

Case Report

International Journal of Clinical & Experimental Dermatology

Pediatric Leukemia Cutis: Darier's Sign

Katia Henostroza-Inga^{1*}, Oscar Cruz-Ballona², Reynaldo Pomar-Morante³, Roxana Lipa-Chancolla⁴, Rosalía Ballona-Chambergó⁵

¹Pediatrician and pediatric dermatology resident physician at Instituto Nacional de Salud del Niño-Brena, Lima, Peru

²Dermatology Resident Physician at the University of Sao Paulo Hospital das Clínicas, Sao Paulo, Brazil

³Dermatologist at Instituto Nacional de Salud del Niño-Brena, Lima, Peru

⁴Pathologist at Instituto Nacional de Salud del Niño-San Borja, Lima, Peru

⁵Pediatrician, dermatologist and pediatric dermatologist at Instituto Nacional de Salud del Niño-Brena, Lima, Peru

*Corresponding author

Katia Henostroza Inga, Avenida Brasil 600, Breña, Lima, Peru

Submitted: 31 March 2021; Accepted: 07 Apr 2021; Published: 12 Apr 2021

Citation: Katia Henostroza-Inga, Oscar Cruz-Ballona, Reynaldo Pomar-Morante, Roxana Lipa-Chancolla, Rosalía Ballona-Chambergó (2021) Pediatric Leukemia Cutis: Darier's Sign, International Journal of Clinical & Experimental Dermatology 6(1): 9-12.

Abstract

Leukemia Cutis (LC) is defined as infiltration and proliferation of neoplastic cells of lymphoid or myeloid lineage in the epidermis, dermis or hypodermis. The case of a 7-month-old infant with Leukemia Cutis, characterized by papules, nodules with a positive Darier's sign, with histopathological findings of an infiltrate of monomorphic lymphoid cells in the dermis and hypodermis, without the presence of mast cells, as a manifestation before acute lymphoblastic leukemia is presented in this article.

Keywords: Skin leukemia. Darier's sign. Acute lymphoblastic leukemia, Leukemia Cutis

Introduction

Leukemia Cutis (LC) associated with acute myeloid leukemia cases (30%) and of unusual presentation in acute lymphoblastic leukemia. This finding has been observed with more frequency in children rather than in adults, for which the early diagnose is necessary due to its implication in prognosis [1-7].

Leukemia Cutis can present as macules, papules, indurated plaques, nodules or unusual lesions that can simulate, for example, pigmented urticaria with hives and positive Darier's sign [4-7]. The exact pathophysiology of Darier's sign in these conditions is unknown, thus it is related to the release of interleukin 3 produced by lymphocytes which would cause proliferation and subclinical infiltration of mast cells [6].

Case report

A 7-month-old male infant, a product of a second and twin pregnancy, first twin, with no relevant history, with a 5-week progressive development of skin lesions: nodules and adenopathy. The physical examination reveals multiple infiltrated nodules, brown and purple, of various sizes (from 0.5 cm to 3 cm), generalized, the nodules on the back show Darier's sign (Figure 1) with satellite urticarial lesions (Figure 2), no mucosa involvement, and mild

hepatomegaly, adenopathy in the cervical and left axillary region are associated. The dermatoscopy revealed fine telangiectasias on an erythematous base. Hemoglobin 10.6 g / dL, leukocytes 6220 / mm³ (Neutrophils 249, Lymphocytes 5287), LDH: 833, AST: 51 U / L, alkaline phosphatase: 677. Serology for hepatitis B virus, human immunodeficiency virus, parvovirus, Epstein Barr, and TORCH (Toxoplasmosis, Rubella, Cytomegalovirus, Herpes Simplex) was all negative.



FIGURE 1: Multiple infiltrated nodules, brown, of various sizes,

the nodules on the back show Darier's sign.



FIGURE 2: Multiple infiltrated nodules, with satellite urticarial lesions.

The histopathology revealed in the dermis, and hypodermis, an interstitial infiltrate made up of cells with a monomorphic lymphoid appearance of medium size, with little cytoplasm, prominent nucleoli, abundant mitosis, and space which was almost free of infiltration between the epidermis, and papillary dermis (Grenz zone) (Figure 3).

