

SHORT COMMUNICATION ΒΡΑΧΕΙΑ ΔΗΜΟΣΙΕΥΣΗ

Dermatological manifestations as a presenting symptom of hematological disease

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Δερματολογικές αλλοιώσεις ως πρώτη εκδήλωση
αιματολογικών νοσημάτων

Περίληψη στο τέλος του άρθρου

Key words: Dermatological manifestations, Hematologic diseases, Leukemia

Dermatological manifestations of hematological diseases present in various forms, including reactive skin lesions, infiltration of leukemic cells, inflammatory reaction and malignant masses such as chloroma or plasmacytoma. The infiltration may be localized or generalized, and is usually a bad prognostic sign. The importance of thorough investigation, including skin biopsy, for diagnosis in these cases cannot be overemphasized.

CASE REPORTS

Patient 1

A 79 year-old male, a retired Sergeant Major, was admitted for paresthesia and weakness in the previous few days. He denied any past medical history and he was healthy taking no medications.

Physical examination showed a healthy looking man, with generalized lymphadenopathy (cervical, axillary, and inguinal) but no hepato-splenomegaly. Neurological inspection showed slight distal weakness (R>L), depressed reflexes, and minimal right drop-foot.

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Laboratory tests revealed: Hemoglobin (Hb) 13.9 g/dL, platelets (PLT) $255 \times 10^9/L$ and leukocytes (WBC) $52,770 \times 10^6/L$ with 18% neutrophils, 21% lymphocytes, 25% myelocytes and 35% monocytes. No blasts were seen on the peripheral blood smear. Blood chemistry was normal except for elevated lactate dehydrogenase (LDH) (679 mg/dL, normal range <450). Kidney and liver function were normal.

Further evaluation included: Chest X-ray, abdominal ultrasound (US) and cranial computerized tomography (CT), which were all normal. Protein electrophoresis and serology tests for hepatitis B and C along with HIV were negative. Bone marrow biopsy and aspirate demonstrated monocytosis with no excess of blasts. PCR for Philadelphia chromosome and translocation (12, 15) were negative. Chronic myelomonocytic leukemia (CMML) was diagnosed.

In the next few days, the WBC rose to $170 \times 10^9/L$. Treatment with hydration, allopurinol and hydroxyurea was initiated, the WBC count quickly fell to $30 \times 10^3/L$ and the patient was discharged in good general condition.

Two weeks later, he was readmitted with weakness, dyspnea and a diffuse rash on his abdomen and extremities (fig. 1).

Laboratory tests demonstrated anemia (Hb 10.8 g/dL), thrombocytopenia (PLT $95 \times 10^9/L$) and markedly elevated WBC, $384 \times 10^9/L$, the majority of which were myeloblasts. Acute renal failure was found with creatinine (Cr) 3.22 mg/dL (normal 0.5–0.9 mg/dL), hyperuricemia of 22.3 mg/dL (normal 2.4–7 mg/dL), hypophosphatemia 0.6 mEq/L (normal 2.8–4.1 mEq/L) and LDH 1900 mg/dL.

Acute monocytic leukemia (M5 FAB) was diagnosed along with a huge expanding tumor load (hence the hypophosphatemia),

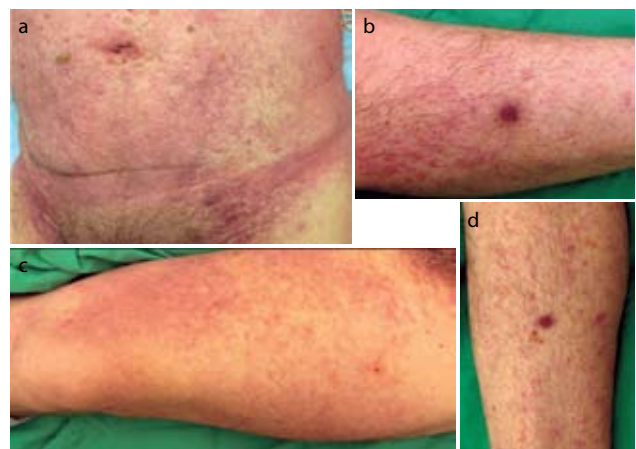


Figure 1. 2nd admission of patient 1. Diffuse purple rash involving trunk and extremities (a, c), along with small purple nodules on the extremities (b, d).

hyperviscosity, probably leukemic skin infiltrate, acute renal failure and disseminated intravascular coagulation (DIC).

