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CLINICAL REPORT

Lichen Planus-like Lesions as the First Manifestation of Adult T-cell Leukaemia/Lymphoma

Hayakazu SUMIDA, Makoto SUGAYA, Masahiro KAMATA, Hiraku SUGA, Tomomitsu MIYAGAKI, Hanako OHMATSU, Hideki FUJITA and Shinichi SATO

Department of Dermatology, Faculty of Medicine, The University of Tokyo, Tokyo, Japan

Cutaneous involvement is frequent in adult T-cell leukaemia/lymphoma (ATLL), a peripheral T-cell neoplasm caused by human T-cell lymphotropic virus type I (HTLV-I). Patients with ATLL manifest different types of skin lesions, including nodules, plaques, ulcers, erythroderma and purpura. It has been reported that the type of skin eruption is an independent prognostic factor for ATLL. We report here a rare case of a 62-year-old Japanese woman with smouldering-type ATLL, first manifested by lichen planus-like skin lesions on the lower leg. This case report highlights the multiplicity of skin manifestations in ATLL. ***Key words: adult T-cell leukaemia/lymphoma (ATLL); human T-cell lymphotropic virus type I (HTLV-I); lichen planus.***

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Makoto Sugaya, Department of Dermatology, Faculty of Medicine, The University of Tokyo, Bunkyo-ku, Tokyo, 113-8655, Japan. E-mail: sugayam-der@h.u-tokyo.ac.jp

Adult T-cell leukaemia/lymphoma (ATLL) was first described in 1977 by Uchiyama et al. (1) as a distinct clinicopathological entity with a suspected viral aetiology, due to the clustering of the disease in the southwest region of Japan. ATLL is one of the aggressive malignancies that may occur in individuals infected with human T-cell lymphotropic virus type I (HTLV-I) (2, 3). Only a small minority of HTLV-I-infected individuals progress to ATLL. The cumulative risks of developing ATLL among carriers are estimated at approximately 6.6% for males and 2.1% for females (4). ATLL has been clinically classified into 4 subtypes, 2 of which are aggressive ATLL (acute and lymphoma types) and 2 are indolent ATLL (chronic and smouldering types), defined by organ involvement, and serum lactate dehydrogenase (LDH) and calcium levels (5). It has been noticed that some patients with indolent ATLL with cutaneous manifestation show a unique clinical course featuring no extracutaneous disease until the advanced stage (6). These cases have been called "cutaneous type", although the term has not been formally accepted. Diagnostic criteria for cutaneous type have been proposed (7). Patients with ATLL manifest various skin lesions, including large nodules, plaques, ulcers and erythroderma (8). The skin lesions can be classified as specific or non-specific. Lesions that are the direct result of infiltration and proliferation of leukaemic cells in the skin are known as specific lesions, and have been described in approximately 50% of patients with ATLL (9). We report here a rare case with lichen planus (LP)-like eruption on the lower leg as the first specific skin lesion of ATLL.

CASE REPORT

A 62-year-old Japanese woman, born in the Saitama Prefecture of Japan, an area where ATLL is not endemic, first presented at our department in November 2010 with generalized pruritic macules and plaques (Fig. 1a). Physical examination revealed bean-sized well-circumscribed violaceous plaques with fine scales on her upper and lower extremities (Fig. 1b). She was clinically diagnosed with LP. In order to confirm the diagnosis, a skin biopsy was taken from a lesion in her lower thigh. The biopsy specimen revealed hyperkeratosis, irregular acanthosis, band-like infiltrate of lymphoid cells at the dermoepidermal junction, and hydropic degeneration of the basal cell layer (Fig. 2a). Lymphocyte infiltration into the deep dermis was not suggestive of LP. Moreover, careful observation revealed that some infiltrating lymphocytes had mild

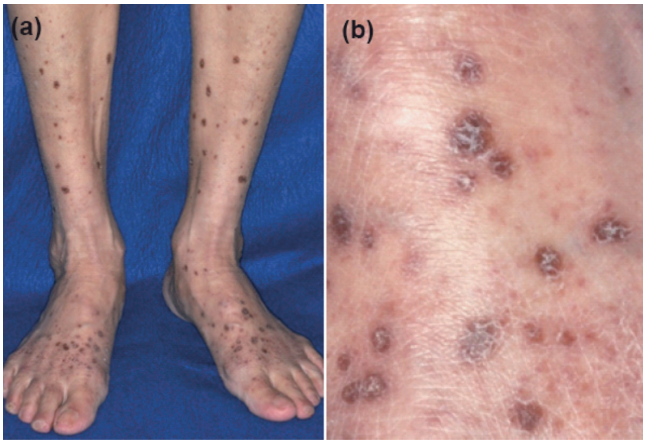

Fig. 1. (a) Generalized pruritic macules and plaques on the lower limbs. (b) Close-up picture of bean-sized well-circumscribed violaceous plaques with fine scales on the left lower limb.

