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Case presentation

Leukemia cutis with lymphoglandular bodies: a clue to acute lymphoblastic leukemia cutis

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Abstract

Leukemia cutis describes cutaneous lesions produced by infiltrates of leukemic cells. It usually manifests contemporaneously with the initial diagnosis of systemic leukemia, but may also precede or follow systemic leukemia. Most cases are associated with acute myeloid leukemia. Adult B-cell lymphoblastic leukemia cutis is very rare. We report a 59-year-old woman with a history of B-cell acute lymphoblastic leukemia who relapsed with aleukemic lymphoblastic leukemia cutis. Lymphoglandular bodies were conspicuous on biopsy and may serve as a morphologic clue to lymphocytic differentiation while molecular and immunophenotypic studies are pending. The patient was successfully treated with local radiation therapy and oral ponatinib.

Introduction

Patients with acute leukemia can present with leukemic infiltration of the skin resulting in clinically identifiable cutaneous lesions. The lesions, commonly referred to as *leukemia cutis*, are variable and manifest as non-tender, diffuse or localized ulcers, nodules, macules, or papules [1, 2].

Leukemia cutis is seen in 10% to 15% of patients with acute myeloid leukemia (AML), but is rare in patients with acute lymphoblastic leukemia (ALL) [3]. Most cases of lymphoblastic leukemia cutis have been reported in children [4]. When identified in ALL patients, it is usually the initial presentation of the disease. To our knowledge, aleukemic cutaneous ALL presenting as an indicator of relapse after allogeneic stem cell transplant has not been previously reported.

Case synopsis

A 59-year-old woman with Philadelphia chromosome positive (Ph+) B-cell ALL was initially treated with combination chemotherapy and dasatinib. Thereafter, she underwent umbilical cord stem cell transplantation in her first complete remission. Low dose (20 mg daily) dasatinib maintenance was started after white blood cell count recovery. On day 236 post transplantation she presented with a 6 x 4 cm violaceous, firm, irregular plaque on her scalp (Figure 1).

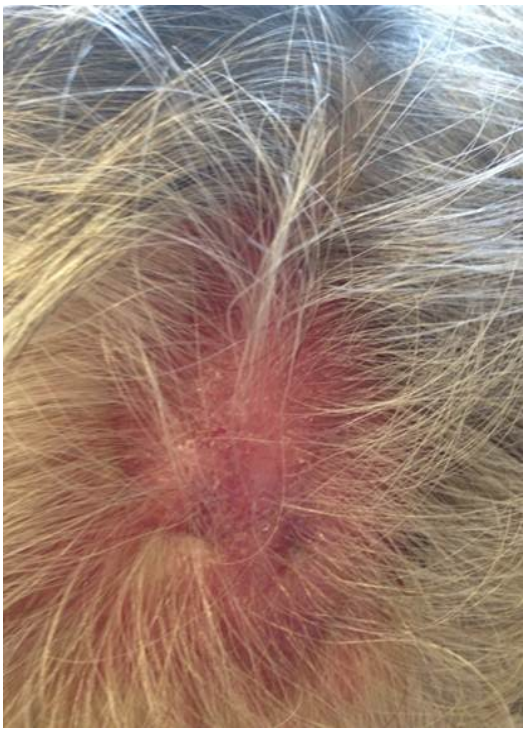

Figure 1. Violaceous, firm, irregular plaque across the scalp.

Punch biopsy demonstrated a dense dermal infiltrate of immature tumor cells with a grenz zone of sparing of the superficial dermis (Figure 2). Tumor cells exhibited high nuclear-cytoplasmic ratios and round nuclei with finely dispersed chromatin (Figure 3). Numerous lymphoglandular (Söderström) bodies, representing discarded cytoplasmic fragments, were identified (Figure 4; lymphoglandular bodies indicated by red arrows). Tumor cells expressed LCA, PAX5 (Figure 5) and TdT by immunohistochemistry. FISH analysis for Ph-chromosome was positive. Bone marrow and CSF studies were negative for ALL. Chimerism analysis of the marrow was of 100% donor origin.

