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REVIEW ARTICLE

Specific skin lesions in hairy cell leukemia at presentation: case report and review of literature

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Abstract Skin involvement in hairy cell leukemia (HCL) at presentation is a relatively rare manifestation of the disease. A 60-year-old male patient in whom cutaneous lesions were the initial manifestation of hairy cell leukemia together with leukocytosis, monocytopenia, massive splenomegaly, and leukemic maculopapulous infiltration of the almost whole skin is described. The present case is the forth mentioned in the literature with specify of leukocytosis in peripheral blood, consisting mostly of hairy cells. The patient was treated with two courses of 2-chlorodeoxiadenosine (2-CdA, Cladribine) and splenectomy and after this cutaneous lesion disappeared and general condition is improved.

Keywords Hairy cell leukemia · Cutaneous manifestation · Clinical course · Leukocytosis · 2-Chlorodeoxiadenosine

Introduction

Hairy cell leukemia (HCL) is characterized by the presence of "hairy cells" (tricholymphocytes) in the circulating blood, bone marrow, and the spleen [1]. Specific skin lesions were reported to occur during the course of the disease in approximately 8% of patients but at presentation they were reported only in three reports pointing the rarity of presenting fourth case [2–4].

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Case report

A 60-year-old male patient presented in January 2008 with malaise, left costal margin fullness, and splenomegaly. Over the next several months he lost 10 kg in weight. The skin changes were initially rare but spread over the next 2 months to involve the extent of almost entire skin. There were painless maculo papular, red brick skin infiltrates 1–2 cm in diameter (Fig. 1). The enlarged spleen (28 × 12 × 20 cm) was found on abdominal ultrasound displacing the left kidney, stomach, and loops of the small bowel.

Laboratory data: Hemoglobin 90 g/l, platelets 73 × 10^9/l, and white blood cells (WBC) 101 × 10^9/l, (differential leukocyte formula: segmented 6%, lymphocytes 4%, and tricholymphocytes 90%). The bone marrow aspirate was normocellular with 70% TRAP positive "hairy" lymphocytes. The immunophenotype of the peripheral blood mononuclear cells was: CD19 + (100%), CD20 + (100%), CD22 + (100%), CD103 + (91%), CD11c + (97%), FMC7 + (83%), CD45 + bright(100%), CD25-(3%), mkappaIg-(1%), and mlambdaIg-(1%). Bone marrow histology revealed hipercellularity with diffuse infiltration of relatively uniform lymphoid cells which presented 80–90% of nucleated bone marrow cells with abundant and bright cytoplasm. The bone marrow immunohistochemistry showed: CD79alfa+, CD20+,CD10−, CD3−,CD5−, CD43−, IgD−, IgM−, DBA44+, anexin+, cyklin D1−,

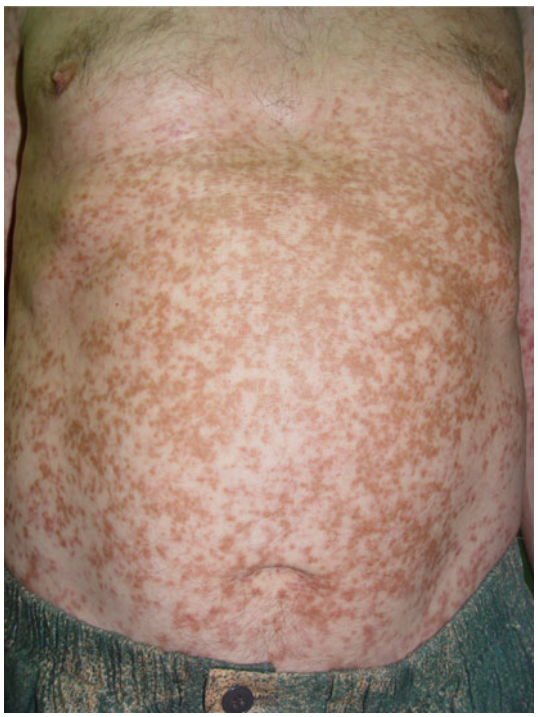

Fig. 1 Erythematous maculo-papular skin lesions

and bcl2+. The biopsy of dermis and hipodermis, showed perivascular and patchy infiltrates, composed of small- to medium-sized lymphoid cells, with an oval or indented nuclei, with homogenous, ground-glass chromatin, inconspicuous nucleoli and abundant, pale blue cytoplasm.These cells were DBA44 positive (Fig. 2). The patient was treated with cladribine 10 mg s.c.(0.14 mg/kg tt) from 1 to 5 day. Two months after treatment skin lesions improved but did not disappear. The spleen temporarely decreased in size but during the following months it started increasing again making mechanical difficulties to the patient particularely when bending. The bone marrow infiltration with hairy cells persisted. The patient was submitted to splenectomy and spleen 4500 g in weight was removed. After splenectomy a second course of cladribine was applied in the same dosage. He is now well with almost normal CBC and skin infiltrates disappeared.

