A Case of Leukemia Cutis in Myelodysplastic Syndrome Evolving into An Atypical Chronic Myeloid Leukemia

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We report a patient who had been initially diagnosed as a myelodysplastic syndrome in 1998 presenting purpuric patches on the left arm that started to develop about a year prior. The purpuric lesions were diagnosed as leukemia cutis by skin biopsy. Her subsequent bone marrow biopsy showed progression into an atypical chronic myeloid leukemia with increased numbers of leukocytes in the peripheral blood. Leukemia cutis typically is regarded as a sign of progression of disease or a manifestation of recurrent disease in treated patients with an established diagnosis of leukemia. We suggest that the skin lesion in this patient could have been a sign of conversion into atypical chronic myeloid leukemia. (Ann Dermatol 15(2) 64~67, 2003).

Key Words: Leukemia cutis, Atypical chronic myeloid leukemia, Myelodysplastic syndrome.

Myelodysplastic syndromes (MDS) are a heterogeneous group of hematologic disorders characterized by dysmorphic and abnormally cellular bone marrow, and cytopenias of the peripheral blood. 6-37% of MDS patients undergo leukemic transformation. On the other hand, atypical chronic myeloid leukemia (aCML) is a disease characterized by a chronic myeloid leukemia-like morphologic picture but it is BCR/ABL and Philadelphia chromosome negative. There have been some reports of cases that have brought confusion between MDS and aCML. It has been also controversial whether aCML should be regarded as distinct from classical CML or chronic myelomonocytic leukemia (CMML). The FAB group has recently published guidelines for distinguishing aCML from CML and chronic myelomonocytic leukemia (CMML), a subtype of myelodysplastic syndrome.

Herein we report a case of a MDS evolving into aCML with accompanying leukemia cutis.

CASE REPORT

A 69-year-old woman visited our clinic in March, 2001 with the complaint of a purpuric lesion on an erythematous patch on the left arm. She had a prior history of MDS by bone marrow biopsy in 1998 and was undergoing blood transfusions as a conservative treatment since then. The purpura on an erythematous patch measured 15 x 5 cm and showed a mottled appearance (Fig. 1). It first appeared a year prior to her visit and gradually increased in size. Skin biopsy of the purpuric lesions disclosed a perivascular infiltration of myeloid cells with variable degrees of maturation (Fig. 2a, 2b). These cells were diffusely reactive for CD15 and many of them were also reactive for Ki-67 (Fig 2c), compatible with leukemia cutis. A repeat bone marrow biopsy showed a hypercellular-for-her age marrow with increased numbers of dysmorphic myeloid elements. Megakaryocytes were normal in number but exhibited dysmorphic features such as separated nuclei (Fig. 3). A complete blood count re-
Fig. 1. Nonpalpable mottled purpuric patch on an erythematous base on 69-year-old female.

Fig. 2B. High power (H & E, ×400) reveals that infiltrating cells are myeloid cells of variable degrees of maturation.

Fig. 2C. Those myeloid cells were reactive for Ki-67.

Fig. 2A. Histopathologic finding of the purpuric lesion on her arm showing perivascular infiltration of cells (H & E, ×40).

Fig. 3. Her second bone marrow biopsy in 2001 shows hypercellular marrow particles for her age, increased number and dysmorphic features in myeloid elements, and megakaryocytes normal in number but with dysmorphic features such as separated nuclei which are the consistent findings of atypical chronic myeloid leukemia.

revealed a hemoglobin of 9.14g/dl, a platelet count of 24.9 × 10^9/l, and a leukocyte count of 25.9 × 10^9/l, which was considerably increased as compared to her leukocyte count in 1998 of 2.72 × 10^9/l. Serial exams of her CBC's since 1998 showed that the leukocyte count started to increase near the end of 2000. Since the patient placed the onset of her skin lesion first a year ago, it can be assumed that her skin lesion preceded the increase in leukocyte count. A Philadelphia chromosome was not detected, and a molecular study for the BCR/ABL rearrangement was negative. Her abdominal sonogram did not show splenomegaly or hepatomegaly. She was given intramuscular interferon on alternate days for 14 days after the purpuric lesion was evaluated. She failed to show any hematologic improvement, but her skin lesion decreased in size
with a reduction in erythema. However, improvement of her skin began prior to the interferon injections.

