

Simultaneous Onset of Chronic Graft Versus Host Disease and Alopecia Areata Following Allogeneic Haematopoietic Cell Transplantation

Hatice Sanli¹, Filiz Kusak¹, Mutlu Arat², Pelin Ekmekci^{1*} and Osman Ilhan²

Departments of ¹Dermatology and ²Hematology, Ankara University, School of Medicine, Ankara, Turkey.

*E-mail: kocyigit@medicine.ankara.edu.tr

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Sir,

Chronic graft versus host disease (cGVHD) is a systemic complication that occurs after allogeneic haematopoietic stem cell or solid organ transplantation. Its incidence after allogeneic haematopoietic cell transplantation ranges between 27% and 72% (1). The immune system itself is a major target for cGVHD and the development of dysfunction may lead to autoimmune disorders. The association of vitiligo, myasthenia gravis, thrombocytopenia, autoimmune haemolytic anemia and polymyositis with cGVHD has been reported previously (2–6).

We present three patients with alopecia areata (AA) occurring during the course of cGVHD. To the best of our knowledge, such an association has not been reported previously.

CASE REPORTS

Case 1

A 26-year-old man was diagnosed with acute myeloblastic leukemia in January 2000. He underwent allogeneic peripheral stem cell transplantation from his HLA-matched sibling donor following a conditioning regimen including busulfan (16 mg kg^{-1}) and cyclophosphamide (120 mg kg^{-1}). After transplantation he received cyclosporin A (CsA) ($3 \text{ mg kg}^{-1} \text{ day}^{-1}$ i.v.) and short-term methotrexate for GVHD prophylaxis. On day +135 he developed herpes zoster infection on the T5-L1 dermatomal area and received acyclovir treatment ($5 \times 800 \text{ mg day}^{-1}$) for one week. One month later he presented with purple violaceous papules on the glans penis and white plaques on the lips. A biopsy obtained from the penile lesions showed characteristic findings of lichenoid GVHD. At the same time, liver involvement was determined by liver biopsy and ursodeoxycholic acid was added to the therapy regimen. Within a month, new lichenoid papules appeared on his nose, forehead and cheek and white reticular net-like lesions, white plaques and erosions appeared on his buccal mucosa. In addition, longitudinal ridging of the nails, diffuse defluvium and significant focal non-scarring alopecia on the left parietal area, vertex and the lateral part of the right eyebrow were observed (Fig. 1). Typical tufted hairs were noted at the periphery of the bald patches. The patient stated that although diffuse alopecia developed during the pre-transplant conditioning regimen, patchy alopecic areas occurred within the last month. A biopsy specimen obtained from the alopecic focus on the left parietal area showed no specific pathology, but the clinical appearance was typical for AA. Low-dose corticosteroid therapy was initiated due to the progression of cGVHD. The lichenoid lesions responded well to this therapy. Diffuse alopecia remained unchanged, but spontaneous depigmented hair regrowth occurred on the lateral part of the right eyebrow. Premature graying of hair, eyebrows and eyelashes also appeared within 2 months.

Case 2

A 19-year-old man was diagnosed with chronic myeloid leukemia in January 2000. He underwent an allogeneic peripheral stem cell transplantation from his HLA-matched sibling donor following conditioning regimen and post-transplantation treatment as case 1. CGVHD limited to liver was diagnosed bioptically 3 months



Fig. 1. Focal alopecia on the right eyebrow in case 1.

after transplantation and ursodeoxycholic acid was started. Eight months after transplantation, non-scarring, linear, ophiasis-like hair loss (Fig. 2) developed along the temporal and occipital areas. The biopsy obtained from the alopecic area showed characteristic findings of AA (Fig. 3). Spontaneous depigmented hair regrowth on the alopecic areas occurred within a month and vitiligo was observed on his face, neck, trunk and extremities. The body hair was also depigmented in those areas. One month later he also developed lichenoid papules and erosions on the buccal mucosa. All findings were evaluated as the progression of cGVHD, and mycophenolate mofetil therapy was added to the immune suppressive regimen.

