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CASE REPORT

Ocular relapse in acute myeloid leukemia (M4) with normal bone marrow

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Abstract A patient with the rare occurrence of ocular relapse of acute myeloid leukemia (AML) M4 while the bone marrow was normal is reported in this paper. A 47-year-old woman with AML was treated with chemotherapy and went successfully into remission. Four months later, she presented with pain, redness, and a mass over the left eye. The ocular relapse involved the subconjunctival space and anterior chamber of the left eye and, presumably, the left lacrimal gland. There were also multiple subcutaneous nodules on both of her forearms. Incisional biopsy from the subconjunctival lesion was performed. Histopathological examination of the specimen showed diffuse blast cell infiltration. Her bone marrow was still in remission. Although exceedingly rare, ocular extramedullary relapse in AML M4 heralds bone marrow recurrence and, despite intensive chemotherapy, the prognosis is dismal.

Keywords Acute myeloid leukemia · Granulocytic sarcoma · Leukemic hypopyon · Conjunctiva

Introduction

Granulocytic sarcoma is defined as solid aggregates of blast cells in extramedullary areas in patients with acute myeloid leukemia (AML) [1]. Extramedullary relapse is a recurrence of leukemia while the bone marrow is still in remission. Extramedullary relapse is a rare event in patients treated with chemotherapy alone, and is more often reported after allogeneic bone marrow transplantation [2]. The common sites of extramedullary relapse include the central nervous system, breast, gastrointestinal tract, skin, and spine [3, 4]. In this paper, we report an unusual case of ocular relapse in a patient with AML whose bone marrow was still in remission.

Case report

A 47-year-old woman presented with a 1-month history of fatigue, diarrhea, and supraclavicular lymphadenopathy in November 2004. On physical examination, pallor of the skin, disseminated petechia on the trunk and limbs, and cervical, supraclavicular, and preauricular lymphadenopathy were detected. A blood cell count revealed a hemoglobin level of

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7.6 g/dl, a white blood cell count of 117 $\times$ 10^9/l, and a platelet count of 33 $\times$ 10^9/l. Peripheral blood and bone marrow examinations disclosed an increase in blast cells. Blasts were positive for CD13, CD14, and CD33, and fluorescence in situ hybridization analysis showed the deletion of 17q21. According to the French–American–British (FAB) classification, AML M4 was diagnosed.

Ocular examination which was then performed revealed 20/20 vision in each eye and few retinal hemorrhages in the left eye. Hyperviscosity syndrome for the high white blood cell count was suspected. Leukopheresis for the high white blood cell count and systemic chemotherapy resulted in complete remission.

In March 2005, the patient developed pain and redness, particularly in her left eye. Her vision was unaffected. There was a bright pink-colored diffuse limbal subconjunctival infiltrative lesion and a yellow–white "pseudo-hypopyon" in the left eye (Fig. 1). The posterior segment appeared normal. Magnetic resonance imaging (MRI) studies demonstrated an enlarged left lacrimal gland, suggesting leukemic infiltration. Within a few days, she developed palpable nodular lesions on both of her arms. Histopathological examination of the incisional biopsy specimen from the left conjunctiva showed diffuse blast cell infiltration, which were CD43- and CD68-positive and CD56-negative on immunohistochemical staining (Fig. 2). Bone marrow examination showed no evidence of leukemia. These results strongly suggested that the blast cells stemmed from the same leukemic clone and favored the diagnosis of granulocytic sarcoma. Systemic chemotherapy resulted in the rapid resolution of subconjunctival and dermal lesions, as well as the anterior chamber infiltration.

Three months later, she presented with fever and hypotension. Examination of the peripheral blood and bone marrow revealed a relapse of leukemia. She underwent systemic chemotherapy with no response, and expired as a result of sepsis.

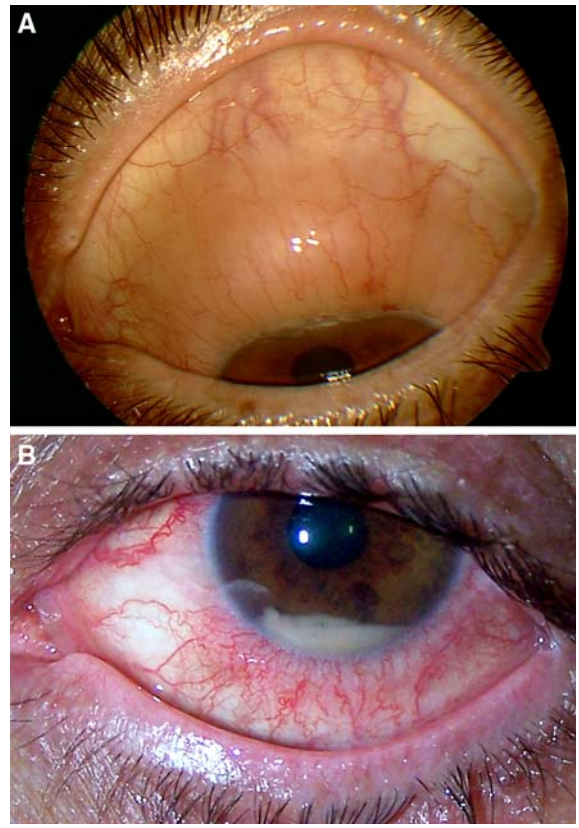

Fig. 1 Left eye of the patient showing (**a**) the superior limbal and subconjunctival infiltrative tumor and (**b**) the "pseudo-hypopyon" in the anterior chamber

Discussion

Extramedullary relapse in AML, excluding the central nervous system, has been reported to have a prevalence of 0.65% in a large series of 3,071 patients [2]. With the introduction of donor lymphocyte infusion, which is used for the graft versus leukemia effect, the incidence of extramedullary relapse is supposed to increase after allogeneic hematopoietic stem cell transplantation [5]. However, the exact incidence of granulocytic sarcoma is hard to assess, since most tumors are discovered at autopsy.

In the present case, ocular relapse of leukemia was documented while the bone marrow was in remission, which is an extremely unusual condition. Previously, ocular adnexal granulocytic sarcoma was noted in an AML patient who underwent autologous bone marrow transplantation [6]. However, our patient received only chemotherapy and, to the best of our knowledge, this seems to be the first case of ocular AML relapse, shortly followed by dermal relapse, without bone marrow recurrence, in a patient who was previously treated with chemotherapy alone.

The mechanisms of extramedullary relapse have not been definitively identified as yet. Possible suggested predisposing factors for granulocytic

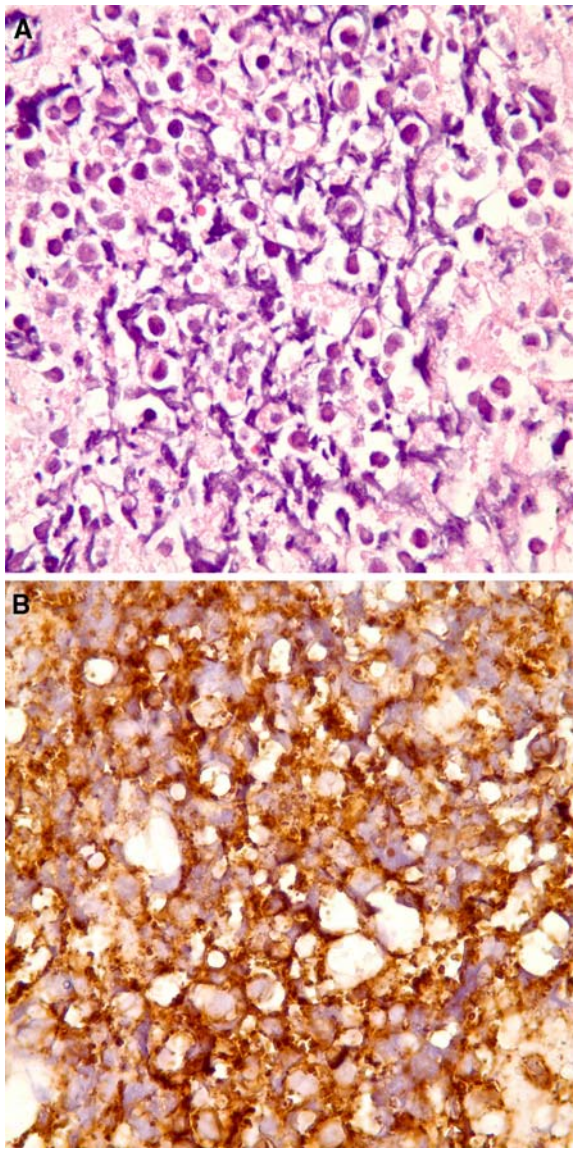

Fig. 2 Histopathological examination demonstrated (**a**) a diffuse blastic leukemic cell infiltration of the subconjunctival space (H&E, 100× original magnification) and (**b**) CD43-positive blast cells (anti-CD43, 120× original magnification)

sarcoma include cytogenetic abnormalities such as t(8;21) and inv(16), the MLL gene rearrangement, and FAB classification M4 and M5 subtypes [7]. One proposed mechanism of isolated extramedullary relapse is the continued effect of graft versus leukemia effect in the bone marrow, but not at the extramedullary sites where chemotherapy or anti-leukemic effector cells given by allogeneic transplantation are unable to function due to the presence of a natural barrier or a micro-environmental condition [7].

It is very important to note that the occurrence of granulocytic sarcoma is almost always followed by marrow relapse. The time between the onset of granulocytic sarcoma and bone marrow relapse ranges from a few days to more than 2 years. In our case, the onset of ocular and cutaneous leukemia was 3 months, except for bone marrow recurrence. Furthermore, ophthalmic involvement is very suggestive of meningeal leukemia [1]. This patient showed that ophthalmic granulocytic sarcoma can occur even if the bone marrow is normal, and that it is definitely advisable to refer the patient to a hematologist, since systemic chemotherapy is needed to prevent, or at least to delay, meningeal leukemia and bone marrow relapse.

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