CASE REPORT

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Small Cell Variant of T-Cell Prolymphocytic Leukemia with Acquired Palmoplantar Keratoderma and Cutaneous Infiltration

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ABSTRACT

T-cell prolymphocytic leukemia (T-PLL) is a rare and aggressive post-thymic malignancy that is characterized by the proliferation of small- to medium- sized prolymphocytes. The classic clinical features of T-PLL are lymphocytosis, lymphadenopathy, hepatosplenomegaly, and skin lesions. Skin involvement varies clinically from diffuse infiltrated erythema. Infiltration is localized to the face and ears, nodules, and erythroderma. We present a case of small cell variant of T-PLL in a patient who presented with unusual cutaneous manifestations of acquired palmoplantar keratoderma (PPK) followed by diffuse erythematous infiltrated papules and plaques involving the trunk. When the etiology of acquired PPK is not clear, the physician should consider the possibility of an underlying malignant disease. In this case, the diagnosis of T-PLL was subsequently confirmed by laboratory and cytological findings, as well as by the immunophenotyping of leukemic cells in skin biopsy. Since paraneoplastic acquired PPK may be the initial evident sign of malignancy, the physician's awareness of this manifestation may be crucial for early diagnosis and treatment. Our case emphasizes the importance of accurate evaluation of skin lesions and early skin biopsy in the diagnosis of some hematological malignancies.

T-cell prolymphocytic leukemia (T-PLL) is a rare and aggressive post-thymic malignancy that is characterized by the proliferation of small- to medium-sized prolymphocytes.[1] It has distinctive clinical, morphological, immunophenotypic, and cytogenetic features and accounts for less than 2% of all forms of small lymphocytic leukemias in adults over the age of 30.[2] It is more prevalent in men, and the median age at presentation is 65 years.[3] The classic clinical features of T-PLL are lymphocytosis, lymphadenopathy, hepatosplenomegaly, and skin lesions.[1,2] Cutaneous manifestation of T-PLL is one of the most frequently involved extramedullary sites. The reported incidence is between 25% and 30%.[4] Clinically, skin involvement varied from diffusely infiltrated erythema, infiltration localized to the face and ears, nodules, and erythroderma.[4] Here, we describe a patient with T-PLL, in which skin involvement was an essential part of the clinical presentation and diagnosis. The clinical, morphological, histopathologic, and immunophenotypic features of the skin involvement in this case are discussed.

CASE REPORT

A 69-year-old Greek male presented with a more than one-year history of thick and cracked palms and soles associated with discomfort and pain. There was no significant past medical history and no family history of keratoderma or other skin disorders. On examination, at initial presentation, he had thick hyperkeratotic palms and soles with fissuring [Figure 1]. He was started on acitretin and topical medication for keratoderma, and showed minimal improvement. Essential workup for acquired palmoplantar keratoderma (PPK) was done including complete blood count (CBC), liver, and renal function tests, hepatitis screening, tumor markers, occult blood, barium swallow, and gastroscopy. Initial laboratory parameters showed normal CBC with a white blood cell count (WBC) of 12.3×10^9 /L and a lymphocyte count of 4.9×10^9/L. Renal and liver function tests were within normal limits. Hepatitis B serologic testing (HBsAg) was positive. Gastroscopy revealed Barrett's esophagus. Since keratoderma is usually associated with malignancy in this age group, tumor markers including alpha-fetoprotein

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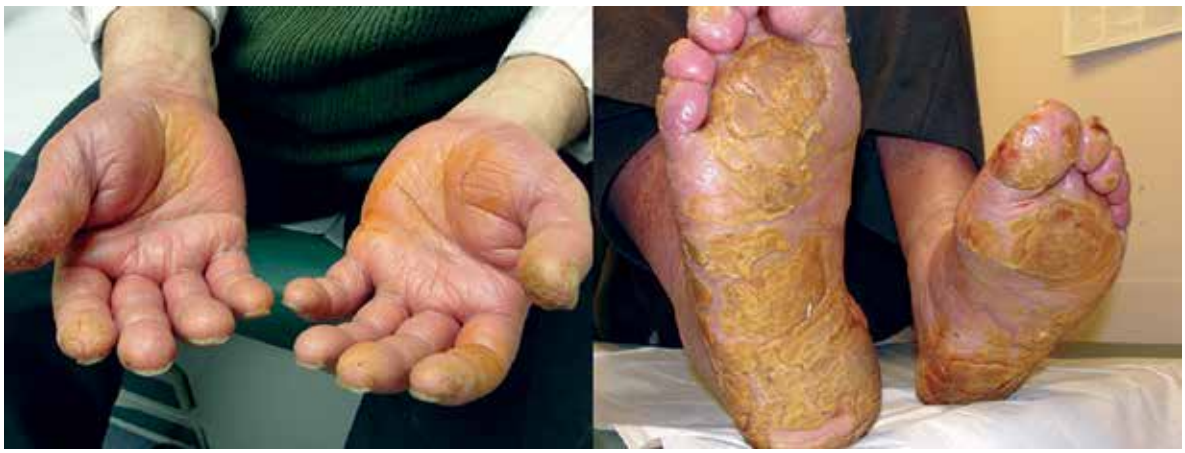

Figure 1: Thick hyperkeratotic palms and soles with fissuring.

