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CASE REPORT

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Leukemia cutis revealing relapse of a chronic myeloid leukemia: A case report

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Key Clinical Message

Clinical presentation of leukemia cutis (LC) is polymorphic and can reveal a malignant hemopathy. More commonly described in cases of acute myeloid leukemia (AML), LC can also occur in case of chronic myeloid leukemia (CML).

Abstract

Leukemia cutis is a rare form of extramedullary feature of malignant hemopathy, seldom associated with CML. Its clinical presentation is pleiotropic and differential diagnosis is broad. It relies on clinical and typical histological and biomolecular concordance. Once confirmed, treatment is based on that of the primary condition. We present a case of a leukemia cutis revealing a relapse of a CML successfully treated by tyrosine kinase inhibitor.

KEYWORDS

chronic myeloid leukemia - acute myeloid leukemia, hematology, immunology, leukemia cutis, myeloproliferative syndrome

1 | INTRODUCTION

Leukemia cutis (LC) refers to neoplastic leukocyte infiltration within the skin and encompasses various forms including myeloid sarcomas, chloromas, or monoblastic sarcomas, each differing in their neoplastic precursors.[1] LC is an uncommon condition depending on the subtypes of leukemia that involve the skin, whether myeloid or lymphoid disorders and is more commonly described in patients with acute myeloid leukemia (AML) but may also be seen with chronic myeloid leukemia (CML), acute or chronic lymphocytic leukemia, and myelodysplastic syndrome.[1–4] It appears to correlate with the progression of leukemia and is concomitant in a large majority of with other associated extramedullary involvement but may occasionally be diagnosed synchronously or months to year before the hematological disease onset and refers to aleukemic LC.[5,6] Etiopathogenesis behind the skin neoplastic leukocyte migration remains unclear but mechanisms involving chemotaxis have been suggested; referring to the concept of skin selective homing.[1] LC is generally asymptomatic and can manifest as either localized or generalized and encompasses various forms, including papules, plaques, and nodules from purplish to brownish color. We report herein a case of LC revealing a relapse of CML in a 62-year-old patient successfully treated by dasatinib.

2 | CASE HISTORY/EXAMINATION

A 62-year-old man presented to our haemato-oncology department for multiple painful and firm subcutaneous nodes on the forearms, the left buttock, and the knee. He first described nodes followed by surrounded hematoma. Past medical history was notable for arterial hypertension treated by amlodipine and CML. The latter was diagnosed in 2006 and initially treated by Imatinib for 3 years with inadequate therapeutic response. He then started dasatinib, which was partially controlled. He also complained about a worsening dyspnea, sub-pyrexia, and arthralgia. There was no history of trauma, travel, infection, or new drug initiation. Furthermore, the patient acknowledged recent irregular medication intake. At physical examination, the patient was not febrile. Chest auscultation was unremarkable. The rheumatological examination did not show any joint effusion. Skin examination showed painful and firm subcutaneous nodes with circumferential purplish discoloration and peripheral hematoma (Figure 1).

3 | METHODS

At this stage and considering the skin features in the context of CML, the most accurate differential diagnoses were the following: LC, cutaneous vasculitis, nodular hypodermitis, and erythema nodosum.

We initiated our investigations with laboratory tests, revealing the following: hemoglobin: 9.5 (13–17 g/dL), white blood cells: 199.33 ($3.5–11\times10^9$/L), neutrophils: 93.05 ($1.5–6.7\times10^9$/L), lymphocytes: 7.18 ($1–4\times10^9$/L), monocytes: 24.32 ($0.2–0.8\times10^9$/L) and 5% of blasts, platelets: 389 ($150–400\times10^9$/L), C-reactive protein: 18.7 (<5 mg/L), haptoglobin: <10 (50–220 mg/dL), creatinine: 1.32 (0.8–1.3 mg/dL), lactate dehydrogenase: 7.268 (50–150 U/L), and uric acid: 12.4 (3.5–7.2 mg/dL). Coagulation tests were consistent with a disseminate intravascular coagulation (DIVC): D-dimer: 23.077 (<500 ng/mL), fibrinogen: 1.07 (1.8–4 g/L), and prothrombin ratio: 40% (85%–100%). Blood hemocultures were negative. Serological assays for HIV, HCV, Rickettsia, and syphilis were negative while he presented immunological scar of contact with CMV, EBV, and HBV. The leukocytosis raised suspicion of a recurrence of CML or even a progression to an AML. The bone marrow aspiration demonstrated a rich marrow with proliferation of the granular lineage, without excess blasts (3.9%), and associated with dysplasia on the erythroid and megakaryocytic lineages (OGATA score = 2/4). Left knee skin biopsy revealed a moderate interstitial infiltrate of the derma and hypoderm, comprising myeloid-like cells at various stages of maturation without excess blasts (Figures 2 and 3). Immunohistochemistry analysis revealed a strong positive reaction against anti-MPO antibody without staining against $CD34^+$ and $CD117^+$. The

