Sparing of the scalp in severe *Demodex* folliculitis after stem cell transplantation

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INTRODUCTION

Facial erythema after allogeneic stem cell transplantation (SCT) is most commonly caused by acute graft-versus-host disease (aGVHD), although viral exanthema, drug reactions, and chemotherapy toxicity are also on the differential.[1] Immunosuppressed patients have higher rates of more severe infestations with *Demodex folliculorum*, and there are few reports of demodicidosis presenting as facial erythema after SCT.[2-5] We report 2 cases of *Demodex* folliculitis presenting as erythematous papules on the face resembling aGVHD but with a distinctive cutoff sign at the scalp that may serve as an important diagnostic tool in differentiating demodicidosis from the other etiologies of facial erythema.

Abbreviations used:

aGVHD:	acute graft-versus-host disease
HSCT:	hematopoietic stem cell transplants
SCT:	stem cell transplantation

CASE REPORT

Patient 1, a 58-year-old Hispanic man with primary myelofibrosis, and patient 2, a 45-year-old white man with acute myeloid leukemia, received haploidentical hematopoietic stem cell transplants (HSCT). Immunosuppressive regimens for both patients consisted of tacrolimus and a short course of mycophenolate mofetil (discontinued on days +27 and +35, respectively). Patient 1 was placed on trimethoprim-sulfamethoxazole, levofloxacin, posaconazole, isoniazid, and valacyclovir for infectious prophylaxis, whereas patient 2 was taking posaconazole, valacyclovir, and pentamidine. There were no recent changes in their medications. New itchy red rashes developed on their faces on days +28 and +38 after transplant, respectively. Of note, patient 1 reported worsening of his rash with application of Vaseline and barrier creams. Both patients had hair loss as a result of chemotherapy, and neither used any antidandruff or medicated shampoos or hair products. The dermatology department was consulted given concern for aGVHD.

On physical examination, both patients had diffuse monomorphic erythematous papules with follicular prominence on their entire faces and necks. The rash on patient 1 was more severe with generalized facial edema and erythema as well as involvement of the shoulders and upper back with erythematous papules and pustules. A sharp demarcation was present at the frontal and temporal hairline with widespread sparing of the scalp in both patients (Fig 1). There were no lesions on the palms and soles or other areas of the skin. The differential diagnosis included aGVHD, drug reaction such as acute generalized exanthematous pustulosis or drug rash with eosinophilia and systemic symptoms, and demodicidosis. A facial skin scraping of both patients found numerous *D folliculorum* mites on potassium hydroxide (KOH) staining (Fig 2). In patient 1, a skin biopsy of a micropustule on the right postauricular area found inflammation surrounding follicular units containing *Demodex* mites with no evidence of aGVHD (Fig 3), and in patient 2, skin biopsy of the neck found folliculitis. Both patients' eruptions resolved within 1 week of treatment with oral ivermectin once and topical permethrin 5% ointment nightly.

DISCUSSION

D folliculorum mites primarily reside within pilosebaceous units of the face and are considered

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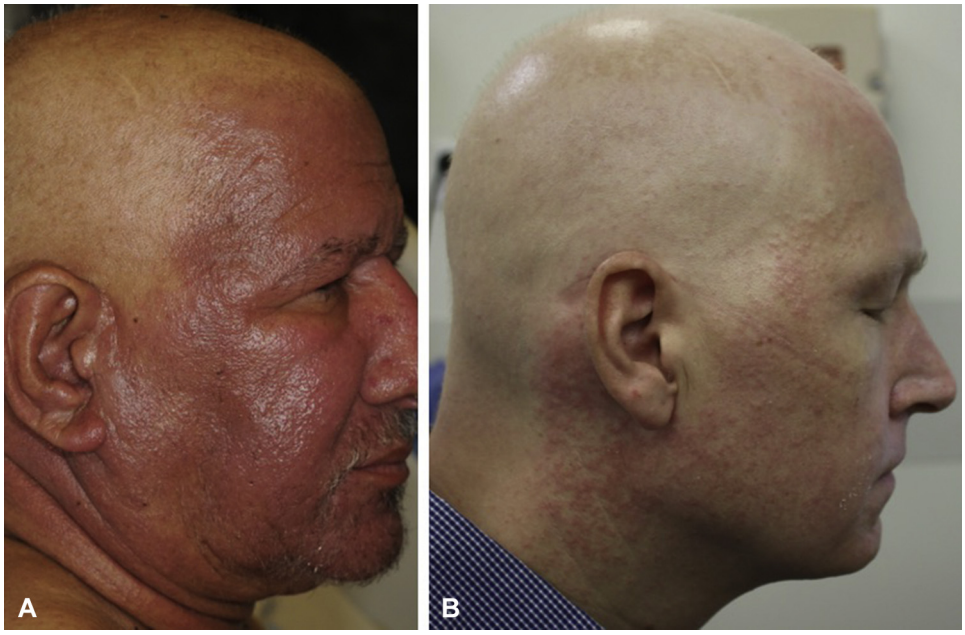

