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Antibody Response to Human Immunodeficiency Virus after Infected Bone Marrow Transplant

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An antibody response to human immunodeficiency virus (HIV) is described in a young woman with T-lymphoblastic leukemia, who received a bone marrow transplant from a donor retrospectively found to be HIV positive.

Epidemiological studies have shown that AIDS and asymptomatic human immunodeficiency virus (HIV) infection are associated with several well-defined high risk groups, including recipients of blood and blood products (1) and bone marrow transplants (2). We report the case of a young woman who received a bone marrow transplant from a donor retrospectively found to be HIV positive.

Case Report. A young 17-year-old woman with T-lymphoblastic leukemia received a bone marrow transplant (4.6×10^8 /kg nucleated cells) in 1983, seven months after the diagnosis in early second remission. The pre-bone marrow transplant chemotherapy consisted of cyclophosphamide and 10 Grays total body irradiation in a single fraction from a ⁶⁰Co source at a dose rate of 4.30 cGy/min. Cyclosporin was the sole agent used to prevent graft versus host reaction and was given for nearly three months after transplantation.

Clinically, the course after transplant was characterized by repeated episodes of hemorrhagic cystitis, with *Escherichia coli* bacteriuria at 2 months, upper respiratory tract infections at 4 to 7 months, pleuro-pericarditis and herpes zoster infection at 14 months, and bronchopneumonia at 17 and 23 months. All episodes resolved promptly following appropriate therapy. At present the patient is well, in complete remission and has a Karnofsky score of 100% five years after transplant. After bone marrow transplant the patient did not receive any further blood or blood products from her donor, but only from blood bank donors, retrospectively found to be HIV seronegative.

In 1987 the bone marrow donor, her 23-year-old brother, was discovered to be an intravenous drug abuser, and retrospective analysis of a frozen blood sample obtained at the time of the bone marrow transplantation revealed the presence of antibodies against human immunodeficiency virus (HIV). Frozen blood samples from the bone marrow recipient taken at diagnosis, immediately before bone marrow transplant, and 5, 16, 19, 24, 30, 36 and 48 months afterwards, were then tested together with the bone marrow donor's serum sample, for the presence of HIV antibody (IgG and IgM) and HIV p24 antigen.

The presence of antibody was first detected by a commercial enzyme immunoassay (Wellcome, UK) performed and interpreted according to the manufacturer's instructions. Analysis of the antibody response against individual HIV polypeptides was performed by immunoblotting using commercial strips (Du Pont, France) with HIV polypeptides blotted after PAGE separation. Each strip was incubated overnight with a 1/100 dilution of serum and the antigen-antibody reaction was detected by a rabbit anti-human IgG biotin-avidin system or by horseradish-peroxidase coupled rabbit anti-human IgM; 4-chloro-1-naphthol was used as substrate. Sera for detection of IgM were tested after pretreatment with *Staphylococcus aureus* protein A (Cowan Strain, Institute Virion, Switzerland) as previously described (3).

All samples were also assayed for the presence of HIV p24 core antigen in a solid sandwich-type enzyme immunoassay with anti-HIV p24 fixed onto microtiter plate wells (Du Pont). All tests with the

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