7 U/mL, respectively). She complained of dry eye and dry mouth. Histopathology of the skin nodules revealed diffuse and intense deposition of monomorphous materials throughout the dermis, surrounded by lymphocytes and plasmacytes (Figure 1C). The deposit was positive with Congo-red staining (Figure 1D), consistent with amyloid. Serum immunoelectrophoresis revealed no monoclonal gammopathy. A whole-body computed tomography showed no systemic amyloid deposition. Ophthalmic examination revealed a reduction of tear productivity and corneal dryness. She was diagnosed as LCNA with primary SS. Her skin nodules were decreased gradually in size and number without treatments, and never recurred thereafter.

LCNA is highly associated with SS (25%–60%), which mostly appears prior to the onset of cutaneous amyloidosis.[2,3] The high incidence of SS may support the prolonged activation of locally infiltrating plasmacytes, leading to the consequence of immunoglobulin overproduction as amyloidogenic protein.[4] To date, there have been 25 cases of SS-plus LCNA, including ours (Table 1). Their clinical characteristics identified a female predominance that may reflect the high incidence of SS. The skin lesions tended to develop on the trunk and extremities (18 and 13 cases, respectively), especially the abdomen, waist, and lower limbs. The onset of SS had no obvious tendency; 13 patients developed SS prior to LCNA, while 10 patients had SS after the development of LCNA. For the former, the period from the diagnosis of SS to the onset of LCNA varied (1-30 years). The number of male Japanese patients was much higher in SS-minus LCNA than in SS-plus disease (20/31, 64.5% vs 3/20, 15.0%, respectively; Table 2). Moreover, a majority of SS-minus LCNA developed on the head alone (*eg*, scalp, lip, nose, and neck) (24/31, 77.4%) but not on the trunk where the most affected site in SS-plus LCNA, although a limitation of our reviewing includes inconclusive statements for the diagnosis of SS in 16 of 31 SS-minus LCNA. The predisposition of gender and affected site differences is likely due to local irritation and minor traumatization,[5] as much as sun exposure. Together, LCNA may represent the clinical profile highly susceptible to SS.

INFORMED CONSENT

Obtained.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

Yasuyuki Yoshida MD
Noritaka Oyama MD, PhD
Minoru Hasegawa MD, PhD

Department of Dermatology, Faculty of Medical Sciences, University of Fukui, Fukui, Japan

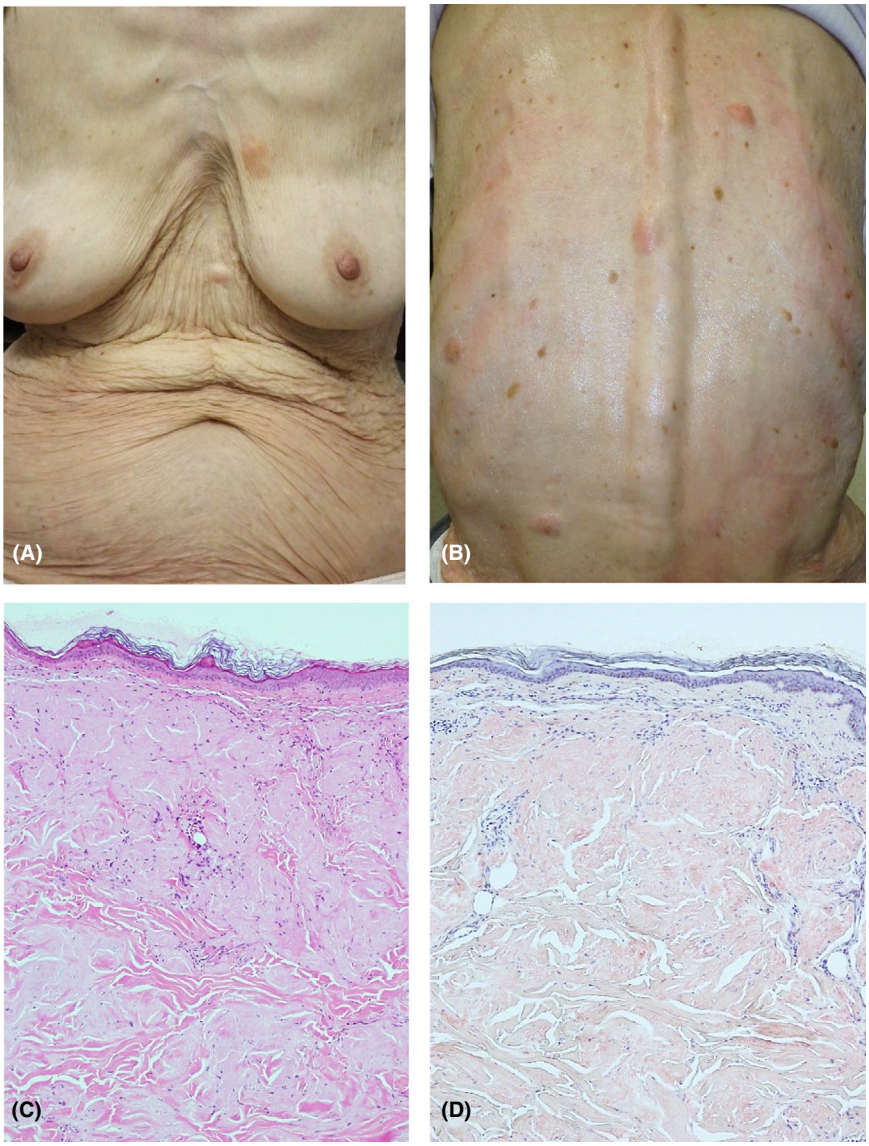

FIGURE 1 Multiple subcutaneous nodules on the chest (A) and back (B). The lesional skin pathology showing the excess deposition of monomorphous materials throughout the entire dermis, surrounded by lymphocytes and plasmacytes (HE × 100) (C). The materials showing positive with Congo-red staining (×200) (D)

TABLE 1. Summary of 25 cases of LCNA with SS

Sex	Male: 3, female: 22
Age	35-88 years (average 59.3 y)
Numbers of LCNA lesions	Multiple: 18, single: 7
Affected site of LCNA	Trunk: 18, extremities: 13, head: 2, genitalia: 2
Association of the onset between LCNA and SS	SS prior to the onset of LCNA: 13 Post-diagnosis of SS after the onset of LCNA: 10 Unknown: 2
Amyloid immunostaining	Positive: 16 (both kappa/lambda: 5, kappa: 5, lambda: 6) Negative: 5 Unknown: 4

LCNA, localized cutaneous nodular amyloidosis; SS, Sjogren syndrome.

TABLE 2. Comparison of clinical features of Japanese LCNA with and without SS

	With SS (n = 20)	Without SS (31)
Sex	Male: 3, female: 17	Male: 20, female: 11
Age	38-88 y (average 60.5)	31-87 y (average 62.1)
Affected site of LCNA	Trunk: 17, extremities: 10, genitalia: 2, head: 1	Head: 24, extremities: 6, genitalia: 1

LCNA, localized cutaneous nodular amyloidosis; SS, Sjogren syndrome.

Correspondence
Noritaka Oyama, Department of Dermatology, Faculty of Medical Sciences, University of Fukui, 23-3 Matsuoka-Shimoaizuki, Eiheiji-cho, Yoshida-gun, Fukui 910-1193, Japan.
Email: norider@wine.plala.or.jp

ORCID
Noritaka Oyama https://orcid.org/0000-0003-4934-5205

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