Syngeneic Acute Graft-versus-Host Disease

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Sir,
Graft-versus-host disease (GVHD) can be seen in recipients of syngeneic or autologous bone marrow transplantation (BMT) (1, 2) and occurs in 8% of patients given this type of BMT (3, 4). Most cases are self-limiting, have a good prognosis and involve mainly the skin. Some authors consider that most cases of GVHD are related to cyclosporin A (CsA) therapy given for prophylaxis of GVHD (5). We report a patient who, without prior cyclosporine therapy and after receiving a syngeneic BMT, developed skin changes consistent with GVHD.

CASE REPORT

A 51-year-old woman was diagnosed as having severe paroxysmal nocturnal haemoglobinuria. She was treated with antithymic immunoglobulin, CsA and granulocyte-colony-stimulating factor for one year and showed a partial response. The patient had an identical twin sister, and studies confirmed that they were genotypically and phenotypically identical. One year after diagnosis, a syngeneic BMT was performed. She was conditioned with busulphan and cyclophosphamide, and received irradiated blood products. CsA was not given. On day 9 after leukocyte engraftment, she developed a generalized erythematous pruritic rash and severe diarrhoea up to 3 l/day. On day 11, elevated serum bilirubin (2.1 mg/dl) was observed.

Physical examination showed an erythematous maculopapular, confluent rash, without palmoplantar or mucous involvement (Fig. 1). A biopsy specimen showed slight alterations with discrete basal cell degeneration and hyperpigmentation, isolated necrotic keratinocytes and a sparse perivascular infiltrate in dermis (Fig. 2). On day 15 she was started on treatment with high-dose corticosteroids (methylprednisolone 60 mg i.v. daily), which led to disappearance of the rash and the diarrhoea, and to normalization on bilirubin levels.

DISCUSSION

Differential diagnosis of GVHD includes skin changes due to chemotherapy or radiation, and drug reactions or infections (3). These possibilities are eliminated in our patient, and transfusion-induced alloreactivity was excluded by adequate irradiation of all blood products. The skin rash, the gut involvement with diarrhoea following leucocyte engraftment and the complete remission after treatment with corticosteroids strengthened the GVHD diagnosis.

Studies in animal models have demonstrated a systemic autoimmune syndrome resembling GVHD, which paradoxically elicits after CsA therapy (5, 6). This syndrome is related to the development of cytotoxic T lymphocytes that erroneously recognize MHC class II molecules. These T cells are presumably exported from the thymus during CsA treatment (7, 8).

In autologous and syngeneic BMT there is an

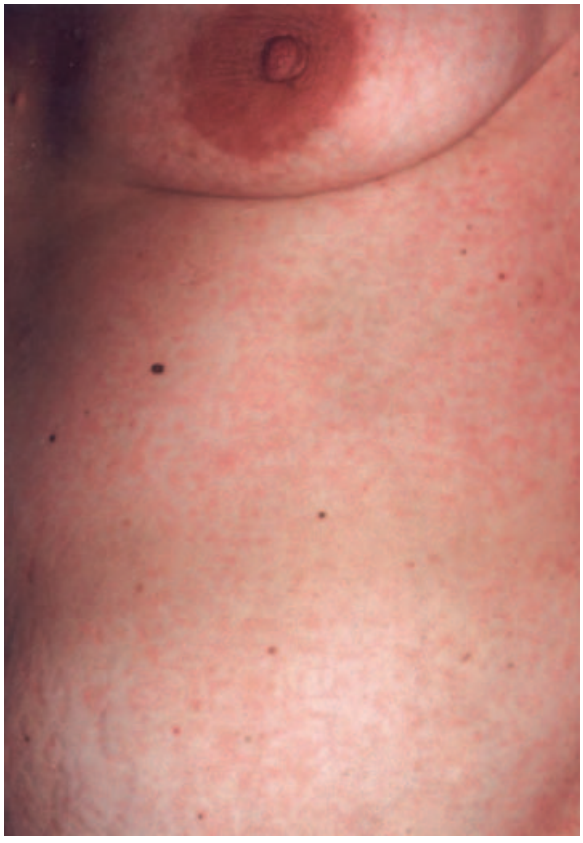

Fig. 1. Erythematous maculopapular rash affecting predominantly the trunk.

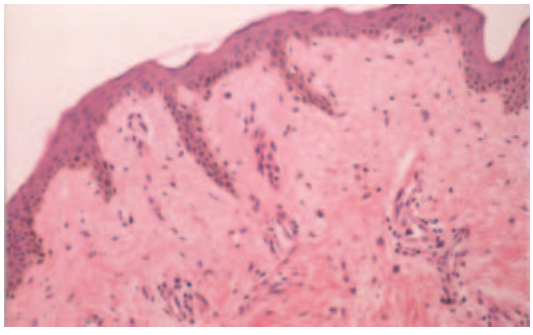

Fig. 2. Histopathological changes consistent with grade I graft-versus-host disease. H&E 40×.

absence of HLA disparity, as both graft and host are identical and do not possess alloantigens to stimulate each other by direct T-cell cytotoxicity (9). Several alternative mechanisms have been suggested such as viral triggering, thymic alteration related to chemotherapy and damage to host tissues produced by cytokines released during the conditioning therapy of the recipient (2, 9, 10).

In our patient, CsA was not given after BMT, but given one year before. There are several reports in haematological journals describing syngeneic GVHD reactions, all speculating on the above-mentioned theories (4, 9–11).

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