

Generalized Vitiligo after Allogeneic Bone Marrow Transplantation

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Sir,

Vitiligo is a common, depigmenting disorder characterized by well-circumscribed cutaneous macules devoid of melanocytes on the epidermis. Bone marrow transplantation (BMT), which has significant therapeutic benefits in haematologic disorders, such as leukaemia and aplastic anaemia, provides convincing evidence for the role of the immune system in some autoimmune diseases (1). In this report we describe four patients with haematologic malignancies in whom generalized vitiligo developed after allogeneic BMT from siblings or unrelated donor without depigmentary disorders.

CASE REPORTS

Patient no. 1

A 15-year-old Korean man was previously diagnosed as having acute lymphocytic leukaemia (ALL) and received a histocompatibility leukocyte antigen (HLA)-matched allogeneic BMT from an unrelated donor after conditioning with total body irradiation (TBI) and cyclophosphamide. Neither the recipient nor the donor had a history of depigmentary conditions. On the eighth day after BMT, the patient was found to have acute graft-versus-host disease (GVHD) presenting with generalized cutaneous lesions and diarrhoea. GVHD was controlled with cyclosporin A and corticosteroids. Three months after BMT, he presented generalized well-circumscribed white macules, which had a chalky white appearance

with Wood's lamp. A skin biopsy specimen was taken from one of the macules on the back and showed complete disappearance of melanocytes. Narrowband UVB therapy was given as monotherapy twice a week. The starting dose was 280 mJ/cm², with 15% dose increments at each subsequent treatment. He achieved >75% repigmentation with 26 treatments.

Patient no. 2

A 30-year-old Korean man with chronic myeloid leukaemia received HLA-matched allogeneic BMT from his sister after conditioning with TBI and cyclophosphamide. Neither the recipient nor the donor had a history of depigmentary conditions. Ten days after BMT, the patient developed acute GVHD with generalized cutaneous lesions, liver enzyme elevation and diarrhoea. He was treated with a short course of methotrexate, cyclosporin A, tacrolimus and corticosteroids. Two years after BMT, he presented well-circumscribed white macules on the whole body. A skin biopsy was performed on the forearm and showed complete disappearance of melanocytes. The patient refused any treatment for the vitiligo.

Patient no. 3

A 28-year-old Korean man with ALL received HLA-matched allogeneic BMT from his sister after conditioning with TBI and cyclophosphamide. Neither the

recipient nor the donor had a history of depigmentary conditions. With cyclosporin A and corticosteroids for prophylaxis, he showed no sign of acute GVHD. He suffered from progressive vitiligo on the whole body from 26 months after BMT. Two months later, the patient presented indurated, atrophic patches on the forearms and palms, which was pathologically confirmed as sclerodermoid chronic GVHD. Liver biopsy was performed due to the elevation of liver enzymes, which revealed chronic GVHD. The patient was treated with systemic and topical corticosteroids and showed clinical improvement. However, the vitiligo lesions still persisted and the patient refused further treatment.

Patient no. 4

A 43-year-old Korean man with myelodysplastic syndrome received HLA-matched allogeneic BMT from his sister after conditioning with TBI, busulphan and cyclophosphamide. There was no history of depigmentary conditions. Methotrexate, cyclosporin A and corticosteroids were administered as a prophylaxis for acute GVHD. Three months after BMT, the patient presented crusted, whitish patches on the lower lip, liver enzyme elevation and gastrointestinal discomfort. Biopsy specimens were obtained from the skin, liver and gastric mucosa, all of which revealed chronic GVHD. Two months later, although GVHD was controlled with systemic corticosteroids, he showed slowly progressive vitiligo on the face and upper extremities, which presented a chalky white appearance on Wood's lamp examination. The patient was treated with topical steroids and is planned to have narrowband UVB therapy.

DISCUSSION

Allogeneic BMT is widely used in the treatment of various haematologic disorders. The major complication of BMT is GVHD, which results from an interaction between donor immunocompetent cells and the recipient's cells showing disparate antigens (1). BMT is known to transfer autoimmune disease such as autoimmune thyroiditis, immune cytopenia, insulin-dependent diabetes, autoimmune polyendocrine failure and vitiligo from donors to recipients with such diseases (2, 3). Previous reports showed a high frequency of various autoantibodies in long-term survivors after allogeneic BMT. However, GVHD is known to be

associated with modulation of the host immune system and could act as a triggering factor for the appearance of autoimmune diseases such as vitiligo (4). Vitiligo is not a common complication of GVHD or immunosuppression, and extensive leucoderma is only rarely reported (5, 6). In our patients, two experienced acute GVHD and two had chronic GVHD. In the former two patients, time intervals between the onset of vitiligo and acute GVHD were 3 and 48 months, respectively, and the latter two patients showed 2- or 3-month intervals between the onset of vitiligo and chronic GVHD. All four patients showed progression of generalized vitiligo even after achievement of improvement in GVHD with immunosuppressive therapy. This suggests that GVHD, especially chronic GVHD, might have a role in the triggering of autoimmune-mediated vitiligo. The disease progression tended to occur independently of GVHD activity in our patients, which is similar to the previously reported cases (7).

We conclude that GVHD might have a role in the triggering of autoimmune-mediated vitiligo and this observation adds new support for the role of autoimmunity in the pathogenesis of some forms of vitiligo.

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