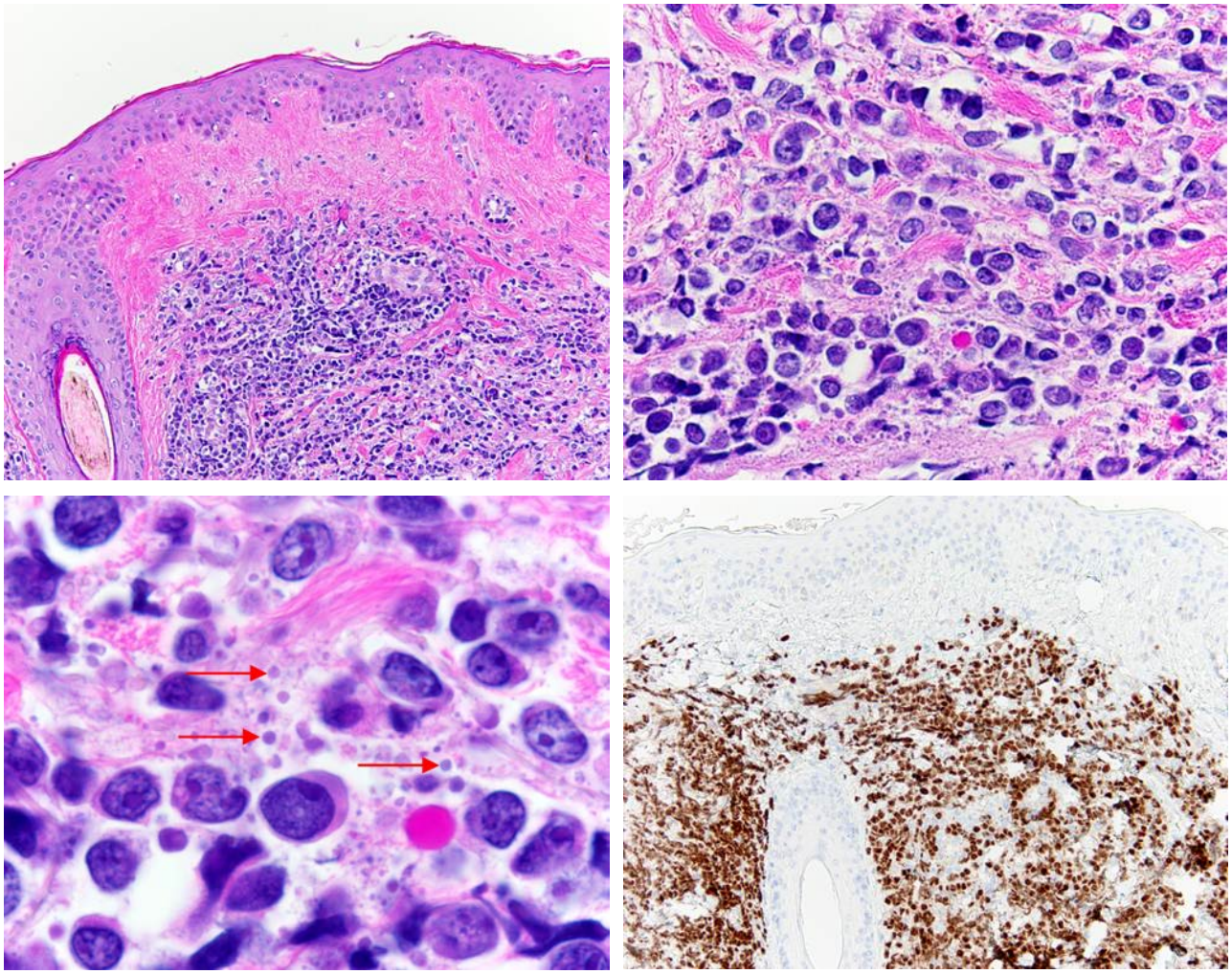

Figure 2. Dermal infiltrate with a grenz zone (H&E, X100). **Figure 3.** Tumor cells exhibited high nuclear-cytoplasmic ratios and round nuclei with finely dispersed chromatin (H&E, X400). **Figure 4.** Lymphoglandular bodies are indicated by red arrows (H&E, X1000). **Figure 5.** Tumor cells expressed PAX5 by immunohistochemistry (PAX5, X100).

