

Periorbital Lupuslike Presentation of Graft-versus-host Disease

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PRACTICE POINTS

- Lupuslike graft-versus-host disease (GVHD) is a rare manifestation of chronic GVHD that predominantly affects the lower eyelids and malar regions.
- Antinuclear antibody (ANA) testing is unhelpful in diagnosis as numerous chronic GVHD patients can develop ANA antibodies.
- A lupuslike manifestation of GVHD may portend a poor prognosis with possible development of sclerodermatous GVHD.

To the Editor:

A 79-year-old man presented with a scaling eruption in the periorbital area, on the bilateral forearms, and on the chest of 4 weeks' duration. The patient denied systemic symptoms including lethargy, muscle weakness, and fevers. His medical history was notable for blastic plasmacytoid dendritic cell neoplasm, a form of acute myeloid leukemia, diagnosed 3 years prior to presentation. The patient received an allogeneic hematopoietic stem cell transplant 8 months later. His posttransplant course was complicated by gastrointestinal graft-versus-host disease (GVHD); progressive graft loss requiring a donor lymphocyte infusion after 1 month; and leukemia cutis, which spontaneously resolved after 1 month. The patient was taken off all immunosuppressive therapy 5 months after the transplant and had been doing well for 2 years with only mild mucosal GVHD affecting the oral mucosa and the head of the penis.

Physical examination at the current presentation revealed linear, atrophic, scaling, purplish plaques with adherent white scale on the upper and lower eyelids (Figure 1). The patient also had scattered purple scaling patches on the bilateral forearms and chest. Laboratory tests including complete blood cell count, comprehensive metabolic panel, and lactate dehydrogenase demonstrated no gross abnormalities. Two shave biopsies of the right

lower eyelid (Figure 2) and left arm (Figure 3) were performed for histologic examination and revealed basket weave hyperkeratosis, irregular acanthosis, sawtooth rete ridges, and scattered dyskeratotic cells. Vacuolar changes and smudging of the basement membrane zone along with a bandlike lymphocytic infiltrate in the upper dermis also were noted in both biopsies. A diagnosis of lupuslike grade 1 GVHD was made.

Graft-versus-host disease remains a notable cause of morbidity and mortality in allogeneic hematopoietic stem cell transplant patients.¹ Skin manifestations represent the most common manifestation of GVHD and have been reclassified as acute or chronic disease based on clinical and histologic findings rather than time of onset. Although acute GVHD classically presents as diffuse morbilliform papules and macules, chronic GVHD has a large range of clinical presentations most commonly mimicking the skin findings of lichen planus, morphea, scleroderma, or lichen sclerosus.¹



FIGURE 1. Graft-versus-host disease characterized by linear, atrophic, scaling, purplish plaques with adherent white scale on the upper and lower eyelids.

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The authors report no conflict of interest.

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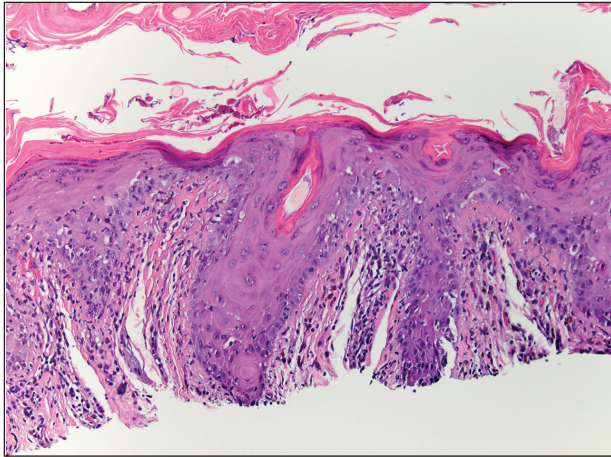


FIGURE 2. Biopsy from the right lower eyelid demonstrated hyperkeratosis, irregular acanthosis, sawtooth rete ridges, and scattered dyskeratotic cells. There were vacuolar changes and smudging of the basement membrane zone (H&E, original magnification $\times 100$).

