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CLINICAL REPORT

Generalized Leukaemia Cutis from a Small Cell Variant of T-cell Prolymphocytic Leukaemia Presenting with Exfoliative Dermatitis

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T-cell prolymphocytic leukaemia (T-PLL) is a rare, aggressive neoplasm of mature T lymphocytes. The small cell variant occurs in approximately 20% of T-PLL patients. The skin findings of leukaemia consist of leukaemia-specific skin lesions, which are infiltrated by leukaemia cells, and non-specific lesions. The former type of lesion signifies leukaemia cutis. Leukaemia cutis presents clinically as tumours, nodules, or patches on the scalp, face and trunk. We report here an 82-year-old Korean male patient who presented with erythema, erosion, vesicles, and scales on his entire body with no clear underlying cause. He had been treated with oral retinoids, steroids, and phototherapy for the diagnoses of drug eruption, pityriasis rubra pilaris, and exfoliative dermatitis at other hospitals. We suspected a hidden malignancy and diagnosed small cell variant T-PLL through blood and bone marrow examination. A skin biopsy specimen showed dense infiltration of small lymphocytes in the dermis. Most of the atypical lymphocytes stained positively with CD markers such as CD2, CD3, CD4, CD5, CD7 and CD8, thereby confirming the presence of leukaemia cells. To our knowledge, this is the first case of generalized leukaemia cutis from small cell variant of T-PLL presenting with exfoliative dermatitis over the whole body. ***Key words: exfoliative dermatitis; leukemia cutis; T-cell prolymphocytic leukemia.***

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T-cell prolymphocytic leukaemia (T-PLL) is a rare lympho-proliferative disorder that accounts for only 2% of small lymphocytic leukaemias in adults (1). It is characterized by an accumulation of monoclonal lymphoid cells in the peripheral blood, bone marrow, and other organs. The common manifestations are striking leukocytosis, hepatosplenomegaly, and lymphadenopathy. A small cell variant of T-PLL is recognized in which cells are small and the nucleous is not readily apparent by light microscopy (2). It is a rare and aggressive clinical entity, but the cutaneous findings have not yet been studied. We describe here a patient who presented with extremely uncommon clinical manifestations of generalized leukaemia cutis from a small cell variant of T-PLL.

CASE REPORT

An 82-year-old Korean man presented with a 6-month history of pain and discomfort, erythema with erosions, ulcers, vesicles and scales. The cutaneous lesions first appeared on the soles of his foot and became widespread, affecting his trunk, limbs, face and scalp. The lesions developed as vesico-bullae and progressed as exfoliative dermatitis. His past treatments included oral retinoids, steroids, and phototherapy, which were given for presumed drug eruption, pityriasis rubra pilaris, and exfoliative dermatitis. However, there was no improvement, and the skin lesions progressed to exfoliative dermatitis. At initial presentation, he had erythema with thick, coarse scales covering his entire body. A few tense blisters and many erosions were observed on the trunk and extremities (Fig. 1). Because the exfoliative dermatitis was resistant to treatment, we suspected a hidden malignancy and decided to do further evaluations. A physical examination revealed no hepatosplenomegaly. Laboratory parameters revealed a white blood cell (WBC) count of 16,000/mm^3, with 90% lymphocytes. Haemoglobin was 10.2 g/dl and platelet count 113 ($\times 10^3/\mu l$). Serology for HIV and HBsAg was negative. Liver and kidney function tests were within normal limits. The peripheral smear revealed 90% small lymphocytes with smudge cells and basket cells compatible with chronic lymphoproliferative disorder. The bone marrow biopsy and aspirate were hypercellular with 78% small lymphocytes with clumped chromatin, round nuclear contours, inconspicuous nucleoli, and scant cytoplasm. By flow cytometric immunophenotyping, the cells expressed CD45, CD2, CD3, CD5, CD7, CD4 (dim) and CD8 (dim). They were negative for TdT, CD10, CD19, CD20, CD23, FMC7, kappa and lambda light chains and CD56. From these findings, a diagnosis of small cell variant T-PLL was made. Chromosomal analysis of bone marrow cells showed a clonal karyotype abnormality: 47,XY,+4[5]/46,XY[15].

