

A Case of Eczematoid Graft-Versus-Host Disease

Jin Ho Chong, M.B.B.S., M.R.C.P.C.H. (UK),* Khawn Tawng, M.B.B.S., M.Med.Sc. (Paed),† Hui Min Liew, M.B.Ch.B. (Dundee), M.R.C.P. (UK),* Shui Yen Soh, M.B.B.S., M.R.C.P.C.H. (UK),† Ah Moy Tan, M.B.B.S., M.Med. (Paed),† and Mark Jean Aan Koh, M.B.B.S., M.R.C.P.C.H. (UK)*

**Dermatology Service and †Paediatric Haematology / Oncology, KK Women's and Children's Hospital, Singapore*

Abstract: A 13-year-old boy underwent allogeneic hematopoietic stem cell transplantation (HSCT) for underlying acute lymphoblastic leukemia and achieved neutrophil engraftment 28 days after HSCT. He developed ichthyosis 6 weeks after HSCT and then keratotic follicular papules, palmoplantar keratoderma, and a seborrheic dermatitis-like eruption 18 weeks after HSCT. From skin biopsies he was diagnosed with eczematoid graft-versus host disease (GVHD), which showed spongiosis with scattered necrotic keratinocytes. He responded to oral and topical steroids and an increase in cyclosporine dose. Although uncommon, eczematoid GVHD must be considered in children who have undergone HSCT and then develop an atypical eczematous eruption, especially in the absence of a history of atopy.

Graft-versus-host disease (GVHD) occurs more commonly as a major complication of hematopoietic stem cell transplantation (HSCT) in adults than in children (1), but recognition of GVHD, including cutaneous GVHD (cGVHD) in children, is still important because it can lead to significant morbidity and mortality (1). We describe a case of eczematoid GVHD, an uncommon presentation of cGVHD.

A 13-year-old boy underwent allogeneic HSCT for his underlying condition of high-risk acute lymphoblastic leukemia with hypereosinophilia. He had no personal or family history of atopy. The HSCT conditioning regime consisted of cyclophosphamide,

etoposide, and rabbit antithymoglobulin. Cyclosporin and methotrexate were given for GVHD prophylaxis. He achieved neutrophil engraftment 28 days after the cord blood infusion.

He developed pruritic, ichthyosiform, erythematous scales over his limbs and torso 6 weeks after HSCT associated with fever. There was no gastrointestinal complaint. He had not been taking any new medications associated with acquired ichthyosis. A skin biopsy specimen (Fig. 1) showed spongiosis with scattered necrotic keratinocytes. Complete blood count showed a hemoglobin level of 10.2 g/dL (normal range 13.5–17.5 g/dL), a white blood cell count of

Address correspondence to Jin Ho Chong, MBBS, KK Women's and Children's Hospital, 100 Bukit Timah Road, Singapore 229899, Singapore, or e-mail: chong.jin.ho@singhealth.com.sg

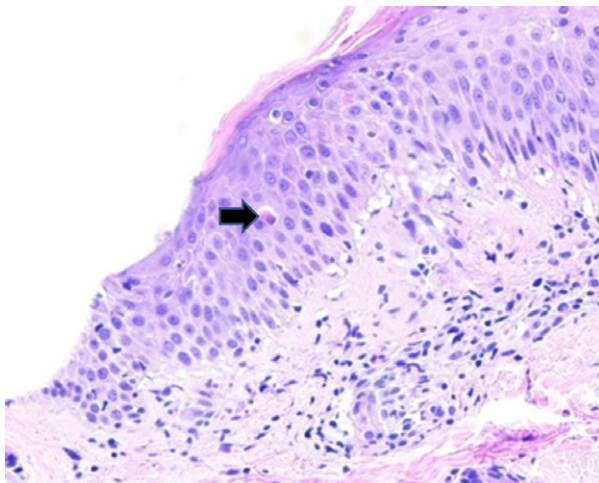


Figure 1. Spongiosis with necrotic keratinocyte (arrow) and perivascular inflammation.

3,150/ μ L (normal range 4,500–11,000/ μ L), neutrophils 60%, lymphocytes 17%, monocytes 20%, eosinophils 1%, and a platelet count of 44,000/ μ L (normal range 150,000–450,000/ μ L). Liver function tests showed total protein of 64 g/L (normal range 65–81 g/L), albumin of 35 g/L (normal range 37–47 g/L), aspartate transaminase of 35 U/L (normal range 14–35 U/L), alanine transaminase of 31 U/L (normal range 9–24 U/L), alkaline phosphatase of 127 U/L (normal range 127–517 U/L), total bilirubin of 30 μ mol/L (normal range 3–20 μ mol/L), direct bilirubin of 12 μ mol/L (normal range 2–7 μ mol/L), and gamma-glutamyl transferase of 35 U/L (normal range 7–21 U/L). Blood and urine cultures did not yield growth of any microorganisms.