Fig 1. Cutoff sign in *Demodex* folliculitis. A sharp demarcation between erythematous skin and spared scalp was present at the frontal and temporal hairline for both patients.

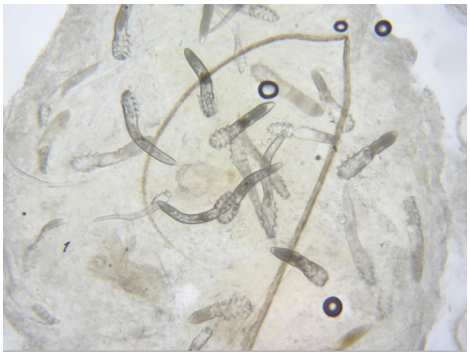

Fig 2. Skin scraping of the face of patient 1 with KOH staining showed numerous *D folliculorum* mites.

part of normal skin flora, with prevalence of infestation increasing with age.[6] *Demodex* mites are associated with development of facial folliculocentric papules and pustules that can mimic various other inflammatory skin conditions, including rosacea, acne, and bacterial folliculitis. Rosacea patients in particular have higher rates of *Demodex* infestation, with both mite density and serum immunoreactivity positively correlated with severity of disease.[7]

In immunocompetent patients, *Demodex*-associated eruptions are often limited to the face with mild erythema. However, in immunocompromised patients, *Demodex* mites are found in greater density and are more pathogenic, specifically in patients with HIV/AIDS and hematologic malignancies.[6] Immunosuppressive therapy has also been associated with increased risk of demodicidosis, with reported cases following epidermal growth factor receptor inhibitors, topical steroids, and topical calcineurin inhibitors.[6] The increased risk in immunocompromised patients may be owing to a combination of impaired immune defenses leading to more infestation and aberrant immunologic responses to existing mites.[6]

To date, there are only 5 reported cases of *Demodex* folliculitis after HSCT, all of which were initially believed to be aGVHD.[2-5] The clinicopathologic features of the cases are summarized in Table I. Our patient 1 had the most severe involvement, with erythema, papules, and pustules extending down to his neck, shoulders, and upper chest and back, whereas patient 2 had involvement of the face and neck, similar to 2 other reported cases.[2,5] The striking severity of our first patient's demodicidosis is possibly a result of his unusually extensive antimicrobial prophylaxis regimen that may have altered normal skin flora and occlusion from Vaseline and barrier creams. The development of these lesions in our patients at days +28 and +38 after transplant is consistent with the timeframe seen in 2 other cases, although this did not appear to coincide with immune reconstitution in any of these patients.[2,5] In most cases, skin biopsy was performed to rule out aGVHD, although Aisa et al[3] relied on microscopic examination showing high density of *Demodex* mites and resolution of skin lesions after topical sulfur to

