

Case report

Leukemia cutis exhibiting Darier's sign: a rare presentation of acute monoblastic leukemiaİdil Sena Canver,¹ Turan Bayhan,² Esra Karakuş,³ Esra Kiratli Nalbant^{1,4}✉¹Department of Dermatology and Venereology, Ankara Bilkent City Hospital, Ankara, Turkey²Department of Pediatric Hematology and Oncology, Ankara Yildirim Beyazit University, Faculty of Medicine, Ankara, Turkey³Department of Pathology, Ankara Bilkent City Hospital, Ankara, Turkey⁴Department of Dermatology and Venereology, Ankara Yildirim Beyazit University, Faculty of Medicine, Ankara, Turkey**Abstract**

Leukemia cutis is a rare cutaneous manifestation of acute myeloid leukemia, most frequently associated with monocytic differentiation. Darier's sign, a wheal-and-flare response classically linked to cutaneous mastocytosis, has only rarely been reported in leukemia cutis and may represent a diagnostic pitfall. We report a pediatric patient diagnosed with acute myeloid leukemia that developed multiple violaceous papules on the extremities and trunk. Mechanical stimulation induced erythema and edema consistent with a positive Darier's sign. Histopathological examination revealed dermal infiltration by myeloperoxidase (MPO)-positive leukemic blasts, confirming leukemia cutis. Bone marrow aspiration and flow cytometry were compatible with acute monoblastic leukemia (AML-M5). This case highlights that Darier's sign may rarely occur in leukemia cutis and should not be considered exclusive to mastocytosis.

Keywords: acute myeloid leukemia, Darier's sign, leukemia cutis, pediatric dermatology**Received:** 26 November 2025 | **Returned for modification:** 27 January 2026 | **Accepted:** 3 March 2026**Introduction**

Acute myeloid leukemia (AML) is an aggressive hematologic malignancy characterized by impaired differentiation of hematopoietic stem cells and uncontrolled proliferation of blast cells (1). Cutaneous involvement, termed leukemia cutis, occurs most commonly in AML with monocytic differentiation, including acute monoblastic leukemia (AML-M5). It may precede, accompany, or follow systemic leukemia and can present as nodules, papules, or plaques, generally indicating disease progression and poor prognosis (2).

Darier's sign, characterized by localized erythema and edema following mechanical irritation, is typically associated with cutaneous mastocytosis and is rarely reported in hematologic malignancies (3). Here, we report a pediatric case of leukemia cutis associated with AML-M5, exhibiting a positive Darier's sign.

Case report

A 15-year-old male patient that had been hospitalized in the pediatric ward was referred to our dermatology clinic for evaluation of papules noted on the skin. According to his medical history, hemophagocytic lymphohistiocytosis had initially been suspected at an outside center due to prolonged fever,

hepatosplenomegaly, and laboratory abnormalities. After an unsuccessful course of treatment with anakinra and cyclosporine, he was transferred to our tertiary-care hospital.

On physical examination at the time of admission to our hospital, hepatosplenomegaly and bilateral cervical lymphadenopathy were noted. Dermatologic examination revealed 10 to 15 non-tender, non-pruritic papules (skin-colored to violaceous), up to 1 × 1 cm in size, distributed over the legs, arms, and trunk. Figure 1A shows the mechanically stimulated papule (red arrow) together with other non-stimulated papules (black arrows) on the lower extremity. Mechanical stimulation of one papule on the left anterior leg induced erythema and edema within five minutes, demonstrating a positive Darier's sign (Fig. 1B). Laboratory investigations revealed marked leukocytosis (white blood cells $70.22 \times 10^9/l$; reference range: 4.2–10.8) with anemia and thrombocytopenia (hemoglobin 11.7 g/dl; reference range: 13–16.6, platelets $30 \times 10^9/l$; reference range: 160–385), elevated ferritin (3,000 µg/l; reference range: 22–322), hypofibrinogenemia (0.67 g/l; reference range: 1.7–4.2), hypertriglyceridemia (359 mg/dl; reference range: 47–210), and elevated lactate dehydrogenase (2,259 U/l; reference range: 120–265). Given the concurrent extreme leukocytosis and cytopenias, an underlying hematologic malignancy was also considered.

A skin biopsy was obtained from an unstimulated lesion on the right distal leg. Differential diagnoses included cutaneous mastocytosis, leukemia cutis, cutaneous metastasis, and Langerhans cell histiocytosis. Histopathologic evaluation demonstrated dense dermal infiltration by blast cells (Fig. 2A), with strong cytoplasmic myeloperoxidase (MPO) positivity (Fig. 2B) and negative for CD117, CD3, CD34, PAX5, and TdT, consistent with leukemia cutis. Serum tryptase levels were within normal limits (4.9 µg/l; reference range: 0–11.4), excluding systemic mastocytosis. Bone marrow aspiration revealed monoblastic blasts, and flow cytometric analysis was compatible with AML-M5, showing diffuse infiltration by CD33-positive blasts. Diffusion magnetic resonance imaging revealed central nervous system involvement with concurrent facial paralysis. Additional imaging demonstrated renal and testicular infiltration. Based on all findings, induction chemotherapy with cytarabine and idarubicin was initiated. During treatment, the patient developed acute-onset painful erythema followed by extensive epidermal detachment with mucosal involvement, consistent with toxic epidermal necrolysis. Suspected medications were discontinued, and treatment with prednisolone (1 mg/kg/day) and intravenous immunoglobulin (0.4 g/kg/day) was started. Due to rapid clinical deterioration, plasmapheresis was performed on day 5. Unfortunately, the patient succumbed to progressive disease within a few days.

