Acute Leukemia and Erythropoietin Cause or Casual Relationship?

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Dear Sir,

No references have been found on the clinical association between leukemia and treatment with erythropoietin (Epo) in patients with renal anemia. We describe a case with such a condition, and etiological aspects are discussed.

A 62-year-old woman with a history of arterial hypertension, mild proteinuria, and small kidneys reached end-stage renal failure with clinically predominant anemia, and was started on maintenance hemodialysis (HD) in November 1988. Arterial normotension and good metabolic control were achieved with 12 h HD/week, but severe anemia persisted. She was given Epo (1,500 IU s.c.) at each HD session when hematocrit was 21.6%, hemoglobin 70 g/l, white blood cell count 6,000/mm³, platelet count 337,000/mm³, serum iron 21 µmol/l, transferrin saturation 29%, and serum ferritin 1,500 ng/ml. The hematocrit value rose to 24.8% after 3 weeks of treatment with apparent stabilization. Two months later, dyspnea and fever appeared associated with a sudden fall of the hematocrit and extreme leukopenia. Anisocytosis, circulating blasts, and isolated megaplatelets were observed. There was 60% blastic substitution in bone marrow, and acute (type 4) nonlymphoblastic leukemia was diagnosed. Two cycles of cytosine arabinoside and dau-norubicin were given, besides daily HD, blood replacement, and antibiotics. The patient died 2 months later.

Could exogenous Epo play a role in the leukemic transformation of bone marrow blasts? Possibly our patient had a subclinical leukemic disease under physiological control, until the administration of Epo might have altered the existing balance between bone marrow mitosis and cellular destruction.

Although Epo has a predominant effect on the erythroid cell line, several authors reported an increase in number, size, and function of platelets [1]. It may also modify leukocyte distribution and the capacity of immunologic response [1-4]. Stockenhuber et al. [2] observed an increase not only in precursors of erythroid lineage induced by Epo, but also in circulating granulocyte-macrophage colony-forming units [2]. A possible relationship between Epo and acute leukemia is suggested by the findings of Asano et al. [3] and Motoji et al. [4] who studied in vitro stimulation of myeloblastic cells obtained from patients with acute leukemia. Epo alone did not induce leukemic blast colony formation, but when it was used in the presence of colony-stimulating factors, the number of leukemic blast colonies was

significantly increased. The proliferative response to Epo was not only restricted to the erythroid lineage, but also involved acute leukemia blast cells [3,4].

The therapeutic availability of recombinant growth factors requires a deeper knowledge of their action at the cellular level and of their possible interaction mechanisms under normal and pathological conditions.

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