(AFP), carcinoembryonic antigen (CEA), prostate-specific antigen (PSA), cancer antigen (CA) 19–19, and alkaline phosphatase (ALP) were tested and found negative. He continued the same treatment and showed slow improvement at the following visits. Six months later, he presented with a pruritic, erythematous eruption on the trunk [Figure 2].

On examination, there were diffuse erythematous infiltrated papules coalescing into plaques involving the trunk, bilateral shoulders and extending to lower extremities, in addition to the previous keratoderma. On systemic examination, there were splenomegaly and inguinal lymphadenopathy. Essential blood investigations were done, which showed a hemoglobin level of 11.9 g/L, WBC of 34.8 × 10^9 /L, lymphocytes count of 19.5 × 10^9 /L and platelets of 189 × 10^9 /L. Because of the progressive increase in WBC and lymphocytosis during follow-up and lymphadenopathy with splenomegaly, a concealed malignancy was suspected. A skin biopsy was done to rule out leukemia cutis. The patient was started on systemic corticosteroids: he did not improve.

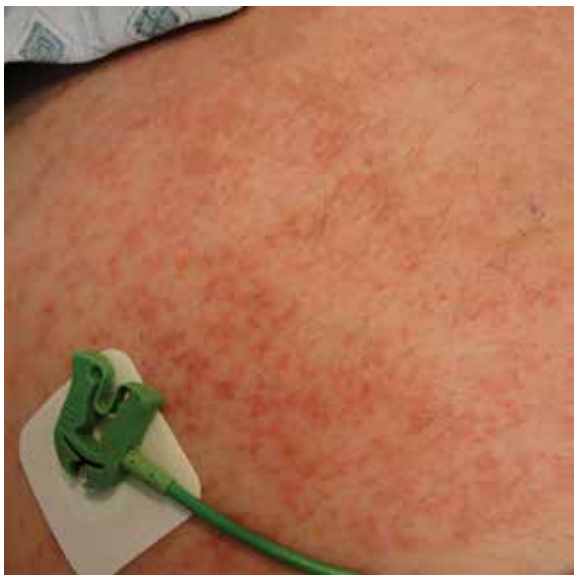

Figure 2: Diffuse erythematous infiltrated papules on the abdomen.

Histopathological examination of the skin biopsy showed a dense superficial perivascular atypical lymphoid infiltrate consisting of small cells with round, oval to moderately irregular nuclear contours and frequent indistinct nucleoli [Figure 3]. There was no epidermotropism.

Immunohistochemical studies were carried out due to the atypical nature of the lymphocytes. The lymphocytes in the dermis stained positively for CD3, CD4, and CD8 and negatively for TdT and CD20 indicating that those cells were of T-cell immunophenotype [Figure 4]. The morphologic and immunophenotypic findings confirmed the diagnosis of mature (post-thymic) T-cell leukemia of small cell variant of T-PLL.

Flow cytometric immunophenotyping of peripheral blood samples showed positive CD3 and CD7 expression. Abdominal and chest computed tomography (CT) showed pleural effusion, mild splenomegaly and a large lymphomatous right-sided retroperitoneal mass involving the right kidney extending downwards along the posterior pararenal spaces.

The patient was started on fludarabine/cyclophosphamide. He responded initially with a decrease in his WBC count to 7.1 × 10^9 g/L. However, after the fourth cycle of chemotherapy, he developed sepsis and died.

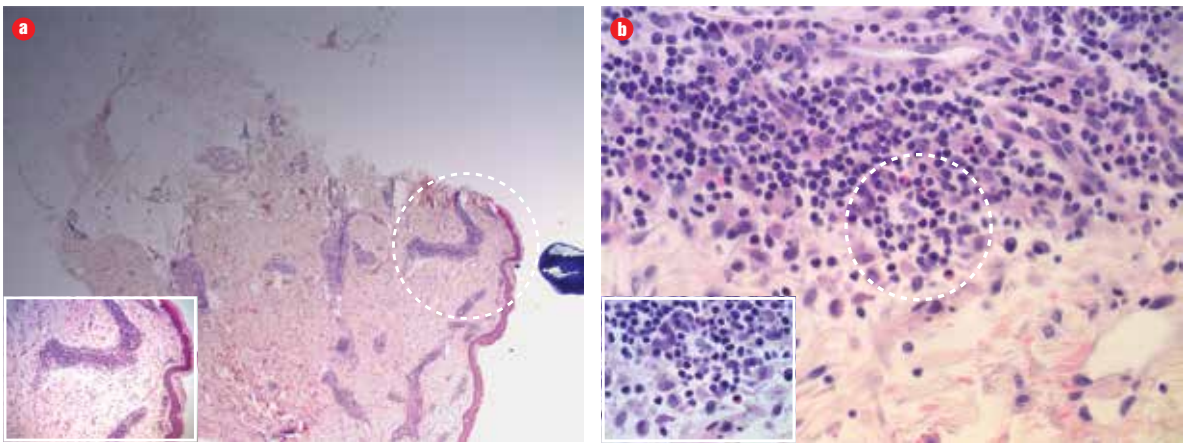

Figure 3: Hematoxylin and eosin staining showing **(a)** dense superficial perivascular atypical lymphoid infiltrate, magnification = 2.5 × (inset = 10 ×), and **(b)** small lymphocytic cells with round, oval to moderately irregular nuclear contours and frequent indistinct nucleoli, magnification = 20 × (inset = 100 ×).

