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Case report

Monocytic aleukemic leukemia cutis

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Abstract

The authors present a case of monocytic aleukemic leukemia cutis in which skin symptoms were the sole manifestation of the leukemia during the first year and a half of the disease. Diagnostic difficulties, the importance of immunhistochemical markers, and the prognosis and therapy of aleukemic leukemia cutis are discussed.

Keywords: Monocytic aleukemic leukemia cutis; Acute monoblastic leukemia

1. Introduction

Leukemia cutis comprises a group of specific symptoms occurring in leukemia indicating dissemination and proliferation of malignant hemopoietic cells in the skin [1,3]. There exists a specific and rare form of this disease identified as aleukemic leukemia cutis, in which leukemic cells are found in the skin prior to the changes in the peripheral blood (or the bone marrow). The English language literature report a total of 64 cases with aleukemic leukemia cutis; of these 30 cases corresponded to the myeloid type, 29 cases to monocytoid type (nine cases of acute monocyte leukemia; 10 cases of chronic monocytic, and 10 cases of myelomonocytic leukemia), and five cases to the lymphoid form of aleukemic leukemia cutis [3–11].

We present a case in which the specific skin symptoms presented a year and half before the diagnosis of acute monoblastic leukemia.

2. Case report

We report on a 39-year-old female patient. A year and half ago the patient had observed cutaneous nodes which caused no complaints. The patient was examined by a few specialists, who failed to diagnose the disease. Histological study of the lesioned skin showed proliferation of immature cells. Peripheral blood and the bone marrow showed no pathological signs. X-ray therapy was performed for the assumed diagnosis of lymphoma cutis. Several months following the involution of the nodes due to the therapy, the skin lesions reappeared all over the body.

2.1. Status at admission

Disseminated, round-shaped, flat, protruding cutaneous and subcutaneous pale-red nodes of 0.5–2.0 cm in diameter, covering the chest and the extensor surfaces of the extremities (Figs. 1 and 2). Lymph nodes, spleen and liver were not palpable. Routine laboratory studies, including RBC sedimentation rate, blood count, smear, blood glucose, renal and liver functions showed no pathologic changes. Chest X-ray and abdominal ultrasound failed to reveal any changes.

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Fig. 1. Papules and cutaneous- subcutaneous nodes on the chest.

Histological studies of the nodular skin lesion indicated atypical lymphoreticular infiltration reaching the subcutis with loose nuclear structure (Fig. 3). Immunhistochemical staining revealed that the atypical cells were positive for leukocyte common antigen (CD45); CD68 indicated hemopoietic origin of the cells. Some of atypical cells yielded a chloracetoesterase positive reaction, which is characteristic of myeloid elements, while others gave a positive lysozyme reaction typical of monocytoid cells. (Fig. 4) Stains with the pan-B-cell marker and the pan T-cell marker were negative. Histological findings suggested an immature blastic myelomonocytic process. At this time the analysis of a sternal puncture sample indicated possible myelomonocytic leukemia.

The patient was transferred to the St. László Hospital. At that time the blood count and the WBC were still normal; serum muraminidase level was 95 μg/ml. (Normal range: 0.7–2.0 μg/ml) Cytological analysis of the bone marrow showed hypercellular marrow, in certain areas of which the ratio of primitive blastic elements comprised 70–80% of the cell count. In 15 of 17 mitoses cytogenetic studies identified 47, XX [10,11] (p11, q13), + 20 type aberrations (reciprocal translocation with an extra 20. chromosome). Immunological typisation of the blasts verified CD33 and HLA A DR surface markers. Bone marrow biopsey showed signs of acute leukemia. The final diagnosis was acute monoblastic leukemia.

Fig. 2. Papules and cutaneous- subcutaneous nodes on the arms.

