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Acute onset of leukemia cutis in a 70-year-old-patient: a case report

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Abstract

We report the case of a 70-year-old man with no significant medical history that presented with a rapid onset of generalized pink to livid papules. No enlarged lymph nodes were observed, and laboratory results revealed a low platelet count. A biopsy was performed, and histopathological examination revealed a cutaneous infiltration with a highly malignant blastoid neoplasm. Further examination performed by hematologists, including cytological analysis of a bone marrow puncture, confirmed acute myelogenous leukemia (AML). Molecular genetic testing revealed a mutation in the gene encoding nucleophosmin (*NPM1*), the most common genetic anomaly in adult AML. He was treated according to protocol with venetoclax and azacitidine, but he died 4 months post-induction due to infectious complications of febrile neutropenia and subsequent sepsis.

Keywords: leukemia cutis, acute myelogenous leukemia, infiltrated papules

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Introduction

Leukemia cutis is an infiltration of neoplastic leukocytes into the skin. The pathogenesis of the disease is not yet fully understood (1–3), and it is more frequently observed in acute myelogenous leukemia (AML) in comparison to other leukemia types (4). In individuals with AML, the prevalence of leukemia cutis ranges from 10% to 15% (2, 5, 6). The incidence of AML is higher in men (7) and increases with age, with a mean age of 67 years (4). Although skin lesions predominantly appear on the trunk and extremities, oral mucosal involvement, particularly gingival hyperplasia, is frequently reported. A conclusive diagnosis involves a comprehensive assessment of the clinical presentation, bone marrow examination, and skin histopathology, with the latter being the most important. Treatment modalities include addressing the underlying disease through chemotherapy alone, chemotherapy followed by stem cell transplantation, or radiation (3).

Case report

A 70-year-old male retiree was referred to our urgent outpatient clinic due to the sudden emergence of skin lesions that had persisted for 5 days. Initial presentation showed pink-to-livid papules on the legs, progressing to widespread involvement of the trunk and extremities. The lesions were not pruritic or painful. The skin manifestations were proceeded by fatigue and weakness. He reported losing 5 kilograms over the previous year, but denied having an elevated body temperature, night sweats, cough, or digestive problems. The peripheral lymph nodes were not enlarged. Upon physical examination, firm pink-to-livid papules and nodules, ranging from 0.5 to 2 cm in diameter, were observed (Figs. 1, 2). The lesions were indurated but devoid of hemorrhagic or ulcerated features.

He had no significant medical history except for arterial hypertension and hyperlipidemia on oral therapy. He had been a smoker since his youth. His family history was negative for skin diseases, and his daughter had multiple sclerosis.

Blood tests revealed impaired renal function, elevated lactate dehydrogenase values (17.84 µkat/l; normal < 4.13 µkat/l), elevated CRP (57 mg/l; normal < 5 mg/l), reduced erythrocytes (4.06×10^{12}/l; normal $4.50–5.50 \times 10^{12}$/l), and a low platelet count (64×10^{9}/l; normal $150–410 \times 10^{9}$/l), with erythroblasts noted (2/100 white blood cells). The differential blood count revealed metamyelocytes (4%), myelocytes (5%), promyelocytes (1%), and blast cells (4%). Tumor markers (alpha-fetoprotein, cancer antigen 19-9, carcinoembryonic antigen, cytokeratin fragment 21-1, neuron-specific enolase, and prostate-specific antigen) were within reference values.

He underwent a biopsy of a skin lesion on his back. Histological examination showed a skin infiltration with a highly malignant blastoid neoplasm (Fig. 3). Immunohistochemistry was positive for $CD4^+$, $CD56^+$, $CD15^+$, and $Bcl\text{-}2^+$ (Fig. 4). According to the morphological picture and immunophenotype, the differential diagnosis included neoplasm of blastoid plasmacytoid dendritic cells and acute myeloid leukemia with monocytoid characteristics.

