Netherlands
The Journal of Medicine

A patient with pure red cell aplasia after allogenic stem-cell transplantation

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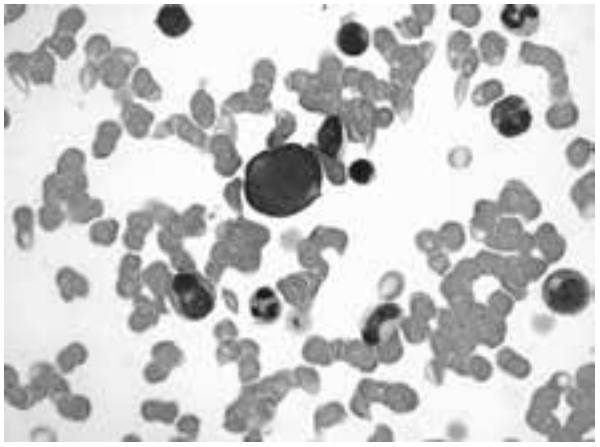
CASE REPORT

A 58-year-old male patient was seen on our outpatient clinic with persistent anaemia after partial T-cell depleted allogenic stem-cell transplantation because of hypoplastic myelodysplastic syndrome (MDS). To keep his haemoglobin level above 5.0 mmol/l he received two units of blood transfusion every two weeks. There were no signs of occult blood loss, infectious diseases or graft-versus-host-disease. The patient was on antiviral medication and trimethoprim-sulfamethoxazole (TMP-SMZ) as *Pneumocystis jiroveci* pneumonia (PJP) prophylaxis. Immunosuppressant drugs were slowly tapered and finally stopped two months after transplantation. His haemoglobin level did not improve after discontinuation of TMP-SMZ.

Physical examination showed no abnormalities. Laboratory investigation revealed: haemoglobin 4.8 (8.4-10.8 mmol/l), leucocytes 4.3 (4.0-11.0 x10^9/l), thrombocytes 283 (150-400 x10^9/l), and reticulocytes 3.8 (25-125 x10^9/l). Vitamin B_{12} and folic acid levels were normal. Ferritin level was high because of repeated blood cell transfusions. Chimerism analysis showed 100% donor chimerism. A crista biopsy and aspiration was performed nine months after transplantation to look for the cause of anaemia.

Figure 1. *Giemsa stained bone marrow smear*



WHAT IS YOUR DIAGNOSIS?

See page 374 for the answer to this photo quiz.

A PATIENT WITH PURE RED CELL APLASIA AFTER ALLOGENIC STEM-CELL TRANSPLANTATION

DIAGNOSIS

The diagnosis is pure red cell aplasia due to Parvo B19 infection.

Giemsa stained bone marrow smear showed a red cell aplasia. Numerous giant proerythroblasts were present in the aspirate, with a high nuclear/cytoplasmic ratio. In combination with pure red cell aplasia, these changes in erythroid precursors are highly suggestive of infection with human parvovirus B19. Immunohistochemistry for parvovirus showed nuclear expression of infected cells. DNA PCR for parvovirus was performed on blood and was positive.

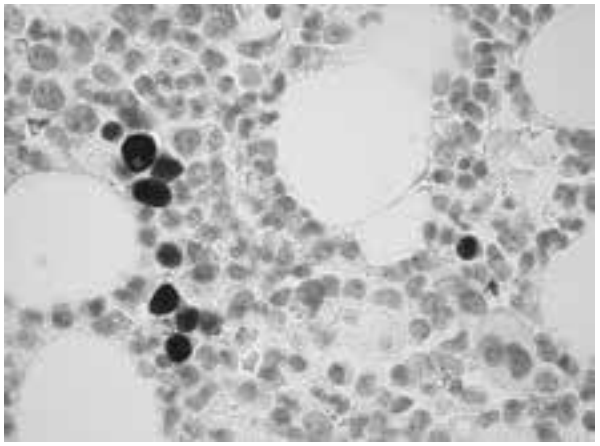
Most cases of parvovirus B19 infection are asymptomatic. The most common presentation of infection is erythema infectiosum, known as the fifth disease, a childhood exanthema characterised by a 'slapped cheek' rash.[1]

In the absence of antiviral immunity, as in our immunocompromised patient, red-cell aplasia can be a manifestation of persistent Parvovirus B19 infection. Parvovirus B19 infects erythroid progenitor cells by binding to the receptor known as the P antigen. Subsequent viral replication in erythroid progenitor cells leads to cellular lysis, which is characteristically manifested as pure red cell aplasia on bone marrow examination.[2]

The anaemia is severe and requires transfusions. A persistent B19 infection often responds to a five- or ten-day course of immune globulin at a dose of 0.4 g per kilogram of body weight.[3,4]

After initiation of immune globulin substitution the haemoglobin level in our patient improved to 6.7 mmol/l within two weeks.

Figure 2. *Immunohistochemical staining for Parvovirus highlights the viral inclusions*



REFERENCES

1. Young NS, Brown KE. Parvovirus B19. New Engl J Med. 2004;350:586-97.
2. Eid AJ, Brown RA, Patel R, Razonable RR. Parvovirus B19 infection after transplantation: a review of 98 cases. Clin Infect Dis. 2006;43:40-8.
3. Kurtzman G, Frickhofen N, Kimball J, Jenkins DW, Nienhuis AW, Young NS. Pure red-cell aplasia of 10 years' duration due to persistent parvovirus B19 infection and its cure with immunoglobulin therapy. New Engl J Med. 1989;321:519-23.
4. Crabol Y, Terrier B, Rozenberg F, Pestre V, Legendre C, Hermine O, et al. Intravenous immunoglobulin therapy for pure red cell aplasia related to human parvovirus b19 infection: a retrospective study of 10 patients and review of the literature. Clin Infect Dis. 2013;56:968-77.