American Journal of Hematology 34:69–70 (1990)

Porphyria Cutanea Tarda After Allogeneic Bone Marrow Transplantation for Chronic Myelogenous Leukemia

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A case of porphyria cutanea tarda (PCT) occurring after bone marrow transplantation (BMT) is reported. A 43-year-old male with chronic myelogenous leukemia received an human leukocyte antigen (HLA)-identical allogeneic transplantation with T-cell depleted marrow. Because of graft rejection, a second transplant was performed 4 months later. A grade II acute graft- vs.-host disease and a cytomegalovirus (CMV) infection were subsequently observed. Two years after the second transplant, cutaneous symptoms of PCT with typical biochemical abnormalities developed. Liver biopsy revealed signs of hepatitis with iron overload. CMV was isolated from liver tissue. The possible roles of underlying disease, BMT, and CMV liver disease are discussed in view of the recently reported cases of PCT in patients with AIDS or hematological disorders.

Key words: immune deficiency, cytomegalovirus infection, hepatic porphyria

INTRODUCTION

Porphyria cutanea tarda (PCT) is a rare dermatological disease characterized by hyperpigmentation and bullous lesions of sun-exposed areas. The disease is caused by an inherited deficiency of uroporphyrinogen decarboxylase (uro-d) and is frequently associated with hepatic disease [1]. Recently, several cases of PCT have been described in patients with acquired immune deficiency syndrome (AIDS) [2–4] or hematological disorders [5–7]. Whether or not this association is merely coincidental is unclear. We report herein a case of PCT in a recipient of allogeneic bone marrow transplantation (BMT) for chronic myelogenous leukemia (CML).

CASE REPORT

A 43-year-old male with previous occupational exposure to benzene presented in May 1982 with splenomegaly and hyperleukocytosis. A diagnosis of Philadelphia-positive CML was made and a treatment by busulfan and then hydroxyurea instituted. On November 7, 1985, an allogeneic BMT was performed from an human leukocyte antigen (HLA)-identical brother, after conditioning by cyclophosphamide (120 mg/kg) and total body irradiation (12 Gy). T-cell depletion and cyclosporine were used for graft-vs.-host disease (GVHD) prophylaxis. Engraftment occurred promptly without evidence of GVHD. In January 1986, a cytomegalovirus (CMV) reactivation was diagnosed by CMV isolation from blood and urine samples and by IgM detection and a fourfold elevation of IgG serum titers in enzyme-linked immunosorbent assay (ELISA). Concomitantly, a mild increase in serum glutamic-oxaloacetic (SGOT) and pyruvic (SGPT) transaminase levels was noted.

In March 1986, a graft rejection necessitated a second BMT with non T-depleted marrow from an HLA-identical sister after preparation by cyclophosphamide, procarbazine, and antithymocyte globulin. Despite cyclosporine therapy, a grade II cutaneous and hepatic GVHD was observed and successfully treated by methyl-prednisone (2 mg/kg for 14 days). In the absence of chronic GVHD, cyclosporine was discontinued after 6 months. A stable engraftment was proved by donor marrow karyotypes. During transplant procedures, the patient received a total of 25 units of packed red blood cells, the last transfusion in May 1986. Mild hepatic abnormalities

Received for publication August 31, 1989; accepted October 19, 1989.

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(SGOT and SGPT between 50 and 150 IU, normal 5–25 and 5–50, respectively) persisted, attributed to chronic CMV infection.

In April 1988, skin lesions typical of PCT developed. The diagnosis was confirmed by elevated urinary uroporphyrin excretion (7,770 mM/24 hr, normal < 10) and decreased erythrocyte uro-d activity (10, normal 21–33). Other biological results included high serum ferritin level (1,788 ug/liter, normal 30–300) and mild hepatic abnormalities (SGOT 65 IU, SGPT 75 IU, alkaline phosphatase 148 IU, normal 30–90). Liver biopsy revealed a moderate steatosis, siderosis, and a moderate granulomatous hepatitis. CMV was detected in liver tissue by indirect immunofluorescence. The patient was bled 6 liters of blood over the next 6 months, with a partial improvement of skin lesions and a return of serum ferritin to normal values. Subsequent treatment by chloroquine resulted in a complete disappearance of dermatological symptoms.

DISCUSSION

The association of PCT with a variety of hepatic pathological conditions is well known. Ethanol, benzene derivatives, and other hepatotoxic drugs can unmask a latent alteration of porphyrin metabolism [1]. Recently, a case of pseudoporphyria attributed to cyclosporine has been described in a renal transplant recipient [8]. Our patient had a history of benzene exposure and received hepatotoxic cytotoxic drugs, irradiation, and cyclosporine at the time of transplantations, but the PCT developed 2 years later and the responsibility of these agents is unlikely. On the other hand, associations between PCT and hematological disorders such as chronic myelogenous leukemia [5], idiopathic myelofibrosis [6], or chronic myelomonocytic leukemia [7] have been reported. Our patient was probably cured of his disease when the PCT was diagnosed, but iron overload secondary to red cell transfusions can be implicated, as stressed by De Rosa et al. [6].

Finally, the main cause of the PCT appears to be CMV hepatitis. The role of viral hepatitis in unmasking porphyria has been described [9]. This observation of PCT in an immunodeficient patient is comparable to those recently published about AIDS patients. In two of the cases reported, evidence of previous exposure to B-hepatitis virus was mentioned [2, 4], and in another case [3] PCT was associated with a *Mycobacterium* hepatitis. Opportunistic infections, including CMV infections, are frequent in AIDS and BMT patients and may impair hepatic porphyrin metabolism. In this setting, the occurrence of PCT patients may be more than coincidental.

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