Skin relapse of acute myeloid leukemia associated with trisomy 8


Acute myeloid leukemia (AML) is a morphologically diverse group of hematopoietic malignancies characterized by proliferation of immature cells that arise in the myeloid progenitor cells of the bone marrow. It shows cutaneous lesions relatively rarely. The most common cutaneous manifestation is the appearance of one or several tumors. An association of AML with skin involvement and trisomy 8 has rarely been reported. We present the case of a 74-year-old woman that presented with fatigue, nausea, dyspnea, and night sweats. On physical examination we found no hepatosplenomegaly, peripheral lymphadenopathy, or skin abnormalities. Hematological examination revealed Hb: 8.4 g/dl, PLT: 35,000/ml, WBC 105,000/ml, and blasts 51%. Bone marrow aspiration showed blasts 88%. Cytogenetic findings in the marrow showed trisomy 8. The patient received 3 courses of systemic chemotherapy with aracytin and idarubicin and then, while she was in remission, multiple red nodules developed on the upper and lower limbs. A skin nodule from the right arm was excised and histology showed a diffuse infiltration of the dermis consisting of large cells with round to oval nuclei and little basophilic cytoplasm. Immunohistochemistry was performed and the neoplastic cells showed strong positivity for MPO but were negative for LCA. Accordingly, a diagnosis of AML involving the skin was made. The patient received another course of systemic chemotherapy with aracytin and idarubicin and is in good condition.
before admission. On physical examination we found no hepatosplenomegaly, peripheral lymphadenopathy, or skin abnormalities. The hematological examination revealed: Hb: 8.4 g/dl, PLT: $35 \times 10^9$/L, WBC: $105 \times 10^9$/L and blasts 51%. Bone marrow aspiration showed hypercellularity with an excess of blasts (88%) that had a positive immunophenotype for myeloperoxidase (MPO), CD14, CD13, and CD33. Chromosomal analysis of the marrow revealed trisomy 8. A bone marrow biopsy showed diffuse infiltration by leukemic blast cells that were positive for MPO, lysozyme, and CD68. Accordingly, a diagnosis of AML (M4 subtype) was made and the patient received three courses of systemic chemotherapy with aracytin and idarubicin. Three months later, although she had normal blood tests and normal bone marrow aspiration, multiple red, painless nodules developed on her upper and lower limbs (Fig 1). A skin nodule from the right arm was then excised and sent for histopathological examination. After a histological diagnosis of skin infiltration by AML blasts was made, the patient received another course of systemic che-

Figure 1: Multiple red nodules on the lower limbs.

Figure 2: Diffuse infiltration of the dermis without epidermotropism (H + E x100).

Figure 3: Higher magnification showing diffuse infiltration of the dermis (H + E x200).

Figure 4: Diffuse, dense infiltration of the dermis by relatively uniform large cells with distinct nucleoli (H + E x400).

Figure 5: Leukemic cells positive for MPO.
Macroscopically, the excised skin nodule had maximum diameter of 7 mm. On the cut surface it was soft and grayish-white. Microscopically, there was a diffuse dense infiltration of the dermis by relatively uniform large neoplastic cells with round to oval nuclei, distinct nucleoli, and little basophilic cytoplasm (Fig 2). There was significant mitotic activity. The epidermis, dermal adnexes, and the subcutis were not involved. Immunohistochemistry was performed and the neoplastic cells showed strong positivity for MPO (Fig 3), lysozyme, and CD68, but were negative for LCA, CD20, CD30, CD3, and S-100 protein. This led to a diagnosis of AML involving the skin according to the WHO classification (1).

The incidence of leukemia cutis is relatively rare (H2%) in AML, appearing mainly as the M4 and M5 subtypes (2, 3). It is strongly associated with the presence of extramedullary disease and it is usually a manifestation of recurrence in treated patients or a late development in association with widespread dissemination.

Typically the skin lesions are not painful, as in our case, and present as red-brown cutaneous papules, nodules, or plaques in a localized or diffuse distribution. The infiltrates are usually confined to the dermis with density varying from low to high, and the pattern may be diffuse or nodular. Uncommonly, there is adnexal infiltration or epidermotropism. The morphological features of the infiltrating cells may vary from uniform to pleomorphic appearance (4). In our case, we had relatively uniform diffuse infiltration of the dermis without epidermotropism or adnexal infiltration.

Histopathological differentiation between specific leukemia cutis and nonspecific cutaneous lesions in patients with AML can be difficult, particularly in cases in which a relatively low number of leukemic cells are present in the skin biopsy. In addition, there may be a substantial morphologic difference between the tumor cells infiltrating the skin and the leukemic cells in the blood or bone marrow (4, 5). In our case, in the bone marrow biopsy, there was infiltration by medium to large cells with round or convoluted nuclei, whereas the skin infiltration was monomorphic with large cells only. The histological differential diagnosis of the skin lesions should include metastatic carcinoma, fungal infections, drug eruptions, and leukocytoclastic vasculitis. Morphological examination, as well as immunohistochemical analysis, is helpful for the distinction.

Trisomy 8 is the most frequently reported numerical aberration in patients with AML. It occurs at a frequency of 3 to 6% as a sole abnormality and twice this frequency in association with other cytogenetic aberrations (6, 7). It is especially prevalent in M4 and M5 subtypes and has an intermediate or poor effect on outcome (7, 8). In our case, the patient is in good condition 10 months after the diagnosis of leukemia cutis was made and is receiving systemic chemotherapy with aracynit and idarubicin.

It has been reported that about 6% of patients with AML and trisomy 8 had skin involvement (8). Another study found an increased incidence of trisomy 8 in AML with skin infiltration (9). To date, there is no clear answer as to what genes or epigenetic effects are impacted by chromosome 8 aneuploidy that potentially predispose to skin infiltration or to specific hematological cell types.

In conclusion, we have described a very rare case of AML with skin relapse associated with trisomy 8.

REFERENCES


AUTHORS' ADDRESSES

Ioannis D. Venizelos MD, PhD, Associate Chairman of Pathology, Hippokration Hospital, 50 Papanastasiou, 54639 Thessaloniki, Greece, corresponding author, E-mail: ivenizel@otenet.gr

Ioannis Klonizakis MD, Professor of Hematology, Department of Internal Medicine, Aristotle University of Thessaloniki, Hippokration Hospital, Thessaloniki, Greece

Efthimia Vlahaki, Lecturer of Hematology, same address

Styliani Haralambidou, Associate Professor of Hematology, same address

Zoi A. Tatsiou MD, Resident of Pathology, Department of Pathology, same address

Elissavet Ioannidou, Associate Professor of Hematology, Department of Internal Medicine, same address