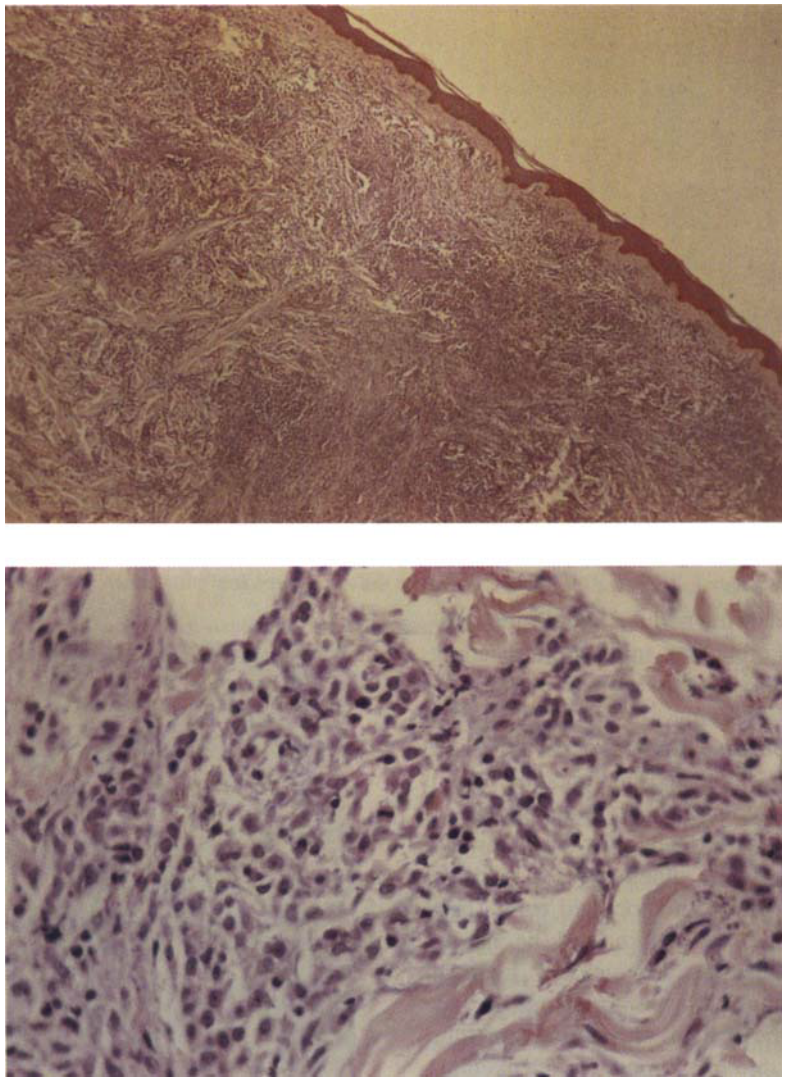

Fig. 3. (A) Atypical lymphoreticular infiltration localized under, but not related to, the slightly atrophic epithelium; the lesions reach the subcutis. (Hematoxylin-eosin stain 10×). (B) Higher power view shows nuclear pleomorphism and mitoses. (Hematoxyline-eosin stain 250×).

After combined chemotherapy (Daunoblastin, Cytosan) the skin symptoms involuted and the bone marrow findings verified remission. The woman refused further therapy. Two months later she was readmitted for reappearance of cutaneous symptoms. After repeated chemotherapy aplasia and subsequent fever (pneumonia) developed. During antibiotic therapy the woman had developed fungal sepsis and died on the 31st day after beginning chemotherapy. Autopsy verified aspergillosis of the lung.

3. Discussion

In regard to specific skin symptoms accompanying leukemia (leukemia cutis) monocytic leukemias (FAB 4,5) are of special importance. A higher incidence of cutaneous leukemias on one hand, and the occurrence of a leukemia-specific muco-cutaneous symptom – gingival hyperplasia – in pediatric monocytic leukemia on the other hand support this view [2].

Monocytic aleukemic leukemia cutis occurs both in

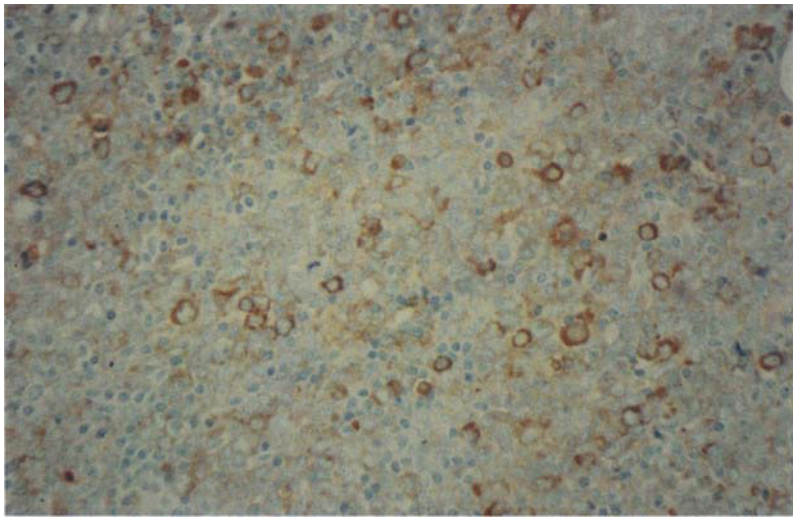

Fig. 4. Monocytoid-specific positive lysozyme reaction (25×).

acute monoblastic and chronic myelomonocytic leukemia. As a rule specific skin symptoms develop 8 (1–30) months prior to the usual symptoms of leukemia. With the use of immunohistochemical markers, this period can be reduced to several months.

Aleukemic leukemia cutis is manifested as pale or livid red, rarely pale-red papules, or cutaneous and subcutaneous nodes 2–4 cm in diameter, which cause no complaints. A characteristic bluish livid color of the nodes can mimic panniculitis. Furthermore, large, hemorrhagic plaques and monomorphic papulous hemorrhagic exanthema can also occur. As a rule the epithelium over the pathologic loci remains intact, and secondary alterations (ulcerations) seldom occur [6,8–10].

Histological findings show infiltration of subepidermal, dermal (with a narrow unaffected zone), or subcutaneous tissues, which can also involve collagen fibers. Infiltration with leukemic cells can spread to the adnexum and be of hemorrhagic character. Differentiation with T and B-cell lymphomas is a crucial point in clinical and histological diagnosis of the disease. In such cases identification of positive monocyte, macrophage or granulocyte markers, as well as lack of pan-T and pan-B markers are important [7,10].

Similar to other types of leukemia cutis, the prognosis of aleukemic leukemia cutis is poor. Cutaneous symptoms indicate extramedullar spreading of leukemia, involvement of other organs, blastic crisis, or leukemic transformation. Death occurs within 3–4 months (1–6 months) following the diagnosis. Tumor cells can return from the skin to the bone marrow or other internal organs. Poor prognosis is expected in cases of rapid reappearance of leukemic papules and nodes following chemotherapy. Chemotherapy per se is insufficient, and thus treatment of leukemic infiltration requires electronic irradiation of the whole body [12].

Why the leukemic cells first appear in the skin, prior to their appearance in the peripheral blood or the bone marrow, is unknown. It is assumed that this marrow pathology is a localized process, in the course of which the tumor cells penetrate into the cutis (due to some cutaneous factors or specific properties of the leukemic cells? A yet unknown 'homing sample'?). Furthermore it is suggested that these leukemic cells are of primary extramedullar origin and can penetrate into the skin and marrow via the hematogenic route. According to another hypothesis the process originates from latent hemopoietic cells, which were transferred to the skin during the embryonal period [9,10].

Our subject lived for only 18 months following the diagnosis of the disease; her intolerance contributed to the outcome. Poor prognosis of aleukemic leukemia cutis is proved by a short (6-month) survival despite combined chemotherapy. We conclude that apart from cutaneous lymphoma, a possibility of aleukemic

leukemia cutis should be considered if livid papulonodose skin symptoms develop. Modern analysis using immunohistochemical markers helps in early diagnosis.

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