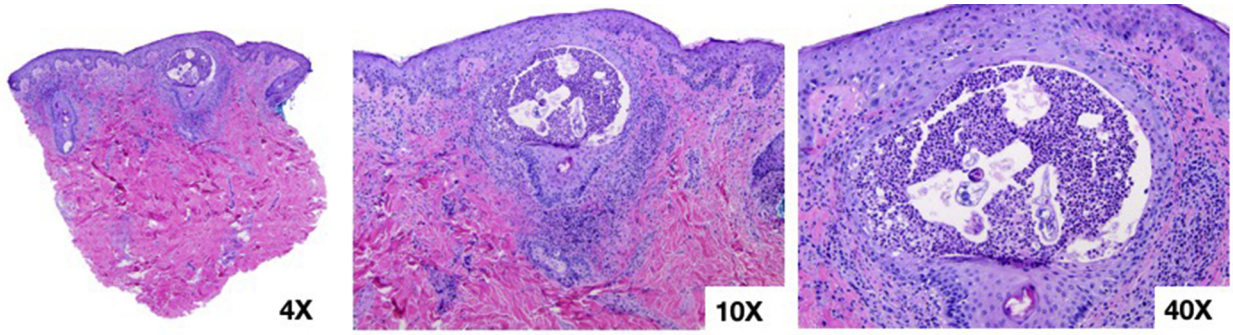

Fig 3. Skin biopsy of a micropustule on the right postauricular area of patient 1 showed inflammation surrounding follicular units containing *Demodex* mites with no evidence of aGVHD.

Table I. Summary of patient characteristics and clinical presentation

	Age/Sex	Affected areas	Days posttransplant	Transplant indication	Immunosuppressive regimen	Scraping or biopsy performed	Treatment
Lotze et al[2]	42/F	Face (cheeks, jaw, chin), neck	+24	Chronic idiopathic myelofibrosis	Cyclosporine, short course of methotrexate	Biopsy	Lindane
Aisa et al[3]	53/F	Entire face	+110	Acute lymphoblastic leukemia	Tacrolimus, short course of methotrexate	Scraping	Topical sulfur
Aisa et al[3]	44/F	Entire face	+110	Chronic myeloid leukemia	Tacrolimus, short course of methotrexate	Scraping	Topical sulfur
Roman-Curto[4]	33/F	Face (forehead, cheeks)	+197	Acute lymphoblastic leukemia	Unknown	Biopsy	Topical permethrin, metronidazole
Cotliar and Frankfurt[5]	46/F	Face (cheeks, jaw), neck	+23	Acute myeloid leukemia	Mycophenolate, cyclosporine	Biopsy	Ivermectin PO x1
Current case 1	58/M	Entire face, neck, shoulders	+28	Primary myelofibrosis	Tacrolimus, short course of mycophenolate	Scraping and biopsy	Ivermectin PO x1, Topical permethrin
Current case 2	45/M	Entire face, neck	+38	Acute myeloid leukemia	Tacrolimus, short course of mycophenolate	Scraping	Ivermectin PO x1, Topical permethrin

make their diagnosis. We performed both skin scraping and biopsy to ensure that an accurate diagnosis was obtained immediately and to evaluate for a potential concomitant aGVHD. Treatment was highly variable, with most cases improving with topical treatment. Our patients exhibited rapid clearance of their lesions after only 1 dose of oral ivermectin, a treatment modality that was previously used in refractory cases, including one post-HSCT case,[5] and may be effective in the more severe demodicidosis seen in immunosuppressed patients.[8]

One particularly unique aspect of our cases is the sharp demarcation or cutoff at the junction between the face and the scalp. Facial distributions of reported post-HSCT demodicidosis cases are summarized in Table I; none specifies whether scalp involvement was present. *Demodex* mites most commonly infest the nasolabial fold, nose, temple, cheeks, forehead, and eyelids, with the neck, chest, and back as the most common nonfacial sites,[9] consistent with the distribution of our patient's lesions. *Demodex* mites have infrequently been found on the scalp with a reported incidence of approximately 5% on scalp biopsies and are rarely pathogenic, although there are few reports of *Demodex*-associated scalp folliculitis.[10] We hypothesize that the mites' physiologic tendency to spare the scalp may be owing to differences in the pilosebaceous units of the scalp compared with those on the face, including the beard and mustache areas. We therefore propose that the cutoff sign may be a helpful clinical clue in cases of suspected demodicidosis and should prompt skin scraping for *Demodex* infestation. Nevertheless, absence of a cutoff sign should not exclude the diagnosis of *Demodex*-associated folliculitis, especially given the difficulty in assessing a sharp cutoff in cases of mild disease.

It is important to consider a *Demodex*-associated eruption in posttransplant patients who present with facial erythema and papulopustular lesions,

especially in the presence of a positive cutoff sign. We recommend prompt skin scraping and skin biopsy given the important clinical implications of a concomitant GVHD diagnosis.

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