DISCUSSION

Myelodysplastic syndromes (MDS) constitute a broad spectrum of hematologic disorders characterized by peripheral blood cytopenias in the presence of a normocellular to hypercellular bone marrow (so-called ineffective hematopoiesis). Recently there have been reports of cases of MDS that apparently converted to atypical chronic myeloid leukemia. This confusion seems to have arisen from the controversy on the existence of a distinct clinical entity called 'atypical chronic myeloid leukemia' (aCML). This disorder is characterized by a chronic myeloid leukemia-like morphologic picture but is Philadelphia chromosome-negative and BCR/ABL-negative. In contrast to chronic myeloid leukemia (CML), some of the myeloid cells have dysplastic morphology, including hypogranular or agranular myelocytes, metamyelocytes, bands, and neutrophils in aCML. Basophils are absent or present in low numbers and the platelet count is often less than 150 x 10^9/L in aCML. There are overlapping quantitative and qualitative features between 'aCML' and 'CMML' (chronic myelomonocytic leukemia) that make it difficult at times to separate these two entities. Bennett et al. developed a statistical model that confirms that aCML and CMML can be distinguished from each other with reasonable success employing five quantitative parameters (WBC, percentage immature granulocytes, percentage monocytes, percentage basophils, percentage erythroid precursors in bone marrow) and one qualitative parameter (granulocytic dysplasia). In aCML, basophils are less than 2%, monocytes ≥ 3-10%, granulocytic dysplasia ++, immature granulocytes 10-20%, and blasts are more than 2%. In contrast, basophils are less than 2%, monocytes usually >10%, granulocytic dysplasia +, immature granulocytes ≤ 10%, and blasts are less than 2% in CMML. Oscier insisted that it was premature to regard atypical chronic myeloid leukemia (aCML) as a distinct clinical entity and that, in some cases, aCML represented an unusual evolution of myelodysplastic syndrome (MDS). The presenting case was first diagnosed as MDS, refractory anemia with excess blast in 1998. Peripheral blood at the time showed pancytopenia. By the time of her second bone marrow biopsy in 2001 after she was diagnosed as leukemia cutis, her peripheral blood showed increased numbers of leukocytes. The peripheral blood smear showed a shift to the left with leukocytosis and increased blasts. That is, this case may have showed conversion from MDS to aCML, but this remains a controversial point.

Cutaneous lesion in MDS can be subdivided into nonspecific and specific groups. Nonspecific skin lesions are often called leukemids. They include cutaneous infection, dermal vasculitis, and neutrophilic dermatoses. Leukemia cutis is a specific lesion of the skin and it results from infiltration by leukemic cells. It is regarded as a sign of dissemination of systemic disease or a manifestation of recurrent disease in treated patients with an established diagnosis of leukemia, but specific cutaneous lesions may occur concomitantly with systemic leukemia and may even precede peripheral blood or bone marrow manifestations of leukemia. Leukemia cutis in aCML has not yet been reported. Tracking of the complete blood count of this case showed a sudden increase of the leukocyte in March, 2001. It might be assumed that this represented conversion to aCML from MDS in this case. That is, the cutaneous lesion appeared a year prior to the change in CBC. In most cases of myelodysplastic syndromes, cutaneous leukemic infiltrates represent either the initial manifestation or a harbinger of acute leukemia, which subsequently develops within 1-20 months of diagnosis of the skin lesion. We believe that leukemia cutis may have indicated a sign of conversion from MDS to aCML in this case.

Most leukemia cutis presents as papules, nodules or infiltrated plaques. Less commonly subcutaneous nodules resembling erythema nodosum, ecchymoses, purpura, or ulceration have been noted. If it is in the form of a purpuric patch as in this case, it is important to differentiate it from senile purpura. There has been a single report of myelodysplastic syndrome which presented as cutaneous purpura in 74-year-old male. Therefore, it is important to fully examine patients and have them undergo a routine laboratory check including CBC if any older patient presents with cutaneous purpura and systemic complaints.
REFERENCES