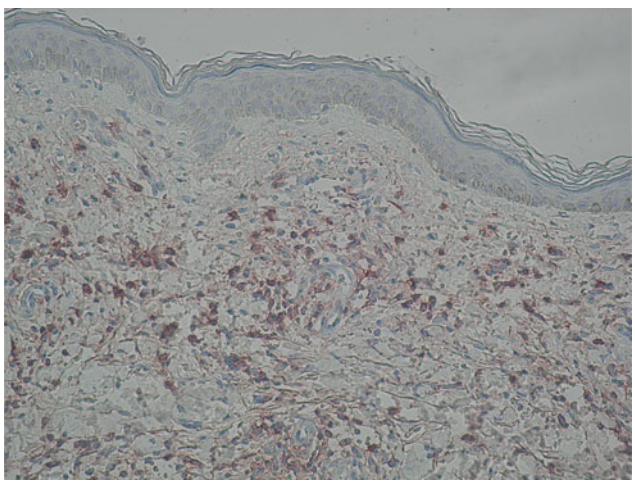

Fig. 2 The skin biopsy showing perivascular and patchy infiltrates in the upper dermis and hipodermis composed of small to medium-sized lymphoid cells (Immunohistochemical staining DBA 44+)

Discussion

Leukemia cutis is infiltration of the epidermis, dermis and the subcutaneous tissue by the leukemic cells. It may be found in a variety of leukemia's. Clinical aspects of specific lesions in HCL show wide polymorphism such as maculopapular eruptions, nodules, infiltrative plaques and ulcers [5–8]. The biopsy indicates that cell infiltrates are perivascular involving the dermis and sparing epidermis [3]. Although skin leukemides in HCL occur during the course of the disease in about 8% of cases they are rare at presentation [2–4, 9–12]. They have been described as evident at presentation only three times prior to the present report [2–4]. Carsuzaa et al. [12] reported that 47 (56%) out of 84 HCL patients had cutaneous symptoms. The majority of them were caused by infection and leukemia cutis was specifically seen in only two patients later in the course of disease [12]. Lawrence et al. [2] reported the first case with specific cutaneous lesions at presentation. He concluded that cutaneous manifestations are not generally recognized as a diagnostic source in patients with HCL because skin biopsy is seldom undertaken. Arai et al. [3] reported a 68-year-old man with HCL and skin lesions and reviewed the literature to estimate the incidence of specific lesions among 600 patients with HCL with regard to the presence/absence of leukemic skin lesions (Table 1). Among this cohort 48/600 patients had such lesions with the incidence of 8%. In the group of 48 patients the specific lesions have been confirmed histologically in eight patients. In another

Table 1 The incidence of specific skin lesions in several series

References	Number of patients	Number of patients with specific skin lesions
Lawrence et al. [2]	1	1
Finan et al. [13]	113	1
Bilsland et al. [4]	1	1
Zak et al. [5]	1	1
Arai et al. [3]	1	1
Damasio et al. [9]	203	15
Raanani et al. [10]	1	0
Carsuzaa et al. [12]	84	2

two patients dermal affection was confirmed by fine needle biopsy making incidence of only 1.6%. The TRAP staining was performed only in 2/10 patients studied. In the remaining 38 patients the lesions were declared as leukemic only based on clinical examination without the supporting histology [3]. Bilsland et al. [4] reported a patient with transient skin lesions at presentation who later developed pulmonary tuberculosis. In three reported cases in the literature [2–4] with specific skin lesions at presentation the number of WBC was low, normal and elevated, respectively. These three presented patients were treated with splenectomy and interferon-α and followed up from 12 to 45 months. The patient reported by Bilsland et al. [4] had elevated WBC the majority of which appeared to be hairy cells. Based on these data and clinical course of our patient we can no more state that cutaneous involvement regardles of stage of disease is not clearly poor prognosis indicator [2, 3, 13]. Leukemia cutis in all presented cases responded to the specific treatment of HCL with disappearing of cutaneous infiltrates.

In the series of 113 patients by Finan et al. only one patient had leukemic skin lesions (1.1%). Consequently, their incidence seems to be different in published series [13].

The other unusual laboratory finding in our patient was leukocytosis at presentation, that was previously reported only in one patient [4]. In a series of 725 cases studies by Italien Cooperative Group (ICGHCL) [9], 80% of patients had pancytopenia at presentation and 13% had leukocytosis with more than 5×10^9/l hairy cells. In the original Bouroncle's series of 116 patients the total leukocyte count superior to 50×10^9/l was found in 3% of patients [1]. Leukocytosis, massive splenomegaly, and relative resistence to therapy is reminiscent of variant HCL (HCL-V). It is not obvious if leukocytosis is a sign of poor prognosis in classic HCL though there is a case of classic HCL who had an extremely high leukocyte count (323×10^9/l) led to leukostasis with intracerebral hemorrhage and death [14]. The HCL-V is excluded in our patient on the basis of positive TRAP staining of the leukemic cells, immunophenotype with CD103, DBA44, and anexin positivity and an absence of monocytes in the peripheral blood. Monocytopenia or complete absence of monocytes is present in the majority of patients with classical HCL. The lack of CD25 positivity marks a single point of possible contention.

Treatment with 2-chlorodeoxiadenosine improved the patient condition and skin lesions improved but did not disappear and he did not achieved remission. In this regard, clinical significant of specific skin lesions is not clearly associated with poor prognosis, except in HCL-variant.

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