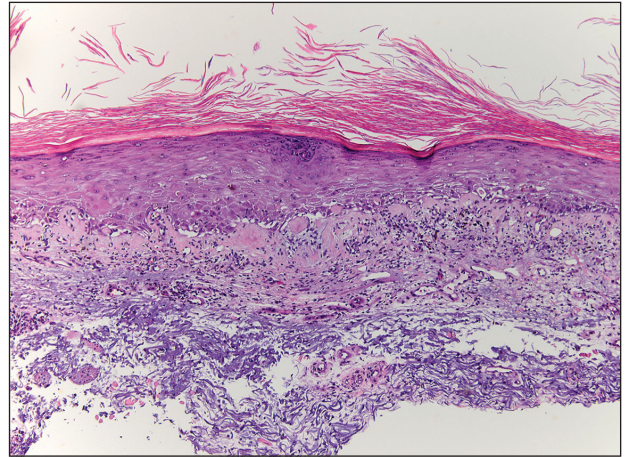


FIGURE 3. Biopsy from the left arm showed irregular acanthosis, sawtooth rete ridges, basket weave hyperkeratosis, a bandlike lymphocytic infiltrate, vacuolar changes, and smudging of the basement membrane zone (H&E, original magnification $\times 100$).

Lupuslike GVHD is a rarely reported manifestation of chronic GVHD that predominantly affects the lower eyelids and malar regions.^{2,3} Our case documents extensive involvement of both the upper and lower eyelids. A lupuslike manifestation of GVHD may portend a poor prognosis. In a case series of 5 patients with chronic GVHD presenting as facial lupuslike plaques, 1 patient died from a relapse of leukemia and 3 patients developed sclerodermatous GVHD. The fifth patient was lost to follow-up.² In another case series, a retrospective analysis discovered that 3 of 7 patients with sclerodermatous GVHD initially presented with hyperpigmented periorbital plaques.⁴ Resolution of skin findings with topical steroids and oral tacrolimus was reported in a case of GVHD presenting with periorbital lupuslike plaques.³ Although further reports are needed to validate the relationship, a lupuslike presentation of chronic GVHD may be an important harbinger for the development of extensive sclerodermatous GVHD.

A diagnosis of lupuslike GVHD is made based on the correlation of a comprehensive medical history, clinical examination, and histopathologic findings. Although other cases of chronic GVHD resembling dermatomyositis presented with purple periorbital plaques, these patients demonstrated dermatomyositislike systemic symptoms including muscle weakness and fatigue, which were not present in our patient.^{5,6} Antinuclear antibody (ANA) testing is unlikely to be helpful in the diagnosis of this uncommon presentation, as 65% (41/63) of chronic GVHD patients developed ANA antibodies in one study.⁷ Also, other patients with lupuslike GVHD who progressed to sclerodermatous GVHD have had both positive and negative ANA serology.² The histopathology of GVHD and lupus erythematosus can exhibit overlapping features, such as lymphocytic infiltrate with interface changes; however, in lupus erythematosus, mucin usually is present, the infiltrate usually is denser and deeper, and a thickened basement membrane zone may be present.

Necrotic keratinocytes also usually are not seen in lupus erythematosus unless the patient's photosensitivity has led to a sunburn reaction.

After his initial presentation, our patient's mucosal GVHD flared in the mouth and on the penis, and he was started on prednisone 50 mg once daily and mycophenolate mofetil 1 g twice daily. With this treatment, our patient's periorbital scaling plaques resolved to residual hyperpigmentation along with remarkable improvement of the mucosal GVHD. He has not manifested any signs of leukemia relapse or sclerodermatous GVHD; however, he remains under close clinical evaluation.

This case highlights an unusual presentation of GVHD with periorbital plaques mimicking hypertrophic lupus erythematosus. A greater recognition of this rare entity is essential to further elucidate its prognosis and its relationship with sclerodermatous GVHD.

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