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Case report

Interferon-α-induced pure red cell aplasia following chronic myelogenous leukemia

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We report a case of pure red cell aplasia (PRCA) that resulted from interferon (IFN)-α therapy for chronic myelogenous leukemia. PRCA improved within 1 month after IFN-α was discontinued. This case indicates the involvement of IFN-α in the pathogenesis of PRCA. [© 2001 Lippincott Williams & Wilkins.]

Key words: Interferon-α, chronic myelogenous leukemia, pure red cell aplasia.

Introduction

Interferon (IFN)-α is now becoming a part of the standard treatment of chronic myelogenous leukemia (CML). In the clinical course of CML, pure red cell aplasia (PRCA) is a very rare complication.[1] Most reported cases of PRCA with CML terminate in acute leukemic transformation.[2] There is only one case report that shows PRCA with CML in the chronic phase during IFN and hydroxyurea therapy.[3] We report here a patient with CML in an accelerated phase who developed PRCA during IFN-α therapy.

Case report

A 47-year-old male was found to have leukocytosis at his routine medical checkup in February 1997. His white blood cell count was 69 600/μl and hemoglobin was 12.4 g/dl. Bone marrow examination revealed a hypercellular marrow with granulocytic hyperplasia, 9.1% myeloblasts and 2.8% promyelocytes, and increased megakaryocytes. Cytogenetic analysis showed the Philadelphia chromosome in 100% of metaphases. Fluorescence *in situ* hybridization studies showed the BCR-ABL translocation in 98.9% of samples. A diagnosis of chronic-phase CML was made. Hydroxyurea was administered as induction therapy for the first 3 months. Simultaneously, IFN-α was started at 3 MU s.c. for 1 week and then increased to 6 MU every day. In August 1999, a new cytogenetic abnormality of der (1;17)(q10;q10) appeared in 15% of metaphases in the bone marrow and we made the diagnosis of progression to accelerated phase.

IFN-α administration was reduced to 3 times a week because it was not felt to be controlling the disease and was continued through to the end of January 2000. In December 1999, the patient's hemoglobin concentration began to decline and he was given transfusions of packed red blood cells. There was no evidence of gastrointestinal bleeding or hemolytic anemia. He presented 10% body weight loss with lassitude. The hemoglobin fell to 7.4 g/dl with the white blood cell count 13.2×10^9/l and platelet count 748×10^9/l. Reticulocyte count was 21 000/μl in November 1999. Bone marrow aspiration and biopsy showed severe suppression of erythroid precursors with myeloid hyperplasia. Giant proerythroblasts characteristic of parvovirus B19 infection were not detected. Myeloblasts and promyelocytes showed no increase in number. The Philadelphia chromosome was found in 100% of metaphases. Trisomy 8 was detected in 15% of metaphases and der(1;17)(q10;q10) had disappeared.

The patient was diagnosed as having PRCA with accelerated-phase CML. There were no midline masses to suggest thymoma on his chest radiograph. At the beginning of February 2000, IFN-α therapy was stopped and hydroxyurea was substituted. Two weeks

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later, his hemoglobin concentration began to rise and he has not required further transfusion. His physical condition and body weight improved. In the following 7 months, he received only hydroxyurea and is still in an accelerated phase with normal hemoglobin. Parvovirus B19 IgG antibody was negative in August 2000.

Discussion

IFN-α is considered to be a first-line drug for patients with CML because it delays disease progression and prolongs overall survival compared with conventional chemotherapy. A few cases of PRCA during the clinical course of CML have been reported and these usually terminate in blast crisis.[2] *In vitro* data suggest that IFN may play a causative role in the development of PRCA.[4] Recently one other case in which IFN-α might have provoked PRCA in the chronic phase of CML has been reported. That patient was on IFN-α and hydroxyurea.[3] In that case, intermittent red blood cell transfusion was required for more than 1 year after discontinuation of both drugs. Our patient received continuous IFN-α for 28 months before the occurrence of PRCA, which improved within 1 month after stopping the drug. We suggest that this is a more valid case connecting PRCA to IFN-α because drug-induced PRCA usually resolves within 1–3 weeks after discontinuation of the causative drug and supportive red blood cell transfusion.[5] We conclude that IFN-α is involved in the pathogenesis of some cases of PRCA.

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