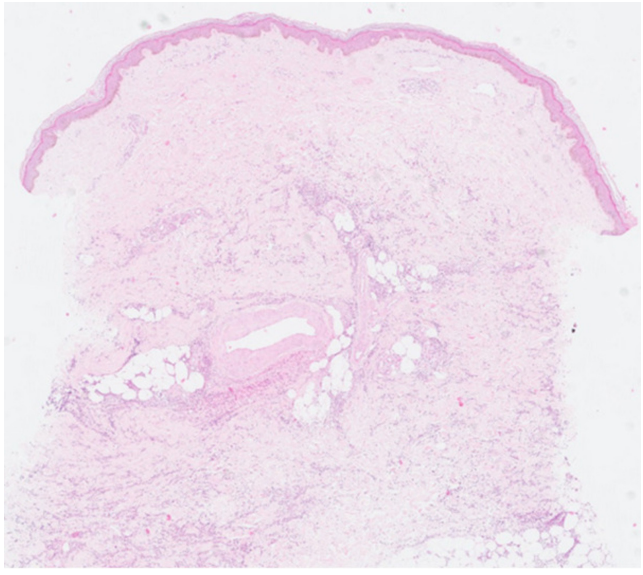

FIGURE 2 Histopathology. Original magnification: ×2,5. Histological examination of the epidermal layer, stratum corneum, and basal membrane is unremarkable. Dermis and hypodermis were sites of significant interstitial infiltration.

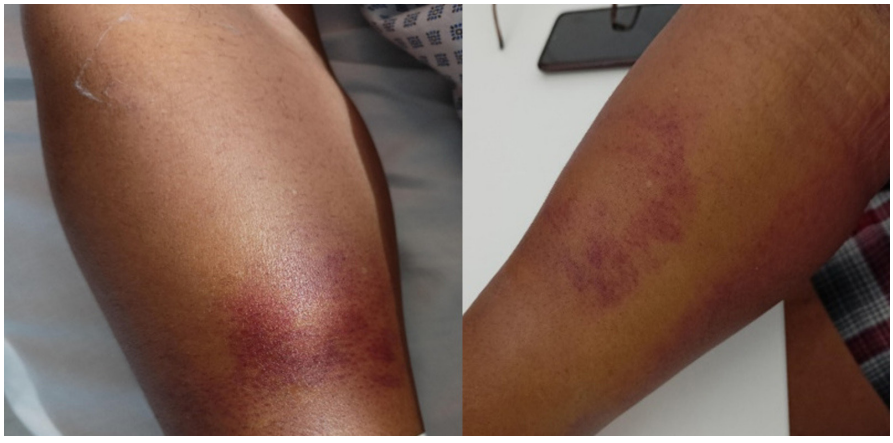

FIGURE 1 Purplish subcutaneous nodes with peripheral hematoma of the limbs.

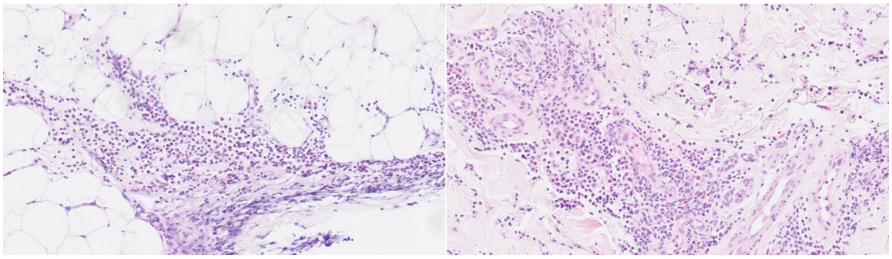

FIGURE 3 Histopathology. Original magnification: ×20. Interstitial infiltrate of the dermis and hypodermis by myeloid-like cells without blasts excess.

epidermis, stratum corneum, and basal membrane were unaffected. Histological appearance was consistent with LC, a dermal, and hypodermal infiltration of CML cells without transformation into AML.