DISCUSSION

We reported a case of small cell variant of T-PLL that presented with unusual cutaneous manifestations of acquired PPK followed by diffuse erythematous infiltrated papules and plaques involving the trunk.

Prolymphocytic leukemia (PLL) is a rare and aggressive type of chronic lymphoproliferative disorder of the B- and T-cell subtype that together account for around 2% of all mature lymphoid leukemias.[5,6] T-PLL is characterized by marked leukocytosis, lymphadenopathy, hepatosplenomegaly, and cutaneous involvement, which occur in about a quarter of patients.[4] The most frequently reported cutaneous manifestations are a diffuse infiltrated erythema, erythematous papules, nodules or plaques, erythroderma, and bullous lesions. The face and ears are typical sites for specific skin infiltration of mature T-cell leukemia.[4] Other reported manifestations include petechial/purpuric morphology and the linear/symmetrical distribution of the lesions.[7]

Skin biopsies of T-PLL cutaneous involvement classically show infiltrate of variable density of atypical lymphocytes in the superficial dermis, with a perivascular and periadnexal distribution with no epidermotropism.[8] The atypical lymphoid cells are small to medium sized with markedly irregular nuclei and visible nucleolus.[2] In 25% of cases, the cell size is small, and the nucleolus is indistinct as in this case.[2]

Immunophenotyping of the T-prolymphocytes characteristically demonstrates a post-thymic T-cell nature (i.e., CD2, CD3, and CD7 positive and TdT and CD1a negative). Sixty percent of cases show a CD4+/CD8- phenotype, but co-expression of CD4/CD8 is seen in 25% of cases.[2,9] In this case,

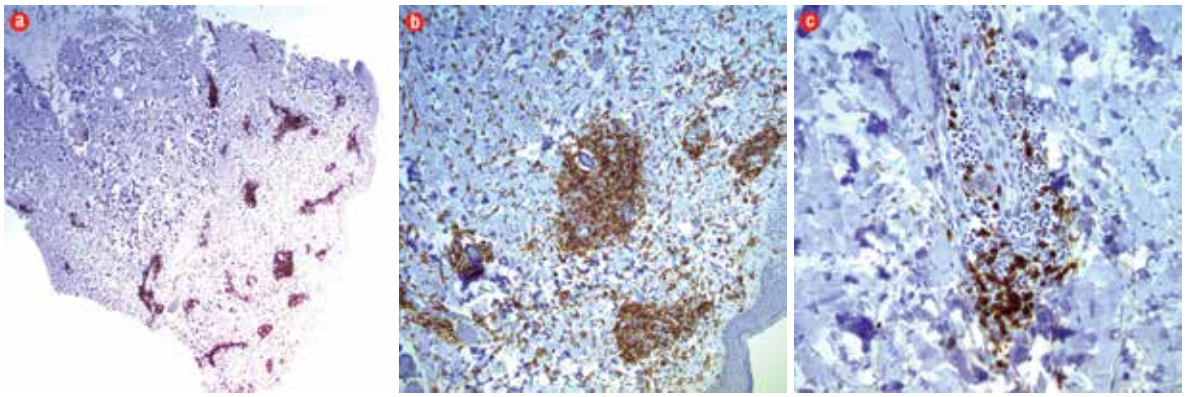

Figure 4: Immunohistochemical studies showed positive expression of **(a)** CD3, magnification = 2.5 ×; **(b)** CD4, magnification = 10 ×; and **(c)** CD8, magnification = 20 ×.

the lymphocytes in the dermis stained positively for CD3, CD4, and CD8 and stained negatively for TdT and CD20, which further supports the diagnosis of T-PLL.

Our patient initially presented with a lengthy history of acquired PPK, which is atypical skin manifestation in T-PLL. However, acquired PPK is considered to be a paraneoplastic marker for internal malignancy such as esophageal, lung, bronchial, breast, urinary bladder, gastric, and colon. Additionally, there have been many reports of acquired PPK associated with Sézary syndrome, cutaneous T-cell lymphoma and non-Hodgkin lymphoma.[10] This patient later developed infiltrated erythematous papules and plaques on the trunk associated with a marked increase in WBC that raised the suspicion of hematological malignancy and confirmed the diagnosis of T-PLL based on typical morphological features and immunophenotyping of leukemic cells in the skin. The patient was managed with steroids before the results of his skin biopsy. He did not show any improvement. We suggest starting systemic treatment only after confirmation of the diagnosis.

CONCLUSION

Our case emphasises the significance of accurate evaluation of skin lesions and early skin biopsy in the diagnosis of some hematological malignancies.

Disclosure
The authors declared no conflicts of interest.

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