Extramedullary relapse of acute lymphoblastic leukemia in the breast after allogeneic stem cell transplantation and concomitant persistence of donor hematopoiesis

Extramedullary relapse (EM) after allogeneic bone marrow transplant (BMT) for acute leukemia is being reported with increasing frequency. The majority of these reports underline the coexistence of EM relapse and marrow remission (CR). Because CR is often obtained by means of donor lymphocyte infusion, it is tempting to suggest an escape from the graft-versus-leukemia (GVL) effect. Here, we report the case of a female patient with acute lymphoblastic leukemia (ALL) who underwent allogeneic BMT. A relapse in the breast occurred which was followed by a subsequent relapse as a nasal lump; it is noteworthy that both extramedullary relapses occurred during persistent complete chimerism.

In November 1997 a 20-year old female patient with ALL in second complete remission received an allogeneic peripheral blood stem cell transplant (PBSCT) from her HLA identical, ABO mismatched, brother. After conditioning with cyclophosphamide 120 mg/kg and fractionated total body irradiation 12 Gy in 6 doses, the patient received granulocyte colony-stimulating factor mobilized peripheral blood stem cells. Cyclosporin A (CSA) and a short course of methotrexate were used for GvHD prophylaxis. Full engraftment occurred and complete chimerism was documented by XY karyotype on day +26 and by a switch in blood group on day +80.

Because of the high risk of relapse, from day +100 the CSA was tapered down with the aim of inducing a GVL effect and within a week mild cutaneous graft-versus-host disease occurred.

On day +140 some nodular lesions were detected in both breasts; a mammography showed multiple nodular formations of medium density, with vague margins in both breasts (Figure 1).

The histological examination was consistent with an extramedullary recurrence of ALL; a bone marrow aspirate showed a cytopenic picture with no morphologic evidence of disease; the karyotype and blood group both indicated the persistence of full chimerism; complete disappearance of the breast masses was obtained with mild systemic chemotherapy and local radiotherapy.

In September 1998 the patient received a second allogeneic BMT from the same donor after fludarabine 30 mg/m^2 for 4 days and busulfan 8 mg/kg as conditioning regimen. Following PBSCT, a low dose of CSA was used for 2 months as GvHD prophylaxis. On day +150 after the second PBSCT, a protruding mass appeared in the right nasal fossa. Histologic examination was consistent with ALL recurrence. At that time, both blood group and karyotype were still of donor origin. A further breast recurrence was observed. The patient was then treated with palliative radiotherapy to the nasal lump. In April 1999, overt hematologic relapse occurred. The cytogenetic study performed on peripheral blood was consistent with mixed chimerism in that mitoses obtained by PHA stimulation still showed an XY karyotype. The patient died a month later of progressive disease.

The breast is an unusual site of extramedullary ALL.[1-3] Reports on patients with EM leukemia with marrow remaining in remisson, or marrow remission obtained by DLI but with concomitant EM leukemia are being increasingly described in the literature.[4-7]

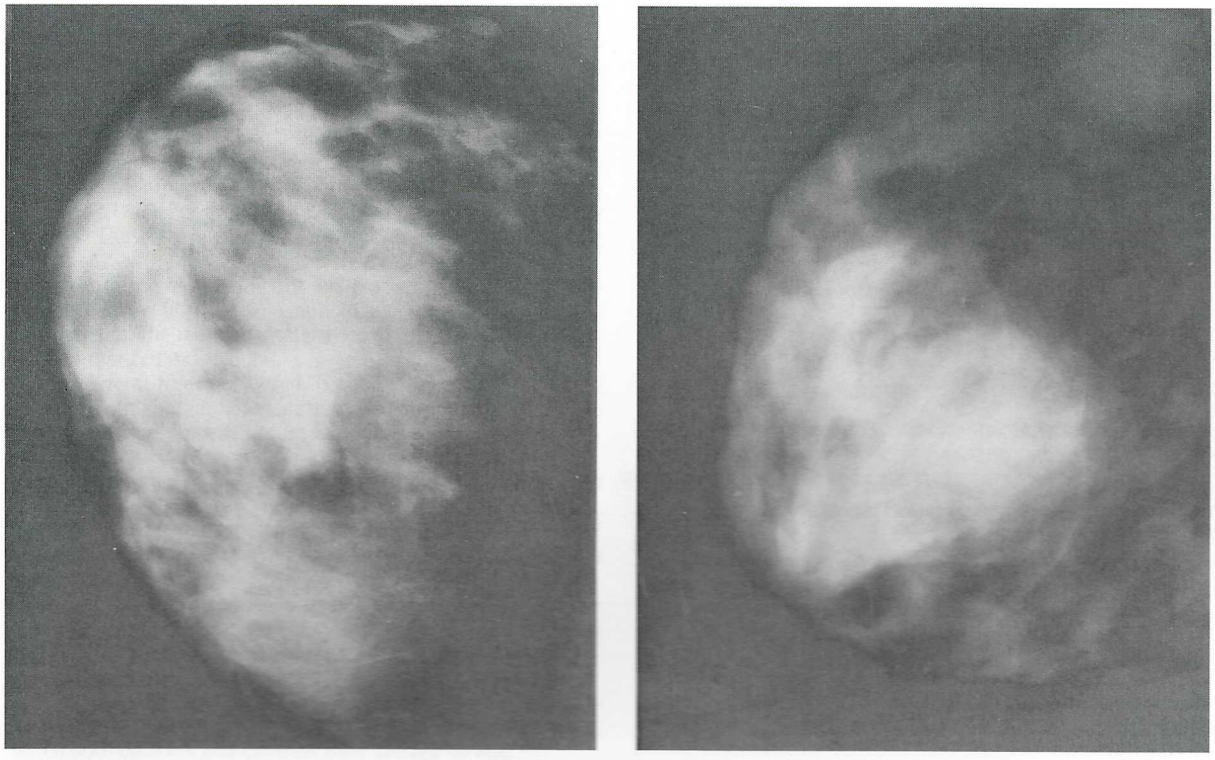

Figure 1.

It is tempting to suggest that in our case the GVL induced by tapering down the CSA resulted in a good control of bone marrow disease while a sort of escape from immunologic surveillance occurred in the breast and soft tissues of the nasal cavity. However, the mechanism by which extramedullary sites are involved remains undefined.

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