To the editor:

Disappearance of chromosomal abnormalities and recovery of hematopoiesis after immunosuppressive therapy for hypoplastic refractory anemia with excess of blasts

We report the disappearance of cytogenetic abnormalities and hematologic recovery after immunosupressive therapy that included antithymocyte globlin (ATG) and cyclosporin A (CsA) in a patient with hypoplastic refractory anemia with excess of blasts (RAEB).

A 57-year-old man presented in June 1986 with pancytopenia. Complete blood count (CBC) showed a hemoglobin (Hb) concentration of 10 g/dL, a leukocyte (WBC) count of 3×10^9/L, and a platelet (Plt) count of 60×10^9/L. The bone marrow was hypocellular without dysplasia and fibrosis. A Ham test (acidified serum lysis) for paroxysmal nocturnal hemoglobinuria (PNH) was negative. Chromosomal analyses of the marrow showed a normal 46,XY karyotype. A diagnosis of aplastic anemia (AA) was made. Oral prednisolone and metenolone acetate were started in August 1986. There was a gradual response of all 3 cell lines. In March 1987, Hb concentration was 13 g/dL, WBC count, 8×10^9/L, and Plt count, 170×10^9/L. Prednisolone was then carefully tapered, although metenolone therapy subsequently was continued.

In August 1988 pancytopenia recurred, and the patient was treated with a second course of oral prednisolone over the next 6 months. In May 1989, Hb concentration was 12.5 g/dL and the neutrophil count, 1.8×10^9/L, but the Plt count showed only a small increase to 30×10^9/L. He was treated with high-dose methylprednisolone. Thereafter, he had been maintaining an Hb concentration higher than 14 g/dL, a neutrophil count higher than 1.5×10^9/L, and a Plt count higher than 100×10^9/L.

In June 2000, there was a rapid decline in his neutrophil and Plt counts. CBC showed an Hb concentration of 9.1 g/dL, reticulocyte count of 40×10^9/L, neutrophil count of 0.18×10^9/L, and Plt count of 24×10^9/L. An excess of blasts (15%) became evident in a severely hypoplastic bone marrow. Megakaryopoiesis was almost absent. A Ham test for PNH was again negative, and expression of CD55 and CD59 on granulocytes was normal. Chromosomal analyses of the marrow showed 47,XY, +8, del(20)(q11q13.3) $^{12}/_{20}$. The diagnosis was changed to myelodysplastic syndrome (MDS) (subtype RAEB). He was given ATG (15 mg/kg/d), administered intravenously once daily for 5 days in July 2000, and oral CsA (5 mg/kg/d) treatment was started. He was clinically well and became transfusion-independent about 1 month later. A slight increase in his Hb concentration (to 9.6 g/dL) and a good response by his Plt count (192×10^9/L) and neutrophil count (2.1×10^9/L) were observed 2 months after ATG/CsA therapy. The bone marrow was normocellular, with relatively erythroid hyperplasia and with a disappearance of dysplastic cells. Chromosomal abnormalities disappeared soon after initiation of ATG/CsA therapy. Cytogenetic analyses of the marrow were serially performed (Table 1). The chromosomal abnormalities remained undetectable 5 months after the initiation of immunosuppresive therapy.

Table 1. Results of cytogenetic analyses

Date	No. of cells analyzed	Karyotypes (no. of metaphases)
June 1986	20	46,XY (20)
August 1988	20	46,XY (20)
May 1989	20	46,XY (20)
June 1996	20	46,XY del(20)(q11q13.3) (2)
		46,XY (18)
June 2000	20	47,XY +8, del(20)(q11q13.3) (12)
		46,XY (8)
August 2000	20	46,XY (20)
September 2000	20	46,XY (20)
November 2000	20	46,XY (20)

ATG therapy with or without CsA has been used successfully to treat hypoplastic MDS, as well as AA.[1-3] Complete trilineage response and transfusion independence were observed in some of the responders. An improvement in cellularity of bone marrow was also observed, whereas myelodysplastic features and cytogenetic abnormalities persisted after treatment. Interestingly, in the present case chromosomal abnormalities disappeared after ATG/CsA therapy. This case is the first report of a patient with MDS who achieved cytogenetic complete remission after ATG/CsA therapy, although disappearance of cytogenetic abnormalities in patients with AA after ATG therapy was previously reported.[4,5] Treatment with ATG and CsA can be effective in restoring hematopoiesis in some hypoplastic RAEB patients, even with excess of blasts.

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