Treatment including forced diuresis, NaHCO_3 , oxygen, allopurinol, antibiotics and hydroxyurea was initiated, along with RBC and plasma transfusion. Within 24 hours massive tumor lysis with hyperphosphatemia was followed by hemodialysis. Treatment started was with low dose Ara-C (cytosine arabinoside) but the patient deteriorated 3 weeks later showing severe neutropenia, DIC and neurological symptoms resembling stroke, and on day 35 the patient died.

Patient 2

A 55 year-old female presented with a painful lesion below her left knee which had appeared one month earlier as a solitary, red, painful lesion and slowly expanded. This was accompanied with marked leukocytosis, but there had been no response to prior antibiotic treatment. Her past medical history was unremarkable.

On physical examination the patient was in general good condition with no findings except for a red, shiny, raised lesion below the left knee, with levido reticularis surrounding it (fig. 2).

Complete blood count showed WBC $20,000 \times 10^6/\text{L}$ (neutrophils predominant) with $3,000 \times 10^6/\text{L}$ monocytes and the blood smear showed monoblasts. Bone marrow biopsy and skin biopsy both showed infiltration of leukemic cells with positive immunohistochemical staining for myeloperoxidase and CD68 (fig. 2c).

Acute monocytic leukemia was diagnosed and treatment was started with Ara-C and idarubicin.³ One month later regression of the lesion was observed (fig. 2b). The patient completed the consolidation treatment and one year later she is in complete remission.

Patient 3

A 53 year-old male presented with skin lesions and arthritis. He had emigrated from Ethiopia four years earlier and was otherwise healthy.

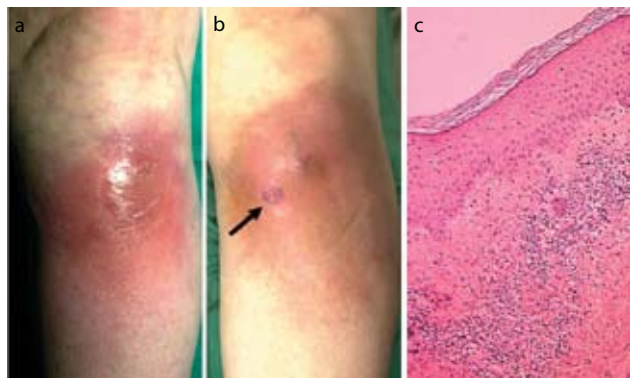


Figure 2. Below knee lesion of patient 2, at presentation (a) and one month after treatment (b). Arrow shows scar of skin biopsy. Skin biopsy of patient 2, showing thick infiltrate of leukemia cells (c).

Three months before presentation, migratory poly-arthritis appeared, accompanied by an itching scaly rash, which began in the scalp and extended to face, trunk and extremities. He lost 8 kg in three months and complained of night sweats and odynophagia.

On physical examination, he was thin and looked ill. A psoriasiform rash was observed on his scalp, face, trunk and extremities (fig. 3a, b). Arthritis was detected on his left knee and in the proximal interphalangeal joints (PIP) bilaterally (fig. 3c).

Complete blood count showed Hb 10.8 g/dL, PLT $153 \times 10^9/\text{L}$, WBC $5.4 \times 10^9/\text{L}$ of which $700 \times 10^6/\text{L}$ were neutrophils, erythrocyte sedimentation rate (ESR) 130/hour, C-reactive protein (CRP) 8.8 mg/dL.

Serology tests for EBV, CMV, HIV, hepatitis B and C were negative. Blood chemistry and protein electrophoresis were normal, INR 1.3 (normal 0.9–1.3), D-Dimer 1000–2000 and chest X-ray normal.

Skin biopsy from a scaly lesion in the arm showed hyperkeratosis and parakeratosis, intradermal congestion with mild lympho-plasmocytic infiltrate compatible with chronic inflammation (fig. 3c).

Bone marrow biopsy and aspirate showed hypercellularity with 90% blasts. Myeloperoxidase staining was positive and Auer rods were observed and FISH t (15, 17) was positive.

Acute promyelocytic leukemia was diagnosed and treatment was initiated with All trans retinoic acid (ATRA) and idarubicin.⁴ Within 2 weeks, the rash and arthritis disappeared completely. More than a year later the patient is in good general condition and in complete remission.