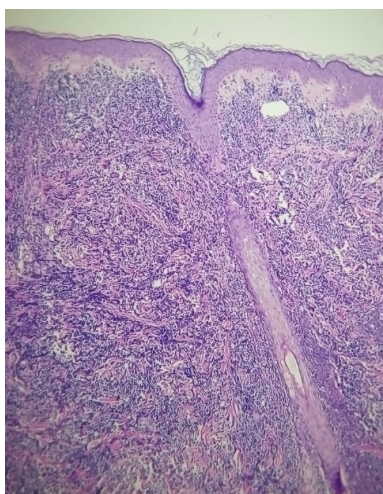


FIGURE 3A: In the dermis and hipodermis an interstitial infiltrate

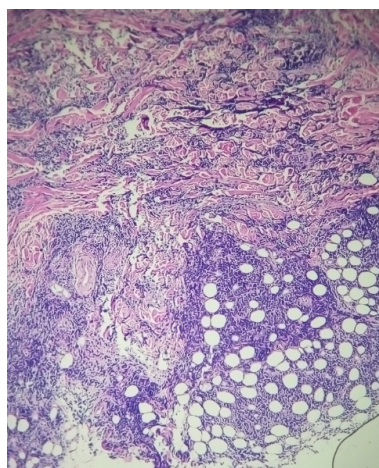


FIGURE 3B: Interstitial infiltrate is made up of cells with a mono-

morphic lymphoid.

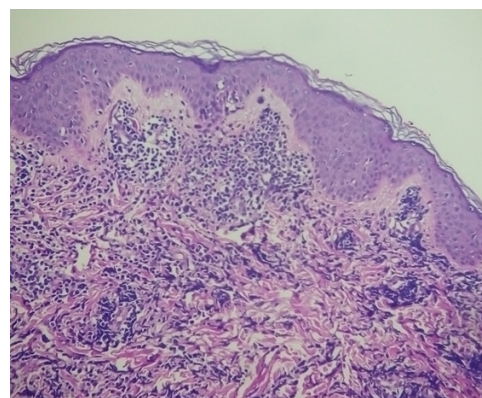


FIGURE 3C: Space which was almost free of infiltration between epidermis and papillary dermis (Grenz zone).

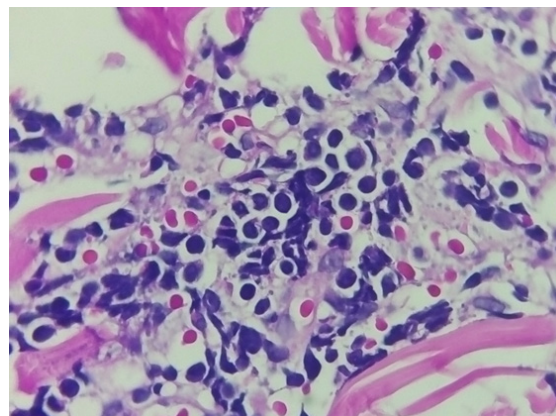


FIGURE 3D: Interstitial infiltrate is made up of cells with a monomorphic lymphoid appearance of medium size, with little cytoplasm, prominent nucleoli.

The immunohistochemistry showed positive CD79a, CD99, KI67, PAX5, TDT (Figure 4); and negative CD20, CD117 as well as negative myeloperoxidase. The flow cytometry reported bone marrow infiltrated by 11.6% of B lymphoblasts with pathological phenotype in Pre-B stage and a subpopulation in the Pro-B stage (Figure 5). The bone marrow study revealed myeloid elements with severe maturation paucity, erythroid elements both forming groups and dispersed, dysmorphic megakaryocytes, presence of immature elements with a multifocal blastic aspect; to which the immunohistochemistry shows positive TDT, CD34, CD117, CD10, CD79a; all these findings result in being compatible with the B-precursor acute lymphoblastic leukemia with cutaneous infiltration.

