Ten year follow up of erythropoietin induced autoimmune pure red cell aplasia

Sir,

Treatment with recombinant human erythropoietin (EPO) carries the risk of development of autoimmune pure red cell aplasia (PRCA). Until 2005, approximately 250 patients have been reported worldwide.[1] We presented India's first patient with EPO-induced PRCA in 2005 at Indian Society of Nephrology Conference ISNCON, 2005, New Delhi. We report the 10-year follow-up of the same patient.

A 53-year-old gentleman was diagnosed with end-stage renal disease due to hypertension. He was initiated on peritoneal dialysis in March 2002. His hemoglobin was 5.2 g/dL.

He was prescribed EPO (Eprex, Janssen-Cilag) at a dose of 50 IU/kg thrice a week for subcutaneous use. His employer provided him with a generic brand of recombinant human EPO-alpha. His hemoglobin in July 2002 was 9.0 g/dL.

In August 2002, he presented with malaise and giddiness. His hemoglobin was 4.9 g/dL. Rest of the reports were as follows: Leucocyte count 7500/mm^3, platelet count 2.3 lakhs/mm^3, absolute reticulocyte count 4300/mm^3,

serum ferritin 873 ng/mL, serum iron 175 μg/dL, total iron-binding capacity 258 ng/mL and transferrin saturation 55%, serum calcium 7.7 mg/dL, phosphorus 5.2 mg/dL, alkaline phosphatase 465 U/L, parathormone 256 pg/mL, and lactate dehydrogenase 125 IU/L. There were no hemoparasites. Serum electrophoresis had not revealed monoclonal spike. There was no serologic evidence of viral infections such as hepatitis B or C, and HIV. He was transfused with two units of blood and the dose of EPO was increased to 75 IU/kg/per dose thrice a week, for subcutaneous use.

During the next few weeks, the patient's hemoglobin level continued to decline and he required repeated blood transfusions. EPO was stopped in the 1st week of October 2002. A bone marrow aspiration and trephine biopsy was carried out. It revealed scanty (<5%) erythroblasts, prominent myeloid precursors, and normal megakaryocytes. Fat spaces and stromal fragments were prominent. Perls' stain showed increased iron stores. Parvovirus serology was not performed. With a suspicion of PRCA, anti-EPO antibody was investigated by radioimmunoprecipitation assay. It was positive with 8.2% cpm (normal value < 0.6% cpm). He was initiated on prednisolone (1 mg/kg/day) and cyclosporine (5 mg/kg/day). The hemoglobin was 6.2 g/dL. Over the next 3 weeks, there was no fall in hemoglobin and after the 4th week, there was a rise in hemoglobin to 7.1 g/dL. In January 2003, the hemoglobin was 9.7 g/dL. The patient was not transfused after the start of immunosuppression. Cyclosporine was stopped in December 2005 and prednisolone in October 2006.

In June 2011, he was diagnosed and treated for tuberculous pleural effusion on the right side. In September 2011, the patient's hemoglobin was 6.5 g/dL. The iron studies were normal, a repeat anti-EPO antibody was negative, and bone marrow aspiration and trephine biopsy was normal. He was started on darbepoeitin 25 mcg once a week. The hemoglobin improved and stabilized at 10 g/dL.

The patient had several features that suggested PRCA.[1] There was a drop in hemoglobin at approximately 1 g/dL per week, no major decrease in leukocyte and platelet counts was found, absolute reticulocyte count was low, and scanty erythroblasts with normal cellularity of myeloid series and the presence of anti-EPO antibodies were found. We hence present successful 10-year survival of first reported patient with EPO-induced PRCA from India.

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