COMMENT

Leukemia cutis (LC) is the infiltration of neoplastic leukocytes or their precursors into the epidermis, the dermis or the subcutis, resulting in clinically identifiable

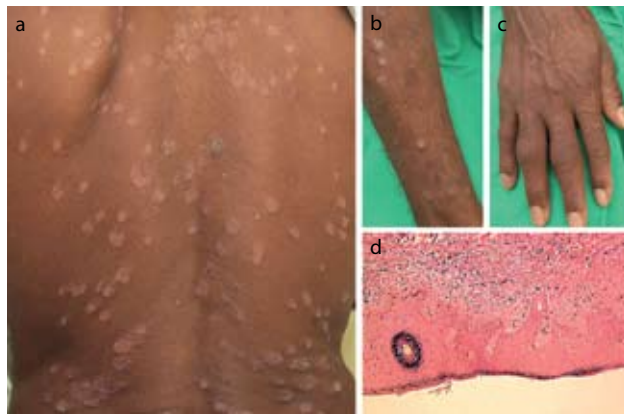


Figure 3. Psoriasiform skin lesions of patient 3 on the back (a) and arms (b). Arthritis of right and left fingers (c). Skin biopsy from a psoriasiform lesion in the arm of patient 3, demonstrating chronic inflammation (d).

cutaneous lesions. The involvement may be localized or generalized. The incidence of LC is 2–4% for AML, but can be up to 30% for M4 and M5.^{1,2} It seldom precedes marrow infiltration,⁵ and is considered a bad prognostic sign.⁶ The exact mechanism of leukemic infiltration of the skin is unknown. In M4 and M5, T-cell-related antigens on the cell surface of leukemic cells may promote selective homing to the skin.⁷

Three patients are described with either leukemic infiltration or reactive inflammation of the skin. All these lesions responded to the chemotherapy regimen given to the patients according to the hematological diagnosis. Patient 1 presented with peripheral neuropathy, which is unusual for acute leukemia. The hypothesis is that leukemia cells infiltrated the peripheral nervous system,⁸ thus presenting as extra-medullary leukemia, which shortly progressed into full-blown AML. The diffuse intense rash at the time of the huge tumor load along with its complete disappearance as the tumor regressed, suggest that the rash was also composed of leukemia cells infiltrating the dermis.

Patient 2 had a classical, biopsy proven, LC with localized infiltration of the skin, which later regressed along with remission of the disease.

Patient 3 had acute promyelocytic leukemia (APL) with a favorable outcome. His psoriasiform rash regressed along with the disease, and probably was para-neoplastic or reactive. This is to our knowledge the first description of such a rash in APL.

Three unique cases are presented here of dermatological manifestations of leukemia. These cases demonstrate the importance of suspicion and of early skin biopsy in the evaluation of skin lesions, especially in hematological patients.

ΠΕΡΙΛΗΨΗ

Δερματολογικές αλλοιώσεις ως πρώτη εκδήλωση αιματολογικών νοσημάτων

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Οι εκδηλώσεις από το δέρμα των διαφόρων αιματολογικών νοσημάτων ποικίλλουν και μπορεί να εμφανίζονται ως αντιδραστικές δερματικές βλάβες, διήθηση από λευχαιμικά κύτταρα, φλεγμονώδεις αντιδράσεις ή ως λευχαιμικές μάζες,

όπως χλώρωμα ή πλασματοκύτταμα. Η διήθηση του δέρματος μπορεί να είναι εντοπισμένη ή γενικευμένη και συνήθως αποτελεί κακό προγνωστικό σημείο. Η σημασία της βιοψίας δέρματος είναι σημαντική για τη διάγνωση. Περιγράφονται 3 ασθενείς στους οποίους η διάγνωση της λευχαιμίας έγινε με βάση τη διερεύνηση των διαφόρων δερματικών βλαβών. Ο ένας ασθενής παρουσίασε διάχυτο εξάνθημα από λευχαιμική διήθηση οξείας μυελομονοκυτταρικής λευχαιμίας, ο δεύτερος μονήρη φλεγμονώδη βλάβη στο γόνατο λόγω οξείας μυελογενούς λευχαιμίας και ο τρίτος μεταναστευτική αρθρίτιδα και ψωριασικόμορφη δερματίτιδα λόγω οξείας προμυελοκυτταρικής λευχαιμίας. Η αξιολόγηση και η ιστολογική διερεύνηση των δερματικών βλαβών είναι συχνά σημαντικές για τη διάγνωση αιματολογικών νοσημάτων.

Λέξεις ευρητηρίου: Αιματολογικά νοσήματα, Δερματολογικές εκδηλώσεις, Λευχαιμία

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