4 | CONCLUSION AND RESULTS

Th final diagnosis was a relapse of CML presented by LC and complicated by DIVC due to dasatinib interruption. In the meantime, the patient was treated with Hydrea before returning to dasatinib. Hematological follow-up was marked by biological and clinical remission of the CML with complete regression of the LC.

5 | DISCUSSION

The patient underwent a relapse of CML simultaneously with the cutaneous involvement that revealed it. LC is less commonly described in adults,[7] particularly in the case of CML. Moreover, the appearance of LC is generally linked to a transformation into a blastic phase, reflecting the progression of the disease,[3] which is not the case here. In our case, there were no additive cutaneous manifestations of bone marrow insufficiency relative to cytopenia that can occur and which may be rigorously interpreted. Other associated extramedullary involvement may be described in a patient with LC as the central nervous system that worsens the prognosis,[6] but this was not observed in our evaluation. Osteoarticular pain is another feature of extramedullary leukemic involvement, typically described by our patient. Joint swelling has to be distinguished from crystal arthropathies given the propensity to develop gout in the context of active leukemia. The particularity of our report lies in the occurrence of LC in a patient diagnosed with CML, without progression to a blast phase and without extramedullary involvement other than the cutaneous manifestation. Furthermore, LC may present in various forms, including papules, plaques, and nodules. Differential diagnosis of those manifestations is broad such as neoplastic, chemotherapy-related, inflammatory conditions (erythema nodosum, neutrophilic dermatosis, etc.) or infectious resulting from immunosuppression, and emphasizes the key role of histology in the diagnosis workup.[1] Diagnosis of LC relies on histopathology, particularly on immunohistochemistry and tissue immunophenotyping. In our patient, cutaneous involvement was localized in the dermis and subcutaneous tissue, characterized by a significant interstitial infiltrate of myeloid-like cells at various and without excess of blasts. Further investigations confirmed the diagnosis of LC showing an increased expression of anti-MPO staining, which is consistent with existing literature.[5] It is not possible to categorize the various forms of leukemia solely through skin biopsy, and therefore, further investigations such as cytochemical and molecular genetic analyses are required.[1] When LC is suspected, a comprehensive biological assessment along with bone marrow aspiration and osteo-medullar biopsy helps to establish the diagnosis of systemic leukemia, which in this case was imputable to the lack of therapeutic observance. The therapeutic approach of the LC relies on the management treatment of the malignant hemopathy, which varies according to the nature of the extramedullary involvement. In the case of contraindicated chemotherapy, radiotherapy can solely be used symptomatically on the pain or pruritus induced by the LC.[8] A combination of radiotherapy and chemotherapy does not provide additional improvement.

Leukemia cutis is a rare manifestation of malignant hemopathies, and even rarer in the case of CML. Diagnosis relies on clinical suspicion and should be confirmed through biological, molecular, and histological investigations in the context of a malignant hemopathy, sometimes antedated by the diagnosis of leukemia cutis.

AUTHOR CONTRIBUTIONS

Amine Chérif: Conceptualization; data curation; formal analysis; investigation; methodology; project administration; writing – original draft; writing – review and editing. **Mohammad Yassine Chérif:** Conceptualization; data curation; formal analysis; investigation; methodology; project administration; supervision; validation; writing – original draft; writing – review and editing. **Anne-Laure Trépant:** Conceptualization; data curation; formal analysis; supervision. **Anne-Pascale Meert:**

Conceptualization; methodology; project administration; supervision; validation; writing – review and editing. **Maxime Ilzkovitz:** Conceptualization; data curation; formal analysis; investigation; methodology; project administration; supervision; validation; visualization; writing – review and editing.

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FUNDING INFORMATION

None declared.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author, Cherif MY, upon reasonable request.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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