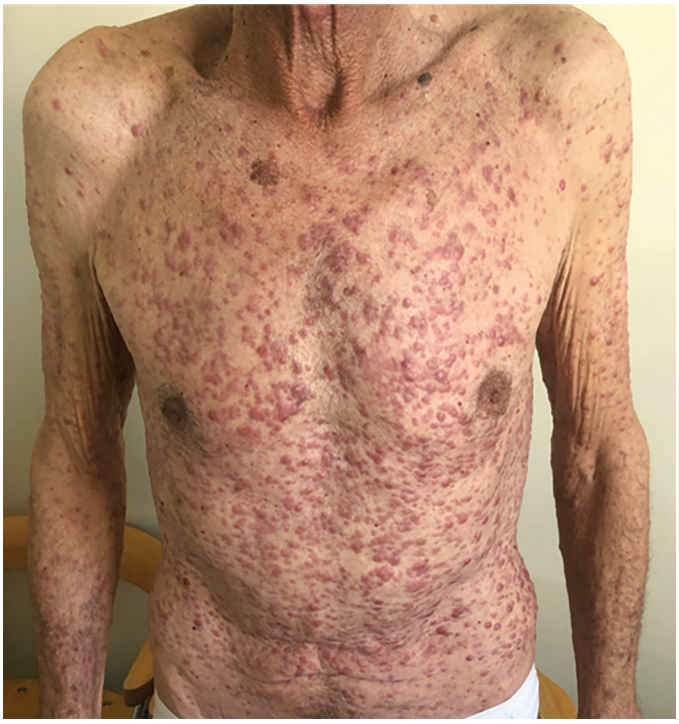

Figure 1 | Generalized involvement of skin on the trunk and extremities.

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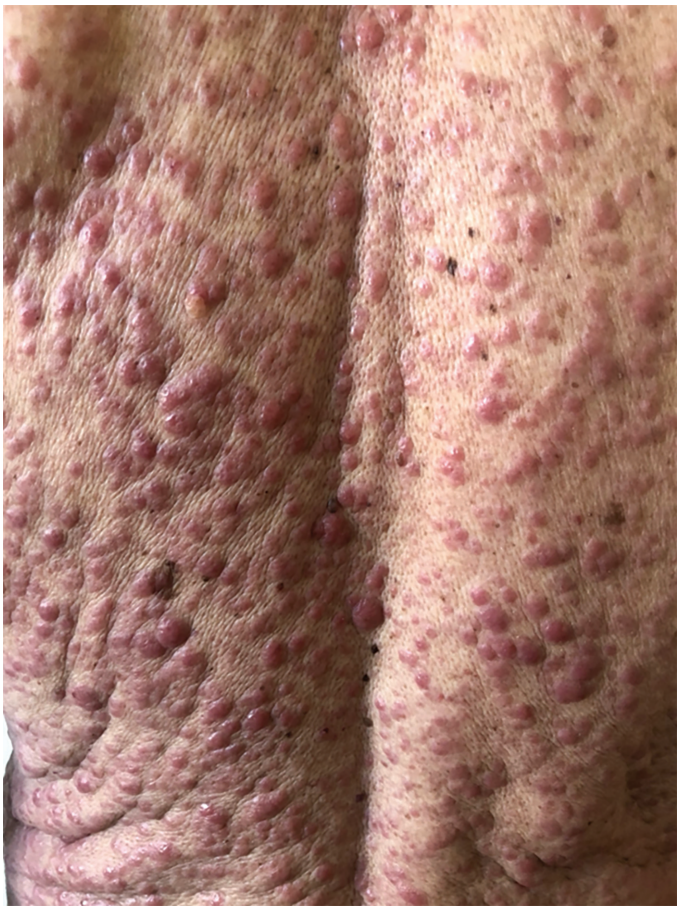

Figure 2 | Firm pink papules on the back.

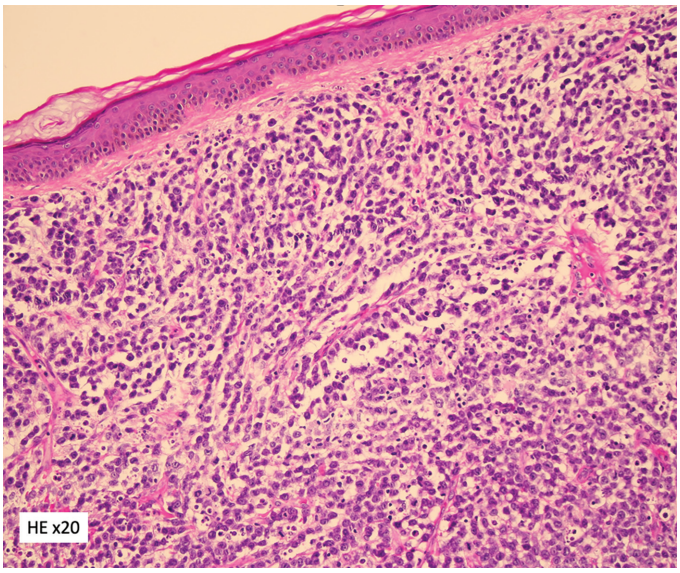

Figure 3 | Hematoxylin and eosin-stained section of skin biopsy (magnification ×20) displaying medium-sized tumor cells with a blastoid appearance.