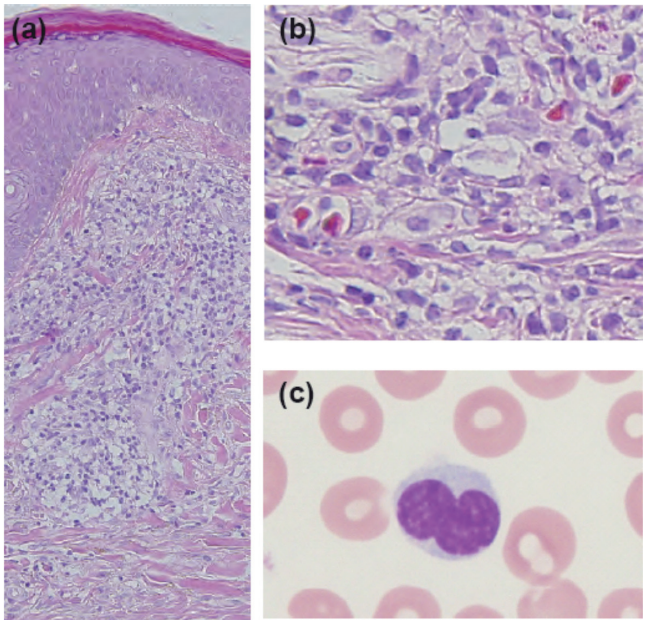

Fig. 2. (a) Histopathology showing hyperkeratosis with band-like infiltration of lymphoid cells (haematoxylin and eosin (H&E) stain; original magnification: ×100). (b) Some infiltrating lymphocytes showing mild atypia (H&E stain; original magnification: ×400). (c) Atypical lymphocytes characterized by lobulated nuclei with homogeneous and condensed chromatin in peripheral blood (Giemsa-stain; original magnification: ×100).

atypia with somewhat irregularly-shaped nuclei (Fig. 2b). Therefore, we performed additional investigations of other possible diagnoses, especially malignant lymphoma.

The laboratory findings were as follows: LDH, 255 IU/l (normal 114–220 IU/l); calcium, 9.7 mg/dl (normal 8.4–9.7 mg/dl); soluble interleukin-2 receptor, 1,301 U/ml (normal 124–466 U/ml). Serological examination was positive for anti-HTLV-I antibody. Giemsa-stained peripheral blood smear showed atypical lymphocytes characterized by lobulated nuclei with homogeneous and condensed chromatin (Fig. 2c). The white blood cell count was 9.1×10^9/l with 20% atypical lymphocytes. Flow cytometry of peripheral blood showed a high frequency of CD4/CD25 double-positive cells in total CD4-positive cells (84.3%). These data suggested that the patient had ATLL. Immunohistochemical staining of a skin biopsy specimen showed that most of the infiltrating atypical lymphocytes were positive for CD3, CD4 (Fig. 3a) and CD25 (Fig. 3b). Moreover, the monoclonal integration of HTLV-I proviral DNA was confirmed by Southern blot analysis in a skin biopsy specimen (Fig. 3c) and whole blood. Bone marrow biopsy showed no infiltration of ATLL cells. Computed tomography, gastrointestinal endoscopy, and whole-body F-18 fluorodeoxyglucose positron emission tomography scan showed no involvement of lymph nodes or internal organs. The diagnosis was ATLL, smouldering-type, with LP-like skin lesions. The patient was followed up with a watchful waiting strategy because of the relatively good prognosis in smouldering-type ATLL. Topical steroids and narrow-band ultraviolet B (UVB) therapy have been performed for the management of skin lesions. To date, the effect of this skin-targeted therapy is minimal.

