CASE REPORT

Aleukemic leukemia cutis preceding acute monocytic leukemia: a case report

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Aleukemic leukemia cutis is an extremely rare clinical presentation in patients who eventually develop acute leukemia, usually of monocytic lineage. This condition is associated with a very poor prognosis and is often difficult to diagnose. We report a case of a 33 years old female with leukemia cutis preceding the onset of acute monocytic leukemia by four months. The patient received induction and consolidation chemotherapy followed by allogeneic bone marrow transplant and has been free of disease for six years. To our knowledge, this is the first documented case in Puerto Rico with the diagnosis of leukemia cutis preceding acute monocytic leukemia.

Key words: Leukemia Cutis, Aleukemia Leukemia Cutis, Acute Monocytic Leukemia.

A 33-years old female with past history of Hashimoto's thyroiditis developed skin lesions localized in the upper right quadrant of the abdomen. She was told that the lesions were precancerous moles and were excised. The initial biopsy report was consistent with "annular granuloma". Ten days later, she developed a non-erythematous papular rash in the upper extremities, which progressed slowly and became generalized. Biopsy of the skin lesions was compatible with a lymphoproliferative disorder. Whole body gallium scan, neck and abdominal computerized tomography were normal. The patient was then referred for hematology consultation.

Review of the skin biopsy revealed a superficial and deep, atypical monocytoid infiltrate most consistent with a leukemic infiltrate. The membrane markers were as follows: negative CD15, CD20 and CD45ra, and diffusely positive lysozyme (Figure 1). The complete blood count revealed: hemoglobin - 13.0 g/dL, platelet count - 332,000/µL and white blood cell count - 8,400/µL. Bone marrow aspiration and biopsy were diagnostic of acute myelogenous leukemia and the patient was referred to our institution.

The patient was clinically stable, and physical examination revealed a fine scattered macular non-erythematous rash in both upper and lower extremities. The bone marrow aspirate was hypercellular, with 89% blasts compatible with acute myelogenous leukemia (Figure 2). Cytochemistry studies were as follows: sudan black B-positive in 72% of blasts, periodic acid Schiff reaction (PAS)-strongly positive with fine and coarse granulation and blocks of activity (Figure 3), α-naphthyl butyrate stain-positive in 93% of cells, with diffuse pattern (Figure 4). Immune markers revealed: 56% of the blasts were positive for CD2, CD4, CD33, CD11b, CD11c, CD15, CD36, CD38, CD56, CD117 and HLA-DR. The cytogenetic study revealed 46XX, t(10;11).

Treatment was initiated according to CALGB protocol # 9621. The induction regimen consisted of: PSC-833, cytarabine, daunorubicin and etoposide. On day 47, complete remission was attained and patient was continued in chemotherapy with three consolidation courses of high

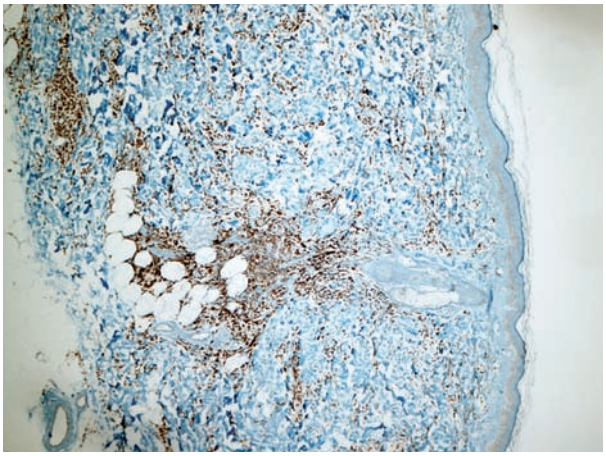

Figure 1. Skin biopsy: lysozyme immunostain-monocytic leukemic infiltrate.

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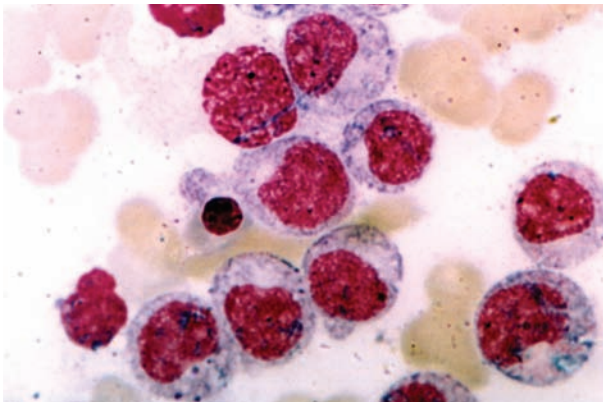

Figure 2. Bone marrow aspirate: Acute myelogenous leukemia.

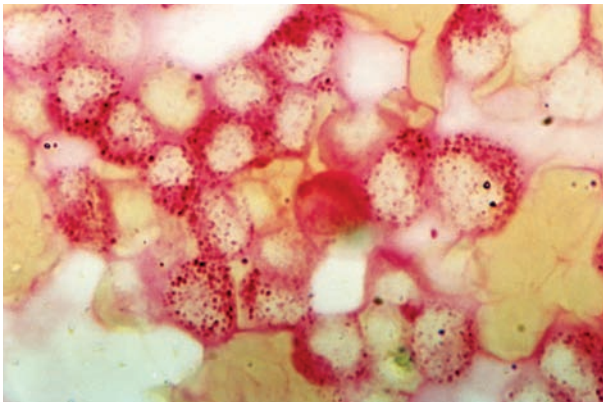

Figure 3. Periodic acid schiff reaction (PAS).

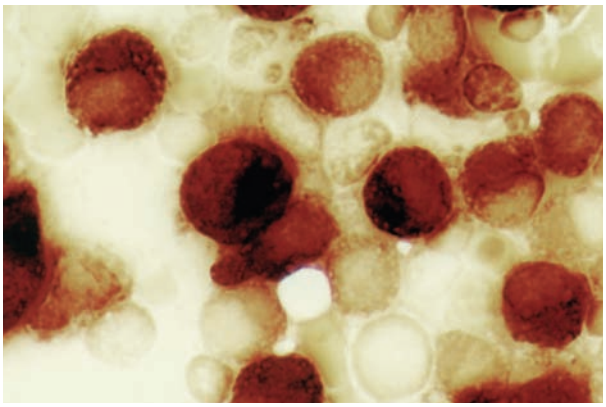

Figure 4. Alpha-naphthyl butyrate stain.

dose cytarabine. All her skin lesions resolved after the first course of chemotherapy. The patient was referred to a bone marrow transplant center in the United States for an allogeneic bone marrow transplantation. There has been no further manifestation of disease since then, and the patient has been free of disease for the last six-years.

Discussion

Leukemia cutis (LC) is an uncommon cutaneous lesion that is often difficult to diagnose. Clinically, skin involvement in systemic leukemia is highly variable and may range from papules, macules, nodules, and vasculitis to a generalized cutaneous eruption and erythroderma, or it can mimic inflammatory dermatoses (1-9). Histologically, LC may be difficult to differentiate from other skin infiltrates and is commonly misdiagnosed (10-11). LC may precede, occur concomitantly or follow the diagnosis of systemic leukemia. It usually occurs in patients with acute myelomonocytic leukemia (FAB, AML-M4) and acute monocytic leukemia (FAB, AML- M5) subtypes.

Aleukemic leukemia cutis (ALC) is defined as the infiltration of the skin by blast cells before their appearance in the peripheral blood and bone marrow. The initial presentation of acute leukemia at a primary extramedullary site is extremely rare, and is usually associated with early bone marrow relapse and poor therapy outcome (12). The incidence of ALC is from 2-7% depending on the series (4.5); the time of progression to acute leukemia varies from 1-20 months, and death occurs usually within a year (6,7,8). Although cases with spontaneous regression of ALC and others with acute myelogenous leukemia (AML) have been reported, this condition is extremely rare (13-14).

ALC can masquerade as a clinically benign skin eruption in a healthy patient with normal blood parameters as occurred in this patient. This case certainly illustrates the difficulties in the diagnosis of LC with routine histological sections, and the cytomorphologic characterization of the leukemic cells in the skin biopsy specimen. It also emphasizes the value of immunohistochemical studies to distinguish ALC from lymphoproliferative disorders, and the high degree of clinical suspicion and follow up required in cases with refractory or progressive skin lesions (10-11).

The histopathologic review of the skin biopsy confirmed the diagnosis of LC in this case, with negative CD20 cell marker and positive chloroacetate esterase reaction and lysozyme markers (9,11-12). The blasts expressed CD56, CD2 and CD4 (T cell markers) in the absence of CD14, this feature has been associated with a higher incidence of extramedullary leukemic infiltration (12, 15). The absence of CD13 and CD14 has been associated with a higher complete remission rate after induction chemotherapy (16).

Cytogenetic abnormalities are among the most important independent prognostic factors in AML (17). This patient presented the translocation t(10;11) which has been identified in acute lymphoblastic leukemia (ALL) and in acute myelogenous leukemia (AML). This translocation is a recurrent event in AML, especially

in M4 and M5 subtypes and is associated with a very poor prognosis (18). Nevertheless, the anti-leukemic treatment given to this patient was successful and a prolonged disease free survival has endured. Patients with extramedullary leukemia (EML), preceding or at onset of acute leukemia, frequently have early relapse after induction chemotherapy. The predisposing risk factors for EML and the optimal therapeutic regimen have been poorly defined. Induction chemotherapy with or without radiotherapy should be recommended for patients with primary ALC, myeloid type, and absence of bone marrow involvement, according to the type of skin lesion. Acute monocytic leukemia has been associated with poor prognosis and frequent extramedullary disease. The outcome of AML-M5 compared to other AML subtypes seems not to differ with current induction and intensive post remission therapy and better supportive care(19).

Conclusions

This is the only documented case of ALC in our institution in the last 20 years. To our knowledge, it is the first reported case in Puerto Rico. Aleukemic leukemia cutis presents a diagnostic challenge. Since the skin involvement is notably variable, a high degree of clinical suspicion is required. The importance of the early recognition of leukemia cutis in aleukemic patients, which should alert the hematologist to treat such patients, should be emphasized.

Resumen

Leucemia aleucémica cutis es una presentación clínica extremadamente rara. Los pacientes, con el tiempo, presentan leucemia aguda, por lo regular, de línea monocítica. Esta enfermedad está asociada a un pronóstico muy pobre. Nosotros informamos el caso de una fémina de 33 años de edad en la que la leucemia cutis precedió por cuatro meses la presentación de la leucemia monocítica aguda. La paciente recibió quimioterapia de inducción y consolidación seguido de un trasplante de médula ósea alogénico y ha permanecido libre de enfermedad por seis años. A nuestro entender, éste es el primer caso documentado en Puerto Rico de un diagnóstico de leucemia cutis precedido por leucemia monocítica aguda.

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