After consultation with a hematologist, we referred him to that department for further diagnosis and treatment. They performed a bone marrow puncture, the cytological result confirmed AML, and molecular genetic testing revealed *NPM1* mutation. Treatment was started following the protocol for patients with newly diagnosed AML that are not candidates for intensive chemotherapy with cytostatic drugs, venetoclax, and azacitidine.

He tolerated the treatment well, experiencing transient improvement in his skin condition. However, 4 months post-diagnosis, hospitalization occurred due to febrile neutropenia. A low leukocyte count (2.3×10^9/l; normal $4.0–10.0 \times 10^9$/l) and only two

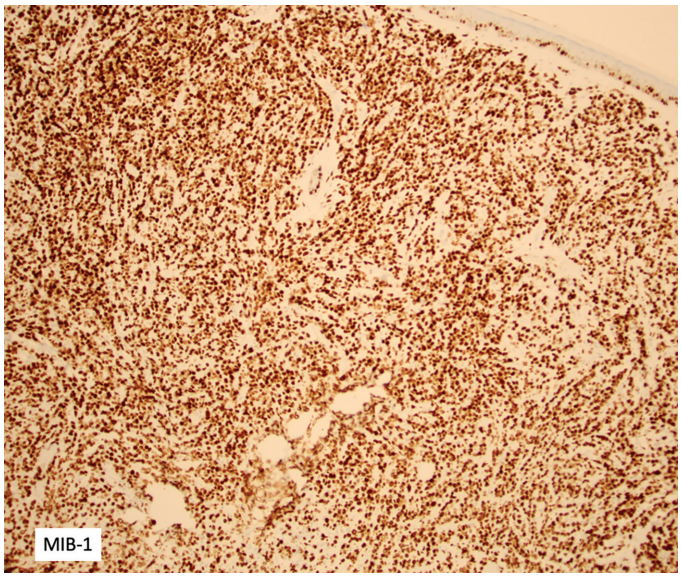

Figure 4 | MIB-1, a monoclonal antibody reactive with cells undergoing DNA synthesis, indicating very high proliferative activity in the figure presented.

neutrophils in the differential were noted. Inflammatory parameters, elevated lactate dehydrogenase, hypokalemia, and hyponatremia were observed. Antibiotic treatment was started, but the patient died 10 days later due to sepsis and general deterioration.

Discussion

An American clinicopathologic study published in 1984 showed that leukemia cutis developed in 55% of patients 1 month to several years after the diagnosis of systemic leukemia (8). In 38% of the patients, leukemia cutis and systemic leukemia were concurrent, and only 7% of the patients had skin lesions prior to the systemic signs, a condition also known as aleukemia cutis (8). In up to 60% of cases, clinical examination reveals nodules or erythematous to violaceus papules, and the central parts may show ulcerative changes. Less commonly, indurated plaques, palpable purpura, erythroderma, ulcers, and gingival hypertrophy may be observed (7). Rarely, some cases may present as a macular rash with minimal infiltrates and may mimic inflammatory dermatoses (9). Unusual presentations such as stasis dermatitis–like eruption, a chilblain-like eruption, cutaneous hyperpigmentation, and macrocheilia have also been described (10). Lesions are usually asymptomatic, although pruritus may be present. Occasionally a myeloid sarcoma (or chloroma or granulocytic sarcoma)—a greenish tumor due to myeloperoxidase-related green pigmentation—may be present (3). Not all cutaneous manifestations are due to leukemic infiltrates; up to 40% of patients diagnosed with leukemia present with non-specific cutaneous signs during the course of the disease (4). The non-leukemic cutaneous features of leukemia are also known as leukemid and are the result of bone marrow failure and drug eruptions (3). These cutaneous findings include neutrophilic dermatoses such as Sweet syndrome and pyoderma gangrenosum, leukocytoclastic vasculitis, and thrombocytopenia-induced petechiae. Patients are susceptible to opportunistic infections due to pancytopenia, leading to common occurrences of cutaneous mycoses and herpes virus infections (3, 5, 9).

