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

Amine Chérif[1], Mohammad Chérif[2], Anne Laure Trépant[2], Anne Pascale Meert[1], and Maxime Ilzkovitz[1]

[1]Jules Bordet Institute
[2]Erasmus Hospital

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Authors:

Amine Chérif[1]; Mohammad Yassine Chérif[2]; Anne-Laure Trépant[3] ; Anne-Pascale Meert[1] ; Maxime Ilzkovitz[1]

Affiliations:

[1]Department of Intensive Care and Oncological Emergencies & Thoracic oncology, Institut Jules Bordet, Université Libre de Bruxelles, Brussels, Belgium. [2]Department of Rheumatology, Erasme University Hospital, Université Libre de Bruxelles (ULB), Brussels 1070, Belgium. [3]Department of Pathology, Erasme University Hospital, Université Libre de Bruxelles (ULB), Brussels 1070, Belgium.

Corresponding author:

Mohammad Yassine Chérif, MD; Department of Rheumatology at Erasme University Hospital, Université Libre de Bruxelles (ULB), Brussels 1070, Belgium.

Tel. +32 2 555 31 11 - Email:*Mohammad.yassine.cherif@ulb.be*

Conflicts of interest and e-mails:

Amine Chérif : None declared. Email : amine.cherif@ulb.be

Mohammad Yassine Chérif : None declared . Email : mohammad.yassine.cherif@ulb.be

Anne-Laure Trépant : Non declared. Email : anne-laure.trepant@hubruxelles.be

Anne-Pascale Meert : None declared. Email : anne-pascale.meert@hubruxelles.be

Maxime Ilzkovitz : None declared. Email :*maxime.ilzkovitz@hubruxelles.be*

Authors involvement:

Amine Cherif has substantial contributions in de drafting and writing of the case report. All authors have equally participated in the correction of the present case report. Mohammad Yassine Chérif and Maxime Ilzkovitz were responsible for the final reading. Final version has been approved by all the authors.

Patient's consent :

The authors obtained written consent from patients for their photographs and medical information to be published in print and online and with the understanding that this information may be publicly available. Patient consent forms were not provided to the journal but are retained by the authors

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Abbreviations used:

DIVC : disseminate intravascular coagulation ; LC : leukemia cutis ; CML : chronic myeloid leukemia ; AML : acute myeloid leukemia

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

LC is a rare form of extramedullary feature of malignant hemopathy, seldom associated to 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.

Introduction

LC refers to neoplastic leukocytes 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 AML but may also be seen with CML, acute or chronic lymphocytic leukemia and myelodysplastic syndrome (1,2). 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 (3,4). Etiopathogenesis behind the skin neoplastic leukocytes 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.

Casehistory/examination

A 62-year-old man presented to our haemato-oncology department for multiple painful and firm subcutaneous nodes on the forearms, the lefts buttock and 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 three years with inadequate therapeutic response. He then started Dasatinib, which was partially controlled. He also complained about a worsening dyspnea, subpyrexia 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. Rheumatological examination did not show any joint effusion. Skin examination showed painful and firm subcutaneous nodes with circumferential purplish discoloration and peripheral hematoma (Fig. 1).

Methods

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

We initiated our investigations with laboratory tests, revealing : Hemoglobin 9.5 (13-17 g/dL), White blood cells 199.33 (3.5-11 x10ˆ9/L), Neutrophils 93.05 (1.5 – 6.7 x10ˆ9/L), Lymphocytes 7.18 (1-4 x10ˆ9/L), Monocytes 24.32 (0.2-0.8 x10ˆ9/L) and 5% of blasts, Platelets 389 (150-400 x10ˆ9/L), C-reactive protein was 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), 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), Prothrombin ratio 40% (85-100%). Blood hemocultures were negatives. 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 (Fig. 2 and 3). Immunohistochemistry analysis revealed a strong positive reaction against Anti-MPO antibody without staining against CD34+ and CD117+. The 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.

Conclusion and Results

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.

Discussion

The patient underwent a relapse of CML simultaneously with the cutaneous involvement that revealed it. LC is less commonly described in adults (5), particularly in the case of CML. In our case, there was no additive cutaneous manifestations of bone marrow insufficiency relative to cytopenia that can occurs 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 (4) 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 with crystal arthropathies given the propensity to develop gout in context of active leukemia. 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, ...) or infectious resulting from immunosuppression, and emphasizes the key role of histology in the diagnosis work-up (1). Diagnosis of LC relies on histopathology, and 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 (3). 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 diagnosis of systemic leukemia, which in this case was imputable to the lack of therapeutic observance. Therapeutic approach of the LC relies on management treatment of the malignant hemopathy, which varies according to the nature of the extramedullary involvement. In case of contraindicated chemotherapy, radiotherapy can solely be used symptomatically on the pain or pruritus induced by the LC. Combination of radiotherapy and chemotherapy does not provide additional improvement.