In view of the clinical presentation and histologic features, a diagnosis of eczematoid GVHD was made. The patient was started on prednisolone for 3 weeks and topical mometasone 1% cream. His skin condition improved, but 18 weeks after transplantation, there was worsening of the ichthyosis, erythema, and scaling associated with keratotic follicular papules (Fig. 2) over his limbs, trunk, and back (Fig. 3). He also developed bilateral thick palmoplantar keratoderma (Fig. 4) and a seborrheic dermatitis-like eruption on his face and scalp. White lacy plaques were seen on the buccal mucosa (Fig. 5). Repeat skin biopsy showed histologic findings similar to those of the previous biopsy.

The rash responded significantly after an increase in cyclosporin dose of 20%. He also resumed treatment with topical mometasone 0.1% cream and emollients. He remained well, with no other complications while on cyclosporine.



Figure 2. Ichthyosiform scaly plaques and keratotic follicular papules on the legs.



Figure 3. Erythematous scaly plaques on the back.

DISCUSSION

The differential diagnoses for a post-HSCT eczematous eruption include an eczematous drug eruption, worsening of existing dermatitis, and donor-related atopy acquisition (2), but these were unlikely given the clinical and histologic picture.

Traditionally, acute GVHD and chronic GVHD are defined as occurring within and after 100 days after transplantation, respectively (2), but these definitions may have become less distinct because of better GVHD prophylaxis, with features of either form appearing at different periods after transplant. Clinically, acute GVHD is characterized by an erythematous morbilliform eruption (3), whereas chronic GVHD usually presents with a sclerodermoid or lichenoid appearance (1). The eczematoid form of



Figure 4. Plantar keratoderma.



Figure 5. Wickham's striae on the buccal mucosa.

GVHD presents as a chronic, generalized, dermatitic eruption and can run a protracted course of up to 20 months, in one adult study (2). It can also present as localized hand and foot eczema or with eczematous and lichenoid papules (4). It does not remit spontaneously and can lead to severe erythroderma, sepsis, and death (2).

Our patient presented with an eczematous reaction with seborrheic dermatitis, ichthyosis, keratotic follicular papules, and thick palmoplantar keratoderma occurring after HSCT. These atypical clinical features should raise the index of suspicion for eczematoid GVHD. The presence of Wickham's striae on the buccal mucosa also suggested that there could be an overlap of the various cutaneous presentations of GVHD. His presentation mirrored the clinical course of another 12-year-old boy who developed acquired ichthyosis 1 month after HSCT (5). Although uncommon, eczematoid GVHD or eczematous dermatitis (1) must be considered in children who develop an atypical eczematous eruption after transplantation, especially in the absence of a history of atopy.

Treatment of eczematoid GVHD in adults includes intensive topical therapy (e.g., potent topical corticosteroids and calcineurin inhibitors), phototherapy (e.g., narrow-band ultraviolet [UV] B light, psoralen plus UVA light), and systemic immunosuppressants (e.g., cyclosporine) (2). Our patient responded well after an increase in immunosuppression with topical corticosteroids.

More studies are needed to learn about the incidence and natural history of cGVHD. With better survival after HSCT, it is important for dermatologists to recognize the protean and unusual manifestations of cGVHD (3,6) in children.

REFERENCES

1. Goddard DS, Horn BN, McCalmont TH et al. Clinical update on graft-versus-host disease in children. *Semin Cutan Med Surg* 2010;29:92–105.
2. Creamer D, Martyn-Simmons CL, Osborne G et al. Eczematoid graft-vs-host disease: a novel form of chronic cutaneous graft-vs-host disease and its response to psoralen UV-A therapy. *Arch Dermatol* 2007;143:1157–1162.
3. Cornejo CM, Kim EJ, Rosenbach M et al. Atypical manifestations of graft-versus-host disease. *J Am Acad Dermatol* 2015;72:690–695.
4. Kim SJ, Choi JM, Kim JE et al. Clinicopathologic characteristics of cutaneous chronic graft-versus-host diseases: a retrospective study in Korean patients. *Int J Dermatol* 2010;49:1386–1392.
5. Huang J, Pol-Rodriguez M, Silvers D et al. Acquired ichthyosis as a manifestation of acute cutaneous graft-versus-host disease. *Pediatr Dermatol* 2007;24:49–52.
6. Ahn HS, Park HJ, Lee JY et al. A case of chronic cutaneous graft versus host disease with the clinical features of exfoliative dermatitis. *Ann Dermatol* 2009;21:319–322.