Case 3

A 31-year-old man was diagnosed with chronic myeloid leukaemia in February 2001. He underwent allogeneic peripheral stem cell transplantation from his HLA-matched sibling donor following conditioning regimen and post-transplant treatment as indicated previously. Three weeks after transplantation, he developed axillary hyperpigmentation and the biopsy showed characteristic



Fig. 2. Non-scarring, linear, ophiasis-like hair loss along the temporal and occipital areas (case 2).

findings of acute GVHD. Dermatological examination on day +90 revealed xerosis, follicular hyperkeratosis and longitudinal ridging and fragility of the nails. The liver biopsy performed at that period also showed histopathological features of cGVHD and ursodeoxycholic acid was added to the therapy. At the control visit 2 months later, in addition to the previous findings diffuse hair loss affecting both eyebrows and new non-scarring patchy alopecic foci had developed on both forearms, which on histopathological examination revealed non-specific findings. Two months later, total spontaneous hair regrowth appeared on all alopecic areas.

DISCUSSION

Chronic GVHD is the most common complication of allogeneic haematopoietic cell transplantation resulting in significant morbidity and mortality, which develops about 100 days after transplantation. Skin, oral mucosa, sub-mucosal glands and liver are the most frequently affected organs (7). Scarring alopecia may be associated with the classical findings of cutaneous GVHD affecting the skin and mucous membranes. It can be in either focal or diffusely progressive form (8).

Diffuse alopecia, especially anagen effluvium, is a frequent finding observed after transplantation due to the conditioning therapy (9). When high doses are given, loss of anagen hairs becomes apparent clinically after 1 to 2 months, but is considered to be temporary, with regrowth occurring 4–6 months after transplantation (10). Our observations of patchy alopecia occurred at least 5 months after chemotherapy. We believe that this hair loss cannot be explained by the cytostatic therapy. Although no specific histopathological finding was observed in two of our cases (cases 1 and 3), the clinical features (patchy, non-scarring alopecia, regrowth by steroid therapy, regrowth with non-pigmented hair) were characteristic of AA. In one of our cases the clinical appearance was different; it was linear alopecia, which is an uncommon type of AA, but characteristic histopathological findings such as peribulbar T lymphocyte infiltration supported the diagnosis. The absence of specific

findings of AA in the histopathological examination of the other two patients may have been due to the variations of lymphocytic infiltration density during the course of the disease (11, 12).

Although AA following organ transplantation has been reported previously (13), to the best of our knowledge AA associated with cGVHD following allogeneic haematopoietic cell transplantation has not yet been reported. In our clinic, we are following 70 patients with cGVHD. Diffuse alopecia is a frequent finding in these patients, but apart from these three cases we have not observed AA.

Neither our patients nor their donors had a history of AA. Their HLA genes were not identical to those strongly linked with AA. However, AA in our cases is unlikely to be just a coincidental association. GVHD probably acted as the triggering factor for onset of the lesions. The development of another autoimmune disease, vitiligo, in one of our patients (case 2) and premature greying (which is seen in association with certain autoimmune diseases) in two patients (cases 1 and 2) also supported this suggestion (14).

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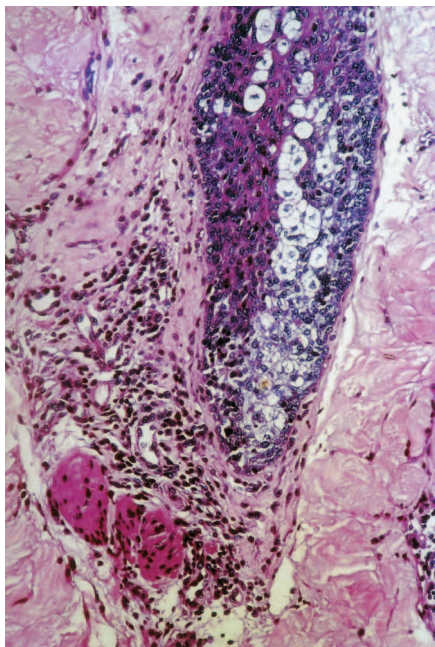


Fig. 3. Lymphocytic peribulbar infiltrate (HE $\times$ 100) (case 2).