Bone marrow and peripheral blood examinations were negative for leukemia. We diagnosed aleukemic B-lineage lymphoblastic leukemia cutis. She was treated with local radiation therapy followed by 45 mg oral ponatinib daily. The scalp lesion completely resolved. She remains on daily oral ponatinib with no evidence of disease by surveillance PET scan 8 months since diagnosis of leukemia cutis.

Discussion

Leukemia cutis may be seen in up to 15% of patients with AML, but is very rare in patients with ALL. Herein we describe an adult patient with relapsed Ph(+) B-lineage lymphoblastic leukemia presenting as aleukemic leukemia cutis. To our knowledge there are only five previous reports of B-lineage lymphoblastic leukemia cutis in adults [5-9]. A previous case series of pediatric ALL patients found 24/1359 cases presented with skin involvement at the time of diagnosis [4]. The most frequent location of skin lesions in children with ALL was on the head, as was the case in our patient. To our knowledge, there are no previous reports of cutaneous ALL as the sole indicator of disease relapse in a post-allogeneic stem cell transplant patient.

Histopathologic diagnosis of leukemia cutis can be difficult and may require immunostaining and molecular testing. Biopsy in our patient was remarkable for conspicuous *lymphoglandular bodies*. Lymphoglandular bodies are round pale basophilic cytoplasmic fragments that vary in diameter from 2 to 7 micrometers. They are associated with B-cell malignancies [10]. They are easily

recognized on routine hematoxylin-eosin preparations. We posit that they are a helpful clue in the diagnosis of cutaneous B-cell acute lymphoblastic leukemia.

The frequency of leukemia cutis is closely associated with specific leukemia subtypes. It ranges from a high of 50% in patients with acute myelomonocytic leukemia to less than 1% in lymphoblastic leukemias [3]. Numerical abnormalities of chromosome 8 in AML are associated with a higher incidence of leukemia cutis, but the exact mechanism by which chromosome 8 anomalies predispose these patients to leukemia cutis remains unknown [11]. The mechanism of skin homing of leukemic lymphocytes is also unknown, but may relate to the expression of cutaneous lymphocyte antigen by the cells of interest [12].

Leukemia cutis portends a poor prognosis. Most patients die within one year of diagnosis. Chemotherapy is usually recommended for leukemia cutis as eventual systemic relapse is inevitable. Small and localized lesions may be treated with surgical removal or radiotherapy [13]. 20% to 30% of adult ALL is associated with the Philadelphia chromosome. Tyrosine kinase inhibitors such as imatinib, dasatinib and ponatinib, which target the BCR-ABL oncogenic protein, have demonstrated promising results in the treatment of Ph(+) ALL [14]. Our patient was treated successfully with local radiation and oral ponatinib and is disease-free 8 months following the diagnosis of aleukemic leukemia cutis.

Conclusion

Allogeneic stem cell transplantation is often complicated by cutaneous disorders such as graft versus host disease, infection, and drug toxicities. We report this case to alert physicians to the possibility of disease relapse manifesting as aleukemic leukemia cutis. Skin lesions in post-transplant patients should be carefully evaluated and there should be a low threshold for cutaneous biopsy even if not typical of leukemia cutis. Lymphoglandular bodies in the biopsy may be a helpful clue to cutaneous B-lineage acute lymphoblastic leukemia while confirmatory molecular studies are pending.

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