To the editor:

Pure red-cell aplasia due to parvovirus B19 infection in a patient treated with alemtuzumab

A 56-year-old woman was diagnosed with mycosis fungoides 10 years earlier. Her cutaneous manifestations were widespread patches, plaques, and ultimately tumor nodules. Her disease was refractory to standard therapies, and she had no histocompatible sibling.

She subsequently entered a phase 2 clinical trial of alemtuzumab (Campath-1H) for cutaneous T-cell lymphoma (CTCL). After 2 weeks’ treatment, she became mentally obtunded with a fever of 40°C. A septic workup including computed tomographic (CT) scan and magnetic resonance imaging (MRI) brain scan, lumbar puncture, and testing for HIV, herpes simplex virus, cryptococcal meningitis, and Mycobacterium tuberculosis were unrewarding. She failed to respond to empirical broad spectrum antibiotics.

Twenty-three days after commencing alemtuzumab, the patient developed a severe, transfusion-refractory anemia (hemoglobin level, 77 g/L), and reticulocytopenia (reticulocyte count, 3 × 10⁹/L), with bone-marrow biopsy revealing features of pure red-cell aplasia (PRCA). Erythropoiesis was markedly reduced, with normal myelopoiesis and megakaryocytes. Giant pronormoblasts were demonstrated, and the myeloid-erythroid ratio was 23:7. (Of note: marrow 8 days prior to commencing alemtuzumab demonstrated normal erythropoiesis.) She had a T-cell lymphopenia of 0.31 lymphocytes per liter affecting both her CD4 and CD8 T-cell subsets. Parvovirus IgM and polymerase chain reaction (PCR) were positive. Intravenous immunoglobulin (1.5 g/kg over 4 days) was administered. Twelve days later, there was a reticulocytosis (reticulocyte count, 226 × 10⁹/L), and the patient became afebrile, alert, and transfusion independent. A repeat bone-marrow biopsy 1 month later was normal.

Pure red-cell aplasia is characterized by severe anemia, reticulocytopenia, and selective deficiency of erythroblasts in an otherwise normal marrow aspirate. Etiologies of PRCA include primary (autoimmune, preleukemic, or idiopathic) and secondary causes such as (a) paraneoplastic ones (thymoma, hematologic malignancies, solid tumors), (b) infections (parvovirus B19, HIV, HTLV, and others), drugs (azathioprine, isoniazid, etc), (d) collagen vascular diseases, (e) chronic haemolytic disorders, and (f) a range of other causes (pregnancy, severe uremia, and nutritional deficiencies).1

Human parvovirus B19 is a small nonenveloped single-stranded DNA virus. It is transmitted via respiratory droplets or, rarely, by blood products.2 Infection is common: 15% of young children, 50% to 60% of young adults, and up to 90% of the elderly population show IgG seropositivity. Parvovirus binds to the blood group P antigens (globoside),2 destroying erythroid precursors. In childhood, it can cause erythema infectiosum (“fifth disease”), hydrops fetalis, an acute polyarthropathy, or a transient aplastic crisis.2 The normal immune system clears the infection before there is prolonged symptomatic anemia. Patients with lymphopenia due to parvovirus B19 in a patient treated with rituximab. The severe CD4 lymphopenia induced by alemtuzumab and other monoclonal therapies such as rituximab for lymphoproliferative diseases is a risk factor for opportunistic infections. Consideration of parvovirus infection as a possible cause of anemia in these patients is important. Treatment with IVIG should be used.

Kirsten E. Herbert, M. Miles Prince, David A. Westerman

Correspondence: Miles Prince, Department of Hematology, Peter MacCallum Cancer Institute, Locked Bag 1, A’Beckett St, Melbourne, Victoria 3006, Australia; e-mail: miles.prince@petermac.org

References