Histopathological examination showed a subepidermal blister that contained a few inflammatory cells and dense atypical small lymphocytes in the dermis, especially the perivascular region and around the skin

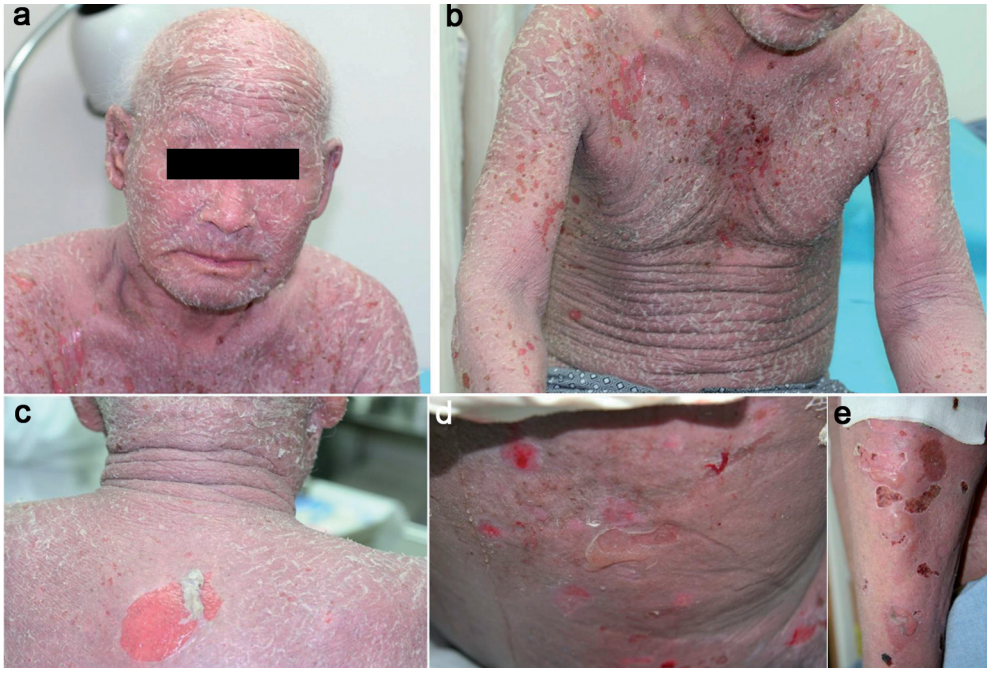

Fig. 1. Thick, coarse, scaly erythematous dermatitis involving the whole body. A few tense blisters and many erosions are distributed along the trunk and extremities.

appendages (Fig. 2). There was no epidermotropism and grenz zone. Because the patient was diagnosed with leukaemia, immunohistochemical staining was carried out. The lymphocytes in the dermis stained positively for CD2, CD3, CD4, CD5, CD7, and CD8, indicating that those cells were T-cell leukaemia cells (Fig. 3). The diagnosis of leukaemia cutis from small cell variant of T-PLL was confirmed by the histopathological findings.

To evaluate systemic involvement, we performed abdominal and chest computerized tomography. Multiple lymph node involvement was observed on the para-oesophageal, hepatic artery, left para-aortic, common iliac, obturator, external iliac, and inguinal areas.

The patient received oral fludarabine phosphate and prednisone, but did not improve. The skin lesions progressed and there was a rapid increase in WBC count to 44,800/mm^3. Two weeks after the start of chemotherapy, the patient died due to sepsis.

DISCUSSION

This case presented several interesting features: (*i*) generalized leukaemia cutis originating from a small cell variant of T-PLL, (*ii*) clinical manifestations with exfoliative dermatitis over the whole body, (*iii*) and the importance of suspecting an underlying malignancy when exfoliative skin lesions of an elderly patient are resistant to treatment.

T-PLL is the most common type of mature T-cell leukaemia and currently encompasses most of the T-cell leukaemias formerly diagnosed as T-cell chronic lymphocytic leukaemia, as well as those with pro-lymphocytoid morphology (3, 4). Patients with T-PLL are generally middle-aged to elderly and present with marked leukocytosis and hepatosplenomegaly (5). One distinctive haematological feature is a rapidly increasing WBC count with doubling times of weeks to months

