Morphologic Evidence of in vivo Differentiation in Acute Myeloblastic Leukemia

G.	Gönül	Hiçsönmez
A.M.	Murat	Tuncer
M.	Mualla	Çetin
F.	Fatma	Gümrük
A.	Abdurrahman	Kara
S.	Songül	Yalçın

Hacettepe Children's Hospital, Department of Pediatric Hematology, Ankara, Turkey

Gönül Hiçsönmez, MD, Hacettepe Children's Hospital, Department of Pediatric Hematology, TR-06100 Ankara (Turkey)

Differentiation of myeloid leukemic cells to mature granulocytes by high-dose methylprednisolone (HDMP; 20-30 mg/kg/day) treatment with remarkable antileukemic effect have been shown by us in children with acute myeloblastic leukemia (AML) [1-5]. It has also been shown that certain steroid hormones (prednisolone and dexamethasone) are among the most potent differentiating agents and can induce differentiation of some mouse myeloid leukemic cells to macrophages and granulocytes [6-8]. Combined HDMP with cyto-toxic chemotherapy increased the remission rate and prolonged the duration of remission in children with AML [9].

Recently Hamidah et al. [10] documented in vivo evidence of differentiation by all-trans retinoic acid in a case of acute promyelocytic leukemia which was characterized by cytoplasmic vacuolation in the neutrophils. We would like to report similar morphologic findings observed during HDMP treatment in a child with AML. A 1-year-old girl was admitted with orbito-ocular granulocytic sarcoma and a generalized nodular leukemic infiltration of the skin. Complete blood count showed Hb 9.8 g/dl, WBC $80 \times 10^9/l$ with 58% blasts and normal platelet count. The bone marrow aspirate was cellular and 35% of the cells were blasts with prominent cytoplasmic vacuolations (fig. 1a). Histochemical examination revealed that the blasts were positive for peroxidase and weakly PAS positive. The vacuoles did not stain. Fifty-six percent of the marrow blasts were CD13 positive, 20% CD34 positive, 16% CD14 positive, 50% CD19 positive and they were TdT, CD2 and CD10 negative (0%).

Induction therapy was begun with oral methylprednisolone at a daily dose of 30 mg/kg. A significant decrease in the circulating blast cell count was noted 2 days after HDMP treatment, however, the WBC count increased to $100 \times 10^9/l$. Because of the increase in the WBCs, possibly due to HDMP effect [2], mitoxantrone 10 mg/m², vin-cristine 0.05 mg/kg and daunomycin 1 mg/kg were added to HDMP treatment on day 3. Four days after initiation of HDMP treatment, the blast cells disappeared from the peripheral blood and numerous abnormally nucleated neutrophils which contained multiple vacuola-

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Fig. 1. a Bone marrow smear at diagnosis. Blast cells containing multiple vacuolations. Wright stain. $\times 675$.

1a

Fig. 1. b Peripheral blood smear. Neutrophils containing multiple vacuolations. Wright stain. $\times 675$.

1b

tions began to increase (fig. 1b). At the same time normal appearing granulocytes also increased. Bone marrow aspirate obtained 1 week after therapy was cellular and the blast cell count declined markedly (16%).

HDMP treatment without using any other antileukemic agents decreased the leukemic cells with concomitant increase in young myeloid elements and neutrophils both in the peripheral blood and bone marrow in various subtypes of AML children [4,5]. Because of an increase in the WBC count, this patient was given one dose of vin-cristine, mitoxanthrone and daunomycin. However, the remarkable

morphologic changes observed within a few days of treatment could not be expected to be a result of the effect of a single dose of these agents. Although the detection of leukemic cell maturation in vivo is rather difficult, the appearance of maturing neutrophils with Auer rods has been identified as a morphologic marker of differentiation of leukemic cells [1, 2,11,12]. In addition, the appearance of abnormally nucleated neutrophils with vacuolations during treatment with differentiating agents could also be considered as an in vivo morphologic evidence of differentiation of leukemic cells as observed in Hamidah et al. [10] and in our patient.

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