Because skin manifestations can present with a variety of clinical features, it is sometimes difficult to recognize leukemia cutis based on clinical findings alone. In addition, bone marrow examination and peripheral blood findings help confirm the diagnosis

(2). AML is diagnosed when more than 20% of blasts are present in the bone marrow (4). The definitive diagnosis of leukemia cutis must be confirmed by histopathology (3). Histopathological examination usually shows infiltration with myeloblasts (2).

Treatment for AML includes chemotherapy alone, chemotherapy followed by stem cell transplantation, or radiation, and it is aimed solely at treating the underlying leukemia (3). Therapy with venetoclax and azacitidine is the treatment of choice for patients with newly diagnosed AML that are not candidates for intensive chemotherapy (11). Remission of hematological abnormalities is followed by complete or partial regression of cutaneous lesions. The prognosis for leukemia cutis is unfavorable because the presence of skin involvement suggests a high probability of extramedullary involvement of internal organs, with the most common site of spread being the central nervous system (12). A recent retrospective study published in 2019 by Wang et al., which included 62 patients with AML and leukemia cutis and 186 patients with AML but no leukemia cutis, showed that the 5-year survival rate was 8.6% in patients with AML with leukemia cutis compared to 28.3% in patients with AML without leukemia cutis (13). In 2021, a retrospective study of 42 patients in Taiwan was published; the median survival rate of the patients diagnosed with leukemia cutis was 7.2 months, and 74.3% of patients died within 1 year (3).

Conclusions

Leukemia cutis, which is most commonly associated with AML, is associated with a poor outcome because it usually means extramedullary involvement. In a small percentage of cases, cutaneous manifestations may be the first sign of AML, and so it is recommended to consider this possibility more often for early diagnosis and treatment.

References

1. Godínez-Chaparro JA, Valencia-Herrera AM, Duarte-Abdala MR, Mena-Cedillos CA, Toledo-Bahena ME. Leukemia cutis and other dermatological findings in pediatric patients with acute myeloid leukemia. Bol Med Hosp Infant Mex. 2021; 78:411–7.
2. Sharma SK, Gupta S, Seth T, Mishra P, Mahapatra M, Singh MK, et al. Leukemia cutis: an unusual presentation. Indian J Hematol Blood Transfus. 2012;28:175–7.
3. Chang YW, Lee CH, Tseng HC. Leukemia cutis in a medical center in southern Taiwan: a retrospective study of 42 patients. J Formos Med Assoc. 2021;120:226–33.
4. Krooks JA, Weatherall AG. Leukemia cutis in acute myeloid leukemia signifies a poor prognosis. Cutis. 2018;102:266.
5. Martínez-Leboráns L, Victoria-Martínez AM, Torregrosa-Calatayud JL, Alegre de Miquel V. Leukemia cutis: a report of 17 cases and a review of the literature. Actas Dermosifiliogr. 2016;107:e65–9.
6. Azari-Yaam A, Safavi M, Ghanadan A. Aleukemia cutis: clinicopathological and molecular investigation of two cases. J Cutan Pathol. 2020;47:747–54.
7. Rao AG, Danturty I. Leukemia cutis. Indian J Dermatol. 2012;57:504.
8. Su WP, Buechner SA, Li CY. Clinicopathologic correlation in leukemia cutis. J Am Acad Dermatol. 1984;11:121–8.
9. Martínez-Escanamé M, Zuriel D, Tee SI, Fried I, Massone C, Cerroni L. Cutaneous infiltrates of acute myelogenous leukemia simulating inflammatory dermatoses. Am J Dermatopathol. 2013;35:419–24.
10. Patterson W. Weedon's skin pathology. 5th ed. Amsterdam: Elsevier; 2021. Chapter 42, Cutaneous infiltrates-lymphomatous and leukemic; p. 1264–5.
11. Cherry EM, Abbott D, Amaya M, McMahon C, Schwartz M, Rosser J, et al. Venetoclax and azacitidine compared with induction chemotherapy for newly diagnosed patients with acute myeloid leukemia. Blood Adv. 2021;5:5565–73.
12. Parsi M, Go MS, Ahmed A. Leukemia cutis. In: StatPearls [Internet]. 2022 [cited 2022 Nov 14]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK541136/.
13. Wang CX, Pusic I, Anadkat MJ. Association of leukemia cutis with survival in acute myeloid leukemia. JAMA Dermatol. 2019;155:826–32.