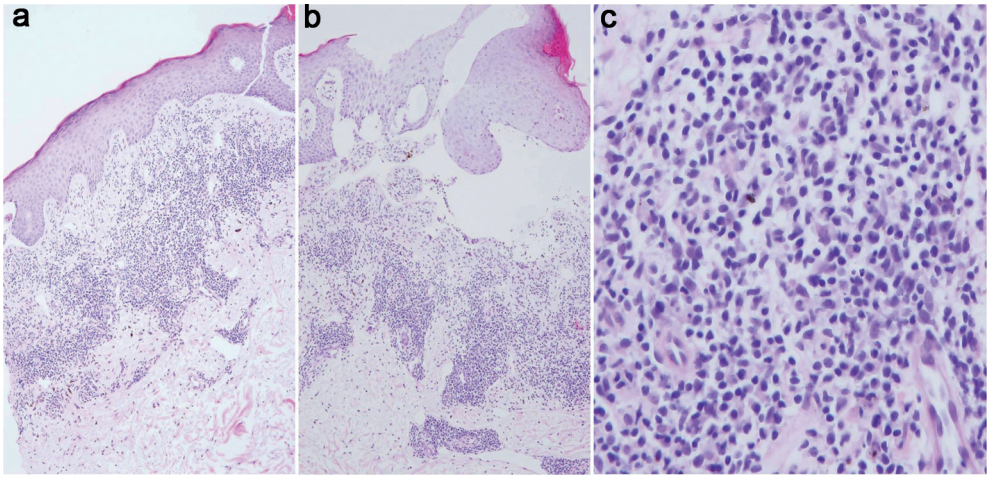

Fig. 2. Sub-epidermal blister containing a few inflammatory cells and a dense infiltration of atypical small lymphocytes in the upper dermis. Epidermotropism and grenz zone are not seen. Haematoxylin and eosin (H&E) stain: a) ×40, b) ×100 and c) ×200).

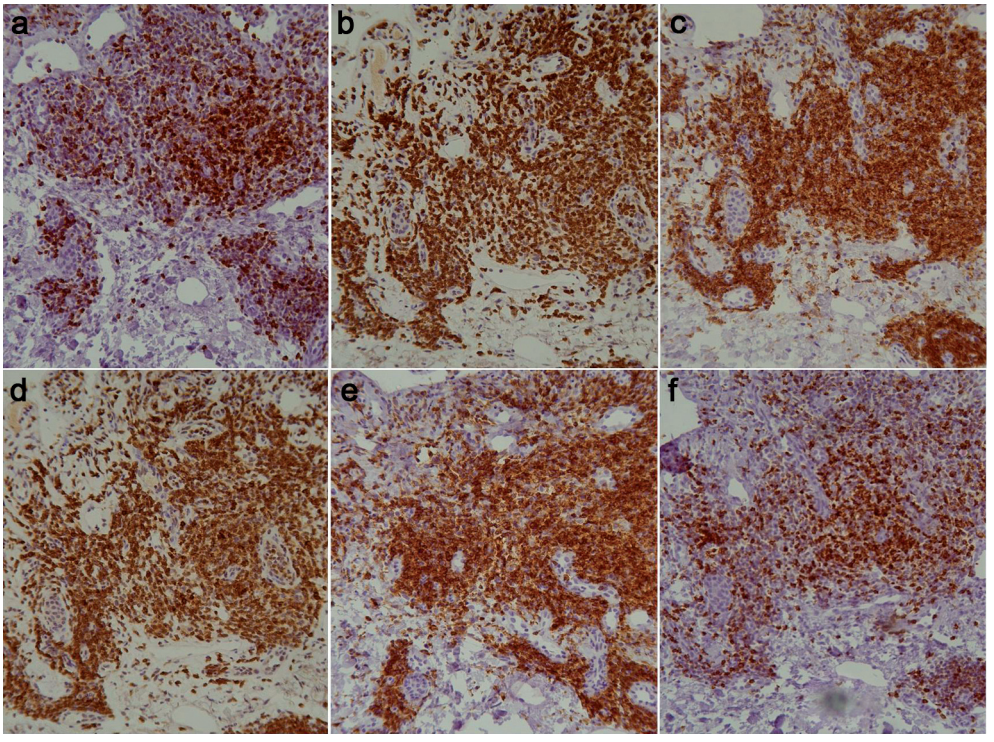

Fig. 3. The atypical lymphocytes in the dermis stained positively for CD2, 3, 4, 5, 7, and 8. (a) CD2 ×200. (b) CD3 ×200. (c) CD4 ×200. (d) CD5 ×200. (e) CD7 ×200. (f) CD8 ×200.

(6). A variant form with small lymphocytes occurs in approximately 20% of T-PLL. The small cell variant of PLL is recognized when cells are small and the nucleolus is not easily visible by light microscopy (3). It is an extremely rare entity with an aggressive course. Our patient was diagnosed with the small cell variant of T-PLL because of the morphological features of the leukaemic cells, a rapidly rising and high WBC count, diffuse lymphadenopathy, skin involvement, and an aggressive clinical course.