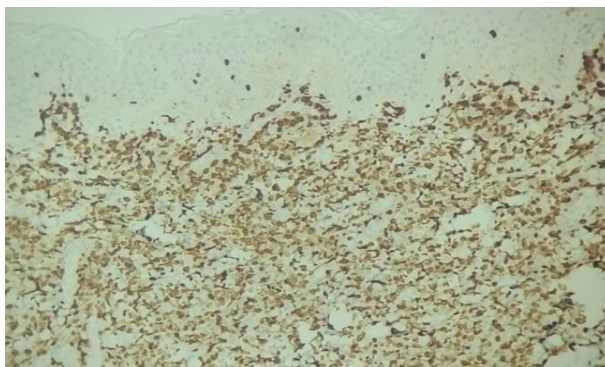


FIGURE 4 A: The immunohistochemistry showed positive KI67.

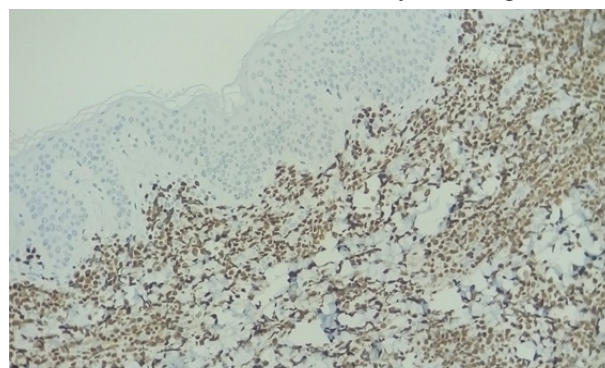


FIGURE 4 B: The immunohistochemistry showed positive PAX5.

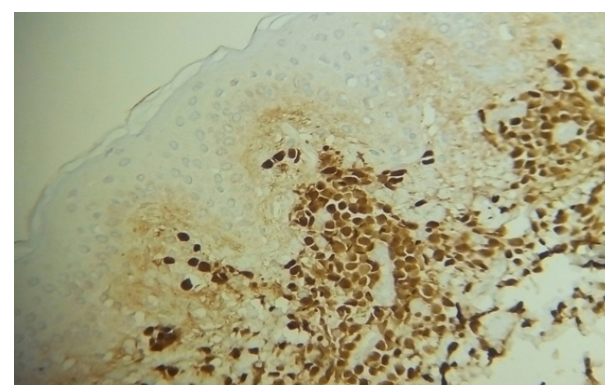


FIGURE 4 C: The immunohistochemistry showed positive TDT.

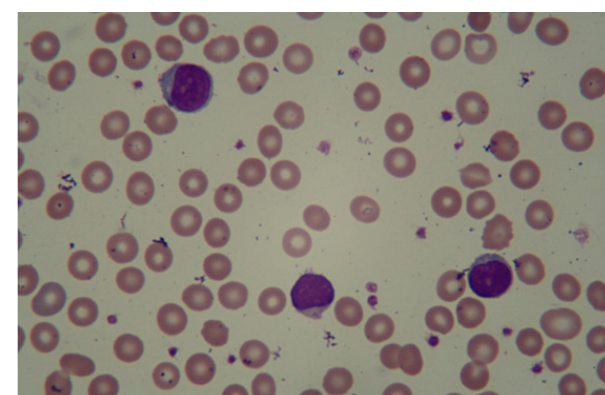


FIGURE 5: The flow cytometry reported bone marrow infiltrated

by B lymphoblasts with pathological phenotype in the Pre-B stage and a subpopulation in the Pro-B stage.

Discussion

LC is a non-frequent entity and the specific cutaneous manifestation of leukemia. It is characterized by the infiltration of immature malignant hematopoietic cells in the skin of patients with some type of leukemia. It occurs in 50% of the congenital leukemia cases, 10-50% of monocytic leukemia, 6-10% of lymphocytic and granulocytic leukemias, and only in the 1.3-3% of acute lymphoblastic leukemias [7-11]. LC lesions can appear before the systemic manifestations of leukemias in 7% of cases and they can be the only sign of presentation. Furthermore, they can even occur in the absence of peripheral blood and/or bone marrow involvement, which is called Skin Aleukemia. LC is considered to be a poor prognostic indicator when it precedes systemic leukemia because it indicates its progression, but when it occurs simultaneously, it indicates relapse; the latter being the most frequent form of presentation since it occurs in more than a third of cases [2-11].