DISCUSSION

The patient described in this report displayed typical clinical findings of LP. The histopathology of the skin lesions showed hyperkeratosis with band-like infiltration of lymphoid cells. Some atypical lymphocytes with slightly irregular nuclei prompted us to perform additional examinations, which revealed that the patient had smouldering-type ATLL. ATLL is characterized by a broad spectrum of cytological features. Diagnosis of ATLL can only be made with the help of serological

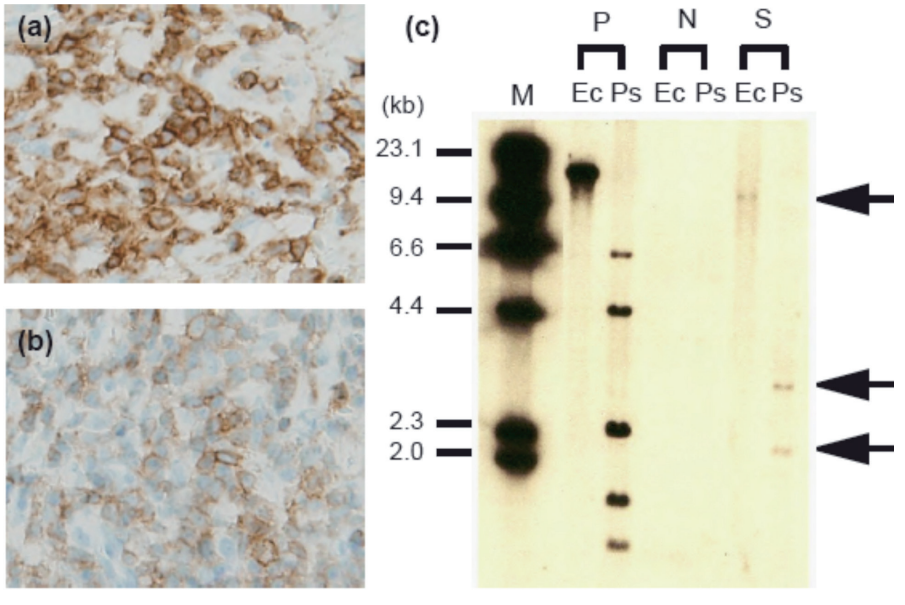

Fig. 3. Immunohistochemical staining of atypical lymphocytes for CD4 (a) or CD25 (b) in the skin biopsy specimen (original magnification: ×200). (c) Southern blot analysis of the skin biopsy specimen for human T-cell lymphotropic virus type I (HTLV-I) proviral DNA. M: size marker (λDNA/HindIII); P: positive control (monoclonal integrated DNA); N: negative control; S: this case; Ec: EcoRI digestion; Ps: Pst I digestion.

and molecular examinations. Moreover, HTLV-I carriers can develop lymphoma other than ATLL (10). Therefore, proof of monoclonal integration of HTLV-I proviral DNA is necessary, as we showed in our patient.

This is the first report describing LP-like skin lesions as an ATLL-specific eruption. Cutaneous involvement is recognized in approximately half of ATLL patients (9). ATLL patients can develop various types of eruptions, including nodules, tumours, plaques, erythrodermas, and purpuric lesions (8). Although a complete understanding of the diverse pathophysiological mechanisms in the skin lesions does not exist, there were some reports of several differences in phenotype and function of infiltrating tumour cells (11, 12). This functional diversity in HTLV-I-infected cells might create an extraordinary variety of skin lesions. More importantly, it has been reported that the type of skin eruption is an independent prognostic factor for ATLL (8). Patch or plaque type eruptions exhibited good prognosis. On the other hand, multipapular, nodulo-tumoural, erythrodermic, or purpuric type eruptions showed poor prognosis. Futher study is needed to determine whether LP type, as seen in our patient, indicates good or poor prognosis. There are many potential skin-targeted therapies, such as topical steroids, psoralen photochemotherapy, narrow-band UVB therapy, or radiation therapy. It has not been proven whether these skin-targeted therapies can improve the prognosis of ATLL patients with skin eruptions. The accumulation of case reports may provide clinically useful information for the prediction of prognosis, patient management, and choice of therapy.

Considering that the skin is often involved in various types of ATLL, skin lesions may represent the first sign of the disease. It is essential that ATLL should be considered during the differential diagnosis of skin eruption, especially in endemic areas. In view of this requirement, clinicians therefore need to be aware of the multiplicity of skin manifestations, including LP-like lesions, that can occur as the first manifestation of ATLL.

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