The immunophenotypic profile of T-PLL reveals its mature T-cell nature, with the most common phenotype being CD2+, CD3+, CD4+, CD5+, CD7+, CD8–, and CD45+ (5). Although most cases are derived from CD4+ helper T cells, up to one-third of T-PLL cases exhibit CD4+, CD8+ co-expression. According to Matutes et al. (2), the small cell variant of T-PLL has a two-fold greater incidence of the CD4+, CD8+ phenotype. Surface marker analysis of the lymphocytes in peripheral blood of our patient was compatible with of the following CD markers: CD2+, CD3+, CD4+, CD5+, CD7+, CD8+, and CD45+.

Leukaemic skin infiltrations in patients with leukaemia are referred to as leukaemia cutis, or, specifically, cutaneous manifestation of leukaemia (7). It can be seen in all types of leukaemia and myelodysplastic syndrome, especially in patients with acute monocytic or myelomonocytic leukaemia (8). It is regarded as a dissemination of aggressive systemic leukaemia to the skin and has a poor prognosis (8). There are a wide range of cutaneous manifestations with variable incidences. The skin lesions usually present as erythematous papules, plaques, nodules, or tumours (7, 9). Rarely encountered cutaneous manifestations include erythroderma, vesicobullous eruptions, and subungual lesions (7). Skin involvement by T-PLL is not unusual. In fact, 25–30% of T-PLL patients have skin involvement with prominent facial preference; oedema and symmetrical distributed petechia or purpura are characteristic (2, 10–12). Other manifestations include diffuse infiltrative erythema and nodules (10). However, erythroderma and bullous eruptions as generalized leukaemia cutis have not been reported thus far. The small cell variant of T-PLL is not a well-recognized entity, and cutaneous lesions have not been studied. To the best of our knowledge, this is the first case of leukaemia cutis from the small cell variant of T-PLL presenting with exfoliative dermatitis covering the entire body.

REFERENCES

1. Catovsky D, Ralfkiaer E, Muller-Hermelink HK. T-cell prolymphocytic leukaemia. In: Jaffe ES, Harris NL, Stein H, Vardiman JW, editors. Pathology and genetics of tumours of haematopoietic and lymphoid tissues. World Health Organization Classification of Tumours. Lyon, France: IARC Press, 2001: p. 195–198.
2. Matutes E, Brito-Babapulle V, Swansbury J, Ellis J, Morilla R, Dearden C, et al. Clinical and laboratory features of 78 cases of T-prolymphocytic leukemia. Blood 1991; 78: 3269–3274.
3. Thorat KB, Gujral S, Kumar A, Nair CN. Small cell variant of T-cell prolymphocytic leukemia exhibiting suppressor phenotype. Leuk Lymphoma 2006; 47: 1711–1713.
4. Keating MJ, Cazin B, Coutré S, Birhiray R, Kovacsovics T, Langer W, et al. Campath-1H treatment of T-cell prolymphocytic leukemia in patients for whom at least one

prior chemotherapy regimen has failed. J Clin Oncol 2002; 20: 205–213.
5. Foucar K. Mature T-cell leukemias including T-prolymphocytic leukemia, adult T-cell leukemia/lymphoma, and Sézary syndrome. Am J Clin Pathol 2007; 127: 496–510.
6. Herling M, Khoury JD, Washington LT, Duvic M, Keating MJ, Jones D. A systematic approach to diagnosis of mature T-cell leukemias reveals heterogeneity among WHO categories. Blood 2004; 104: 328–335.
7. Robak E, Robak T. Skin lesions in chronic lymphocytic leukemia. Leuk Lymphoma 2007; 48: 855–865.
8. Miyoshi I, Uemura Y, Sonobe H, Taguchi H. Leukemia cutis. Intern Med 2007; 46: 65–66.
9. Watson KM, Mufti G, Salisbury JR, du Vivier AW, Creamer D. Spectrum of clinical presentation, treatment and prognosis in a series of eight patients with leukaemia cutis. Clin Exp Dermatol 2006; 31: 218–221.
10. Mallett RB, Matutes E, Catovsky D, Maclennan K, Mortimer PS, Holden CA. Cutaneous infiltration in T-cell prolymphocytic leukaemia. Br J Dermatol 1995; 132: 263–266.
11. Magro CM, Morrison CD, Heerema N, Porcu P, Sroa N, Deng AC. T-cell prolymphocytic leukemia: an aggressive T-cell malignancy with frequent cutaneous tropism. J Am Acad Dermatol 2006; 55: 467–477.
12. Volk JR, Kjeldsberg CR, Eyre HJ, Marty J. T-cell prolymphocytic leukemia. Clinical and immunology characterization. Cancer 1983; 52: 2049–2054.