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ERYTHROPOIETIN IN MYELODYSPLASTIC SYNDROMES: DURABLE RESPONSE IN A YOUNG PATIENT

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Sir,

Barosi *et al.*[1] recently reported guidelines for the clinical use of erythropoietin (rHuEPO); they emphasized that rHuEPO is rarely indicated in myelodysplastic (MDS) patients. However, many recent experienced have suggested it may have a beneficial effect when given alone in some MDS patient.[2-6] The high doses of rHuEPO used in these studies (approximatively 100 times higher than normal serum levels) could conceivably stimulate either the abnormal MDS clone or the remaining normal erythropoietic precursor cells, thereby accounting for the observed responses. We report a good durable response to high doses of rHuEPO in a young patient with a long disease history. A 28-year-old woman with a thalassemic trait (HbA_2 4.19%, HbF 4.57%) was referred to our institution in January 1981 because of anemia (Hb 7.6 g/dL); all other hematological parameters were in the normal range, and bone marrow aspirate showed an increase of erythroblastic cells with significant dysplastic features in the erythroid as well as megakaryocytic series without blasts (RA according to FAB classification). A 3-month period of oral vitamin B6 was given without clinical improvement. In October 1981 spleen enlargement (5 cm below costal margin) was observed, with a decrease in Hb levels (Hb < 6.5 g/dL) and the appearance of thrombocytopenia (Plts < 60×10^9/L); ferrokinetic studies revealed anemia with qualitative and quantitative erythropoietic defects and a reduced red cell life span. Platelet survival was shortened by the presence of hypersplenism. On the basis of these findings a splenectomy was performed in February 1982 and the platelet count subsequently normalized; however, Hb levels and transfusional requirements did not improve. Histological examination of the spleen did not reveal the presence of myeloid metaplasia. To maintain Hb concentration at 8-9 g/dL the patient needed about 3-4 units of packed red cells/month. In October 1991 we started rHuEPO treatment (400 U/kg twice a week sc). Hematological parameters before treatment were: Hb 9 g/dL, WBC 11×10^9/L, Plts 570 $\times10^9$/L, reticulocytes 36×10^9/L and basal serum EPO concentration was inappropriately low for the degree of anemia (44 mU/mL).

As shown in Figure 1, after 3 months of treatment both Hb level and reticulocyte count reached progressively normal values and have remained stable until the pressent writing: 54 months of follow-up. Because of the good response observed, rHuEPO was never discontinued and is still being administered at the same dosage. However, the other hematological parameters as well as erythroid maturation have not been affected by treatment. No functional iron deficiency was noted during the treatment and the patient did not need any iron supplementation. The Karnovsky score for performance status improved together with Hb levels and the patient became transfusion free after 1 month of treatment.

Karyotype analysis was performed before and after 12 months of treatment; on both occasions a mosaicism of normal and tetraploid cells was evidenced (data reported in details elsewhere). Anemia is the most important feature in MDS patients and represents the most frustrating therapeutic problem. Long-term transfusional support is still the mainstay of treatment, even

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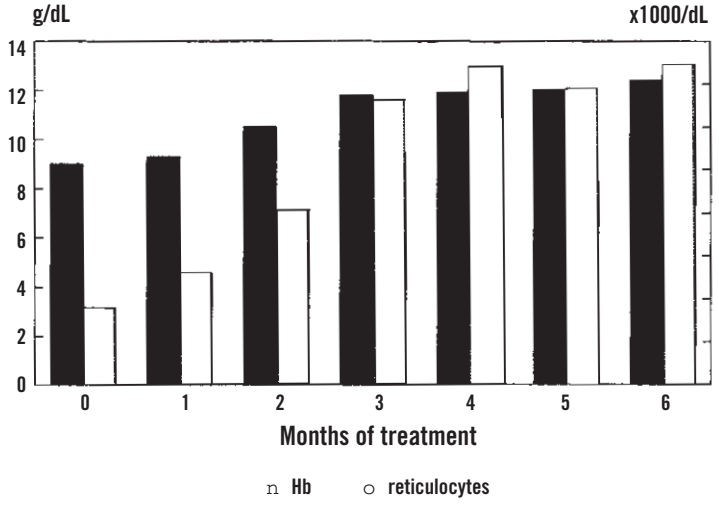

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Figure 1.

though it may induce many side effects, especially in young people. Data from the literature show that rHuEPO has some activity in about 15-20% of MDS patients.[1-6] However, normalization of Hb levels is very rare when rHuEPO is used without other growth factors.[2,4,6]

Little is known about the response mechanism to rHuEPO in MDS; markedly eterogeneity in the biology of MDS may however explain the different results observed when the same treatment was employed. It is possible that younger patients with MDS may have a better chance of improving during rHuEPO treatment because their marrow stem cell reserve is different from that present in elderly MDS patients.

This case illustrates achievement of a long-lasting complete response with high doses of rHuEPO in a young patient with RA that was highly dependent on PRC transfusions. Therefore, in our opinion, even though rHuEPO treatment is more expensive supportive treatment

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