It presents with clinical heterogeneity, with papules and nodules being the most common, as well as macules, plaques, and ulcers. These lesions range from a few to several centimeters large, single, or multiple, yellowish to brown, red, purplish, localized, or disseminated [11]. Unusual findings that simulate other dermatoses have been reported as erythema multiforme, erythroderma, pyoderma gangrenosum, ecthyma gangrenosum, leukocytoclastic vasculitis, paronychias, and, rarely, lesions that simulate urticaria, urticaria pigmentosa, with a positive Darier's sign [5-12]. The diagnosis of LC is based on the correlation of the clinical picture with the histopathological findings, the distinction of the dominant cell type, and the immunohistochemistry.

Our case is of an infant with Leukemia Cutis, with very particular characteristics such as association with acute lymphoblastic leukemia, a rare event; clinical expressions before hematological alterations; and the most striking finding, the presence of multiple nodules with a positive Darier's sign surrounded by a significant urticarial reaction; findings which had not been described in children and that could correspond to premonitory clinical manifestations of the presence of mast cells in the bone marrow. In our patient, this fact was evidenced by the finding of positive CD17 (1-2%) in the immunohistochemistry of the bone marrow study. According to the reference in the literature, in hematological disorders, an increase in mast cells in bone marrow is found in 2% of patients, as a result of the increase in plasma cells and lymphocytes, the latter being a producer of interleukin 3, which intervenes in the proliferation and hyperactivity of mast cells with an exaggerated release of mediators which is considered a secondary characteristic of hematological neoplasms [13].

Conclusion

A case of Leukemia Cutis in an infant, with unusual findings, such as its association with ALL, the presentation of nodules with a positive Darier's sign, and urticarial lesions around these lesions is presented. These previously mentioned and undescribed findings constitute an indicator of aggressiveness and torpid evolution of the ALL picture.

References

1. Andriescu EC, Coughlin CC, Cheng CE, Prajapati VH, Huang JT, et al. (2019) Pediatric leukemia cutis: A case series. *Pediatr Dermatol* 36: 658-663.
2. Jiang X, Wang W, Zhang M (2015) Leukemia Cutis: An Unusual Presentation of Acute Lymphoblastic Leukemia in a Child. *Indian J Dermatol* 60: 636.
3. Mansoori P, Taheri A, O'Neill SS, Sanguenza OP (2018) T-Lymphoblastic Leukemia/Lymphoma with Annular Skin Rash and Epidermotropism. *Am J Dermatopathol* 40: 676-678.
4. Cho-Vega JH, Medeiros LJ, Prieto VG, Vega F (2008) Leukemia cutis. *Am J Clin Pathol* 129: 130-142.
5. Raj S, Khopkar U, Wadhwa SL, Kapasi A (1993) Urticaria-pigmentosa-like lesions in acute lymphoblastic leukaemia (2 cases). *Dermatol* 186: 226-228.
6. Yen A, Sanchez R, Oblender M, Raimer S (1996) Leukemia cutis: Darier's sign in a neonate with acute lymphoblastic leukemia. *J Am Acad Dermatol* 34: 375-378.
7. Ratnam KV, Khor CJL, Su WPD (1994) Leukemia Cutis. *Dermatol Clin* 12: 419-431.
8. Bodemer C, Larralde M, Luk D, Mendiratta V, Purvis D, et al. (2019) *Harper's Textbook of Pediatric Dermatology*, 2 Volume Set. (Hoeger PH, Kinsler V, Yan AC, eds).
9. Jandali S, Kirschner RE (2011) Congenital leukemia cutis presenting as multiple violaceous lesions in a newborn. *Ann Plast Surg* 66: 310-312.
10. Haidari W, Strowd LC (2019) Clinical characterization of leukemia cutis presentation. *Cutis* 104: 326-330.
11. Lamberti A, Miracco C, Scaramuzzino F, Cinotti E, Rubegni P, et al. (2018) Rare clinical manifestations of leukemia cutis. *J Cutan Pathol* 45: 799-801.
12. Kauh YC (1987) Cutaneous Manifestations of Leukemia. *Yonsei Med J* 28: 81-90.
13. Prokocimer M, Polliack A (1981) Increased Bone Marrow Mast Cells in Preleukemic Syndromes, Acute Leukemia, and Lymphoproliferative Disorders. *Am J Clin Pathol* 75: 34-38.

Copyright: ©2021 Katia Henostroza Inga. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.