LC 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 context of a malignant hemopathy; sometimes antedated by the diagnosis of leukemia cutis.

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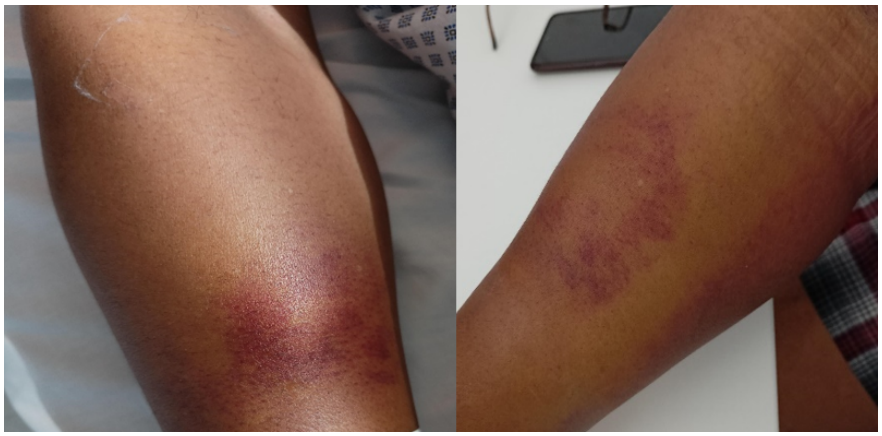

Figure 1 Purplish subcutaneous nodes with peripheral hematoma of the limbs

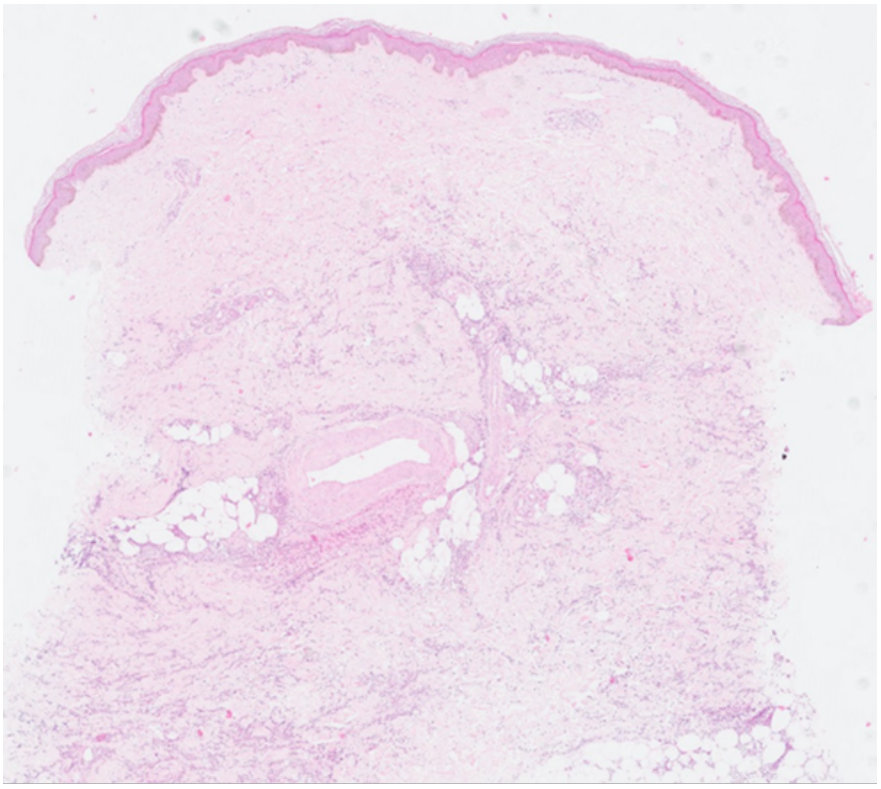

Figure 2 Histopathology. Original magnification : x2,5. Histological examination of epidermal layer, stratum corneum and basal membrane is unremarkable. Dermis and hypodermis were site of significant interstitial infiltration.

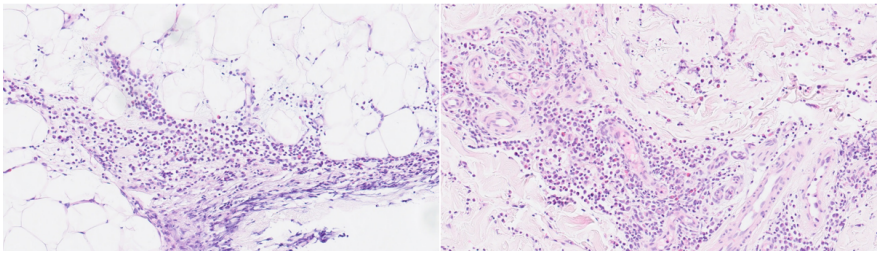

Figure 3 Histopathology. Original magnification : x20. Interstitial infiltrate of the dermis and hypodermis by myeloid-like cells without blasts excess.