Discussion

Darier's sign, caused by mast cell degranulation, is classically linked to mastocytosis but has occasionally been reported in hematologic malignancies (3). Henostroza-Inga et al. described Darier-positive leukemia cutis in an infant with acute lymphoblastic leukemia (ALL), suggesting that lymphoblast-derived interleukin-3 may activate mast cells secondarily (4). Similar Darier-positive or Darier-like reactions have since been described in T-ALL and in primary cutaneous marginal zone lymphoma, including cases without histologic mast cell expansion (5–7).

In our patient, normal tryptase and the lack of mast cell proliferation supported an alternative explanation. We speculate that the provoked erythema and edema may reflect heightened local vascular responsiveness and mediator release within densely leukemic-infiltrated dermis, producing a Darier-like response despite the absence of mastocytosis. Although a limitation is the lack of paired pre- and post-provocation photographs of the same lesion, the wheal-and-flare reaction was clinically apparent at bedside.

To our knowledge, this is one of the very few reported pediatric cases of AML-M5 presenting with a concomitant positive Darier's sign.

Conclusions

This case expands the clinical spectrum of leukemia cutis and suggests that Darier's sign, although rare, may be encountered in pediatric AML-M5. Awareness of this association is important for dermatologists and hematologists because it may guide timely diagnosis and appropriate investigation. When Darier's sign is

observed outside the typical context of mastocytosis, leukemia cutis should be considered in the differential diagnosis.

References

1. Cho-Vega JH, Medeiros LJ, Prieto VG, Vega F. Leukemia cutis. *Am J Clin Pathol*. 2008;129:130–42.
2. Chitapur UG, Athanikar SB, Panchagavi AB, Naveen KN, Athanikar VS. Leukemia cutis: a sign of relapse. *Clin Dermatol Rev*. 2022;6:53.
3. Surjushe A, Jindal S, Gote P, Saple DG. Darier's sign. *Indian J Dermatol Venereol Leprol*. 2007;73:363–4.
4. Henostroza-Inga K, Zevallos-Giampietri E, Sánchez-García F, Sánchez J. Pediatric leukemia cutis: Darier's sign. *Int J Clin Exp Dermatol*. 2021;6:9–12.
5. Singh S, Taneja N, Kaul S, Arava S, Bhari N. Aleukemic leukemia cutis mimicking urticaria pigmentosa in a patient of T-cell acute lymphoblastic leukemia. *Indian J Dermatol Venereol Leprol*. 2020;86:105.
6. Yen A, Sanchez R, Oblender M, Raimer S. Leukemia cutis: Darier's sign in a neonate with acute lymphoblastic leukemia. *J Am Acad Dermatol*. 1996;34:375–8.
7. Leonard N, Lal K, Luffman C, O'Donnell P, Jolley L, Belazarian L. Darier sign in a teenager with primary cutaneous marginal zone lymphoma. *Pediatr Dermatol*. 2021;38:494–6.

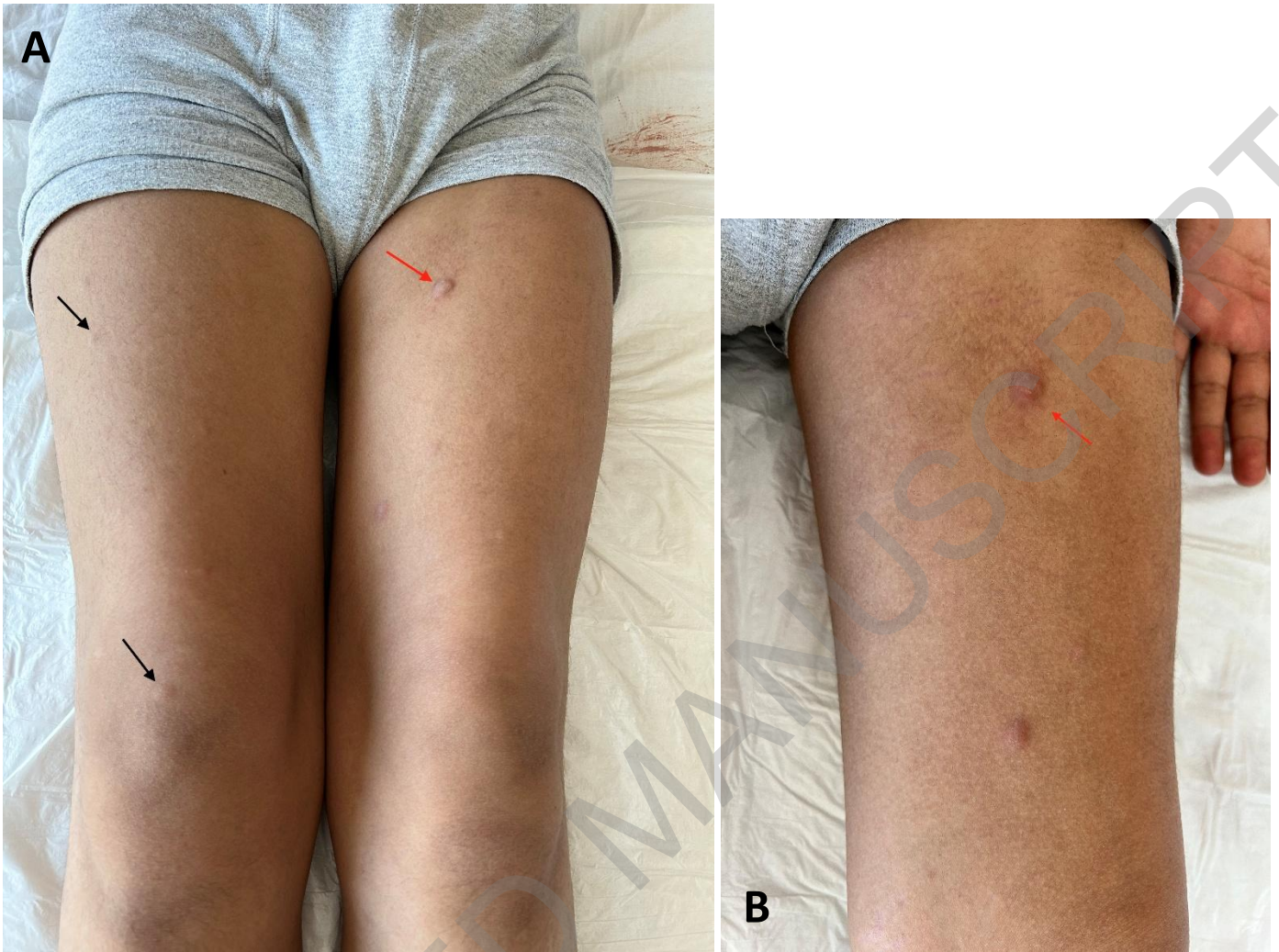


Figure 1. A) The mechanically stimulated papule is indicated by the red arrow and shows erythema and edema consistent with a positive Darier's sign. Additional non-stimulated, skin-colored papules are marked with black arrows, B) close-up view of the stimulated papule (red arrow) demonstrating erythema and edema following mechanical irritation.

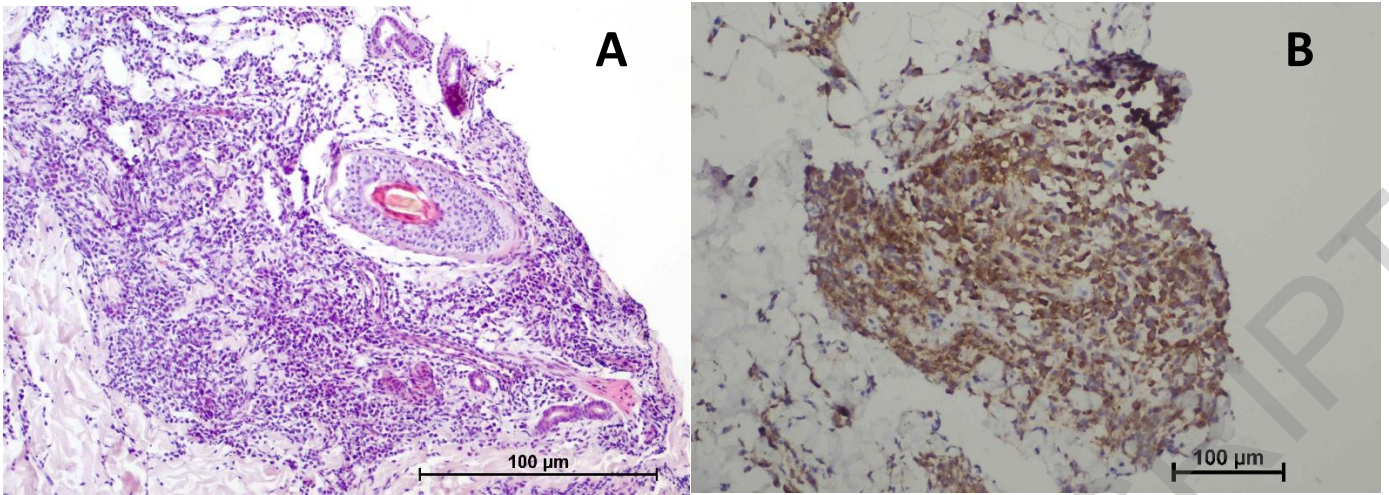


Figure 2. A) Diffuse dermal infiltration by leukemic blasts in the papillary dermis (hematoxylin and eosin, $\times 40$), B) strong cytoplasmic myeloperoxidase (MPO) expression in blast cells (MPO, $\times 40$).