Coexistence of Staphylococcal Scalded Skin Syndrome and Acute Graft-vs-Host Disease

We report a case of adult staphylococcal scalded skin syndrome (SSSS) superimposed on acute graft-vs-host disease (GVHD) and discuss the unique histologic features of both conditions seen on skin biopsy.

Report of a Case | A man in his 60s with a history of myelodysplastic syndrome underwent a matched unrelated donor hematopoietic stem cell transplant (HSCT) after conditioning with fludarabine and total-body irradiation. Prophylaxis against GVHD included cyclosporine A, 175 mg, and mycophenolate mofetil, 1000 mg, both given orally twice daily. On day 35 after HSCT, the patient developed nontender erythematous macules and papules on the thighs, which subsequently spread to the trunk and extremities. The patient later developed diarrhea and mildly elevated serum total bilirubin levels (1.5 mg/dL). Skin and colon biopsies confirmed acute GVHD, and the patient was treated with intravenous methylprednisolone, 200 mg/d, with resolution of symptoms.

On day 144 after HSCT, the patient developed diarrhea and mildly tender diffusely scattered erythematous macules and papules on the trunk, neck, face, and extremities, along with acute kidney injury (creatinine, 2.94 mg/dL). Owing to a recent fever, the patient began treatment with intravenous lidocaine, 1000 mg/d, with resolution of symptoms.

OBSERVATION

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proximal, flexural regions of the arms and thighs (large areas of superficial desquamation, most notable on the 146, the skin lesions progressed to diffuse erythroderma with 147. Treatment with intravenous methylprednisolone, 100 mg/d, 148, nezolid, 600 mg, twice daily and intravenous cefepime, 2 g/d. 149, (hematoxylin-eosin, original magnification ×400). 150, disease with superimposed subcorneal layer separation and acantholysis 151, Epidermal keratinocytes undergoing apoptosis secondary to graft-vs-host 152, (Figure 2). A diagnosis of GVHD with coexisting SSSS was made based on the clinical findings and histopathologic changes. Blood cultures remained negative, and the diarrhea and desquamative changes improved under treatment with systemic steroids and intravenous vancomycin. The patient’s condition deteriorated secondary to a pulmonary embolism and pneumonia, and intubation was required. After discussions with the patient’s family, medical treatment was discontinued. Respiratory support was removed, and the patient died on day 154.

Discussion | Acute GVHD involving the skin can range from patchy erythema to erythroderma with diffuse desquamation. Clinical differentiation of severe acute GVHD from other desquamative eruptions, including SSSS, is difficult because they have similar physical findings. Although SSSS is more common in children, renal impairment and Staphylococcus aureus burden caused by immunosuppression are major predisposing factors for SSSS in adults.1 In these patients, early diagnosis and management of SSSS is critical because treatment with corticosteroids for presumed GVHD may worsen SSSS, and mortality can be as high as 54%.2,3 Clinically, both SSSS and acute GVHD manifest as desquamative dermatoses, though the desquamation seen in SSSS is an immediate phenomenon, and desquamation in acute GