Hypereosinophilic Syndrome Terminating in Acute Myelogenous Leukemia

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Hypereosinophilic syndrome (HES) is defined as a circulating eosinophil count greater than 1,500 cells/ μ l, of duration in excess of 6 months, and with no other identifiable cause of the eosinophilia [1]. In the majority of patients with HES the proliferation of eosinophils is thought to be due to a reaction to an unknown agent rather than to a clonal expansion, although this syndrome often results in marked morbidity and mortality due to eosinophilic infiltration into various organs, especially the heart. Only a few cases of HES have been reported to terminate in acute myeloid leukemia (AML) [2-7], although the diagnosis of acute lymphoid leukemia has recently been noted to be preceded or masked by HES in some patients [8]. In this paper we describe a patient with typical HES who suffered from cardiac symptoms due to hypereosinophilia and thromboembolic complications for nearly 5 years; the disease terminated in AML.

A 55-year-old Japanese man was admitted in July 1984 for the further examination of malaise. On physical examination there was no hepatosplenomegaly or lymphadenopathy. The white blood cell (WBC) count was 39,500/ μ l with 68% eosinophils, 14% neutrophils, 11% lymphocytes and 1% basophils. Hemoglobin was 14.8 g/dl; platelets were 189,000/ μ l. Blood chemistries were normal. Neutrophil alkaline phosphatase score was within normal limits; serum B12 was 1,533 pg/ml. Antinuclear antibodies were not detected and IgE was 219 U/ml. Coprology showed no parasite ova. No antibodies to several worms were detected by the Ouchterlony technique. Bone marrow aspiration showed normocellular marrow with 50% eosinophils at various stages of maturation. Cytogenetic study revealed a normal karyotype. Basophilia, myelodysplasia, and myelofibrosis were not seen. He was diagnosed with idiopathic HES. Hypereosinophilia was treated with prednisolone on an outpatient basis. However, he had been suffering from cardiac failure since October 1984. The cardiac echogram revealed mural thrombi on the myocardial wall and valvular insufficiency. Since a fall in 1988, he also suffered from an ulcer in his right toe. He was readmitted for the control of cardiac failure and the ulcer in January 1989. The ulcer progressed to necrosis and the right lower leg was amputated in March 1989. For the control of

eosinophilia, 1,000 mg of hydroxyurea was administered. The blood and bone marrow examination on March 1984 revealed no increase in immature blasts and no myelodysplastic changes. In October 1989 marked anemia and poikilocytes appeared abruptly. The WBC was 63,300/ μ l with differentials of 96% myeloblasts, 1% neutrophils and 3% lymphocytes; hemoglobin 7.7 g/dl and platelets 27,000/ μ l. Cytogenetic analysis of the bone marrow revealed no chromosomal abnormalities. Blasts were positive for per-oxidase and naphthol ASD chloroacetate esterase and negative for α -naphthyl butyrate esterase. Surface analyses showed that the majority of blasts were reactive only for CD13, CD33, and HLADR. Immunoenzyme cytochemistry using an alkaline phosphatase antialkaline phosphatase technique revealed that the majority of blasts were positive for an antimyeloperoxidase antibody, MPO-7 (Dakopatts, Glostrup, Denmark) (fig. 1). He died of pneumonia on October 27 in spite of intensive chemotherapy including cytosine arabinoside and daunorubicin. He had suffered from tissue damage due to HES for 5 years and ultimately died of acute myeloid leukemia. In this patient hydroxyurea was used for 6 months before leukaemic transformation. However, the AML in this patient was probably not a hydroxyurea-induced secondary leukemia because hydroxyurea seldom causes secondary leukemia and, furthermore, the duration of 6 months from the

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Fig. 1. Morphology of circulating blasts at the terminal stage, a May-Grünwald-Giemsa stain, b Positive reaction for peroxidase. Di-aminobenzidine method, c Positive reaction for an antimyeloperoxidase antibody. Alkaline phosphatase antialkaline phosphatase technique.

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Although there has been a report of a case of eosinoblastic leukemia evolved in HES, in which the eosinoblasts were identified ultrastructurally by the presence of specific granules in blasts [5], the possibility of eosinoblastic transformation in the present case was excluded by the positive reaction for an antimyeloperoxidase antibody.

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beginning of administration to onset of AML is too short for therapy-related leukemia to be induced.

The blasts in this patient were quite different from those in common acute lymphoid leukemia or AML (AML-M4Eo) in both cytology, surface phenotyping, and cytogenetics, although these types of acute leukemia were reported to be often associated with eosinophilia [8, 9].

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