Resistance to Recombinant Human Erythropoietin in a Hemodialysis Patient with Lupus Reactivation

R.	Rafael	Romero
D.	Daniel	Novoa
A.	Alejandro	Perez-Freiria
V.	Victor	Arcocha
R.	Rafael	Alonso
D.	Dolores	Arza
X.M.	Xose M.	Lens
D.	Domingo	Sanchez-Guisande

Service of Nephrology, General Hospital of Galicia, Santiago de Compostela, Spain

Dr. Rafael Romero, Servicio de Nefrología, Hospital General de Galicia, E-15705 Santiago de Compostela (Spain)

Dear Sir,

Recombinant human erythropoietin (rHuEpo) is effective in the treatment of anemia in most patients with end-stage renal disease (ESRD) [1]. However, there is a minority of patients who are resistant to the effects of rHuEpo. This resistance has been associated with iron and vitamin deficiency, aluminum overload, severe hyperparathyroidism, hemo-lysis, infections, chronic inflammatory states, and vasculitis [see refs. 3-5]. We report a case of rHuEpo resistance in a hemodialysis patient with systemic lupus erythematosus (SLE) and no apparent lupus activity.

A 28-year-old woman with ESRD secondary to SLE, who was on hemodialysis since 1987, is described. The anemia had remained stable (hematocrit 26-28%), not necessitating transfusions during the last years. In December 1990 the hematocrit dropped to 20%, and treatment with rHuEpo (50 U/kg s.c, three times a week) was initiated. Because laboratory investigation revealed ferritin 32 ng/ml, transferrin saturation 22%, and serum iron 66 µg/dl, oral ferrous sulfate was also prescribed. Since during the next 2.5 months there was no response, the dosage of rHuEPO was increased to 100 U/kg three times a week, and iron dextran (1 g i.v.) administered, also resulting in no response. In April 1991, the patient developed arthralgias and hair loss, and SLE reactivation was considered. Laboratory analysis showed hematocrit 21%, hemoglobin 7 g/dl, ferritin 207 ng/ml, transferrin saturation 16%, serum iron 47 µg/dl, serum aluminum 52 µg/l, immuno-reactive parathyroid hormone 700 pg/ml, aDNA 100 IU/ml, C3 64 mg/dl, C4 13 mg/dl,

Prednisone

rHuEPO, U/kg

1∞

2 3 4 5 Time, months

Fig. 1. Changes of hematocrit and rHuEpo dose before and after treatment with predni-
anti-nuclear antigen > 1/1,000, haptoglobin 150 mg/dl, and a direct Coombs test was negative.
Prednisone treatment (40 mg/day) was initiated with a dramatic increase in hematocrit (fig. 1)

and disappearance of clinical lupus activity. Subsequently, the rHuEpo dose was decreased to 25 U/kg (three times a week), and the hematocrit stabilized at 33-36%.

Severe hyperparathyroidism and aluminum overload may cause rHuEpo resistance [2]; although this patient had elevated immunoreactive parathyroid hormone and aluminum serum levels, the dramatic response to prednisone ruled them out as causes of resistance. Inflammatory states such as vasculitis rheumatoid arthritis, or occult infection have been described as causes of rHuEpo resistance.

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ance [2-5]. SLE anemia may result from several mechanisms, and more than one may be operative at any time, but anemia of chronic disease is the most common cause. In the present case hemolysis was excluded, and probably the last mentioned mechanism was the cause of rHuEpo resistance. SLE activity decreases with ESRD, although a minority of patients continue to have serological and clinical activity by the 5th year of dialysis [6]. Because some clinical characteristics of SLE, such as fever, pericarditis, arthralgias, anemia, and leukopenia, are also typical of uremia and dialysis-related complications, SLE reactivation may be a difficult diagnosis. The rHuEpo resistance and the laboratory tests were the clue in our patient.

To our knowledge, the present report represents the 1st case of rHuEpo resistance induced by SLE reactivation in a hemodialysis patient, and we conclude that in these patients resistance to rHuEpo must alert the clinicians to the possibility of lupus activity.

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