RECOMBINANT ERYTHROPOIETIN IMPROVES THE ANEMIA ASSOCIATED WITH GAUCHER’S DISEASE

To the Editor:

Gaucher’s disease is the most common inherited disorder of glycolipid metabolism and is characterized by the excessive accumulation of glucocerebroside in organs and tissues throughout the body of affected individuals. Prominent clinical features include splenomegaly, hepatomegaly, anemia, thrombocytopenia, and osteoporotic bone destruction. We describe a patient with type 1 (adult) Gaucher’s disease in whom, because of the presence of multiple alloantibodies and prior splenectomy, recombinant erythropoietin was used to treat a profound and symptomatic anemia.

A 33-year-old woman with known type 1 Gaucher’s disease, status-post splenectomy at the age of 11, underwent an elective revision of a left hip prosthesis at an outside hospital in May 1988. Preoperative laboratory studies showed hemoglobin at 11.3 g/dL, leukocyte count at 14,700 cells/µL, and platelets at 181,000 cells/µL. Her postoperative course was complicated by a presumed transfusion reaction, transient renal insufficiency, anemia, and severe thrombocytopenia. She was treated with gamma globulin and dexamethasone, and was discharged in late June 1988.

Over the next 5 weeks, the patient was admitted in turn to George Washington University Hospital and the National Institutes of Health for the evaluation of right hip pain and intermittent fevers. Pertinent physical findings included a temperature of 38.5°C, a liver span of 16 cm, and increased warmth over the right femur and hip with diminished range of motion secondary to pain. Laboratory studies revealed anemia (hemoglobin 6.0 g/dL), thrombocytopenia (platelets 71,000 cells/µL), serum iron 62 µg/dL, and transferrin 155 µg/dL.

The patient received a total of 5 U of compatible packed red cells over the next week. Because of signs of continued red cell destruction, a re-type and screen was performed and revealed Type O, Rh (D) positive. Direct Coomb’s was weakly positive, score 3.5, with 1 to 2(+) pan-agglutinin in eluant. Antibody screen was positive with anti-JKα, anti-S, anti-F, and anti-Bg.

By August 12, 1988, the hemoglobin was down to 4.9 g/dL, and the patient was complaining of orthostatic symptoms and hepatic tenderness. After informed consent was obtained, the patient was begun on a trial of recombinant human erythropoietin (rHuEpo, Ortho Pharmaceutical Co, Raritan, NJ), receiving a total of eight infusions. A brisk reticulocyte response was evident 24 hours after the first two infusions, peaking on day 5, at which point the hemoglobin and hematocrit began to rise (Fig 1). The orthostatic symptoms abated and the hip pain became more tolerable. Following completion of physical therapy, the patient was discharged on day 51.

The anemia manifested in the present case of Gaucher’s disease was undoubtedly multifactorial in origin. The massive hepatic enlargement probably contributed to both the nonimmune and the subsequent immune red cell destruction. In addition, the apparent prolonged course of Gaucher’s bone crisis in this patient, characterized by fever and unrelenting bone pain, may have resulted in impaired iron utilization, and thus might be expected to respond to erythropoietin therapy. The patient tolerated the infusions well, and there was no evidence of hypertension or elevations in serum creatinine or potassium, previously observed in some renal patients treated with the recombinant hormone. The availability of this cloned growth factor now promises important alternatives to the therapy of a variety of clinical syndromes associated with relative bone marrow hypoproliferation and/or the presence of multiple alloantibodies.

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REFERENCES


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Fig 1. Administration of rHuEpo to a patient with Gaucher’s disease. Epo (105 U/kg) was administered intravenously on day 0 and 1, then thrice weekly for 2 weeks, as indicated. There was a prompt rise in the percentage of reticulocytes that peaked on day 5, followed by a more gradual rise in the hemoglobin (Hgb) and hematocrit (Hct).
To the Editor:

Recently Dessypris et al reported about the effect of recombinant human erythropoietin (rhuEPO) on the concentration and cycling status of human bone marrow hematopoietic progenitor cells in vivo.1 The authors found that in nine patients with transfusion-dependent anemia of end-stage renal failure, administration of rhuEPO at a dose of 150 to 300 U/kg intravenously three times per week for 2 weeks caused an increase of bone marrow erythroid progenitor cells (CFU-E, BFU-E) and also, unexpectedly, an increase of myeloid (CFU-GM) and megakaryocytic (CFU-MK) bone marrow progenitor cells. Furthermore, the increase of progenitor cells was accompanied by an increased cycling status of these cells. Applying an in vitro colony assay as previously described,2 we have measured weekly peripheral blood committed (BFU-E, CFU-GM) and pluripotent (CFU-GEMM) hematopoietic progenitor cells in 11 uremic patients on regular hemodialysis. These patients were treated with rhuEPO at a dose of 80 U/kg intravenously three times weekly because of anemia due to end-stage renal failure. As shown in Fig 1, peripheral blood BFU-E, CFU-GM, and CFU-GEMM were significantly increased within 1 week of supplementation therapy as compared to pretreatment levels. These data indicate that the expansion of bone marrow BFU-E and CFU-GM under the influence of rhuEPO, as shown by Dessypris et al.,1 is accompanied by an increase of the respective progenitor cells in peripheral blood and directly demonstrate the CFU-GEMM compartment as a target for therapeutic doses of rhuEPO. Thus, both studies support the concept that the action of rhuEPO in vivo is not restricted to the erythroid lineage, but includes a broad spectrum of hematopoietic progenitor cells.

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Fig 1. Effect of treatment with rhuEPO on the number of BFU-E, CFU-GM, and CFU-GEMM in the peripheral blood of patients with anemia of chronic renal failure. Values are expressed as means ± standard errors from 11 patients treated with 80 U/kg rhuEPO three times weekly for 12 weeks. Shaded areas represent progenitor cell ranges from 15 normal individuals. All three progenitor cell classes were significantly increased (<.01 by the Mann Whitney U-test) after one week of rhuEPO treatment as compared to pretreatment values.

REFERENCES


Recombinant erythropoietin improves the anemia associated with Gaucher's disease [letter]

GP Rodgers and LS Lessin