AUTOIMMUNE THROMBOCYTOPENIA AND NEUTROPENIA AFTER BONE MARROW TRANSPLANTATION

To the Editor:

First et al.1 recently reported the occurrence of isolated thrombocytopenia after allogeneic bone marrow transplantation in patients who had engraftment of all hematopoietic lines. Their findings reflect those obtained in our laboratory and reported elsewhere.2-5 Our study comprised 14 patients who received autologous buffy coat or bone marrow grafts and 32 patients who received allogeneic bone marrow grafts. The autograft patients received cyclophosphamide and melphalan as pregraft conditioning, while the allograft patients received various combinations of drugs, including cyclophosphamide and cyclosporine A, in addition to total body irradiation.

Investigations for platelet and neutrophil autoantibodies using immuno-fluorescent antoglobulin techniques6 were carried out before and after grafting on all patients. At the time of postgraft antibody testing, only three of the patients had evidence of viral infection and only one had signs of graft-v-host disease (GVHD); in general, such patients were excluded from the study.

There was a high incidence (52%) of antibodies to circulating (donor origin) platelets in the early postgraft period. Furthermore, we demonstrated a high incidence (65%) of antibodies to circulating (donor origin) neutrophils after bone marrow grafting. The cell specificity of these antibodies was demonstrated by cross-absorption experiments. Similar results have since been reported by Bierling et al.7 and Plouvier et al.9 In our own study, such antibodies in the allografted patients were shown, by immunoglobulin allotyping, to be of marrow donor type and were therefore autoantibodies. The antibodies demonstrated after autografting were, by definition, autoantibodies.

We also saw the two categories of thrombocytopenia described by First et al.,1 ie, transient and chronic. In addition, a further late-occurring type of thrombocytopenia was noted in some patients whose follow-up was for longer periods after marrow grafting; IgM platelet autoantibodies developed in one autografted patient at 211 days and in two allografted patients at 335 and 427 days postgraft.

Late-occurring thrombocytopenia has also been described by Spruce et al.10 The effect of autoantibodies on the postgraft platelet or neutrophil counts varied considerably in our study, and the presence of postgraft autoantibodies to circulating cells did not predict the development of a cytopenia. These variable effects probably reflected the in vivo activity of the antibody and the ability of the engrafted bone marrow to compensate for antibody-mediated cell destruction.11

Our investigation did not explain the mechanism of formation of autoantibodies after allogeneic or autologous marrow grafting. Ablative chemotherapy, and in particular radiotherapy, used for pregraft conditioning were common to both allografts and autografts, and may have been contributory factors. Altered expression of "self" antigens may result from stem cell damage due to insufficiency numbers or inadequate function of suppressor T cells in the early postgraft period may also lead to autoantibody formation. Whatever the mechanism, it is likely to be due to the interaction of a number of factors during re-establishment of the normal immune and hematopoietic systems after grafting.

These observations and those recently reported by First et al.1 draw attention to the occurrence and clinical significance of selective thrombocytopenia and neutropenia after both autologous and allogeneic bone marrow transplantation. Our studies also point to the possible autoimmune basis of these cytopenias.

REFERENCES

Autoimmune thrombocytopenia and neutropenia after bone marrow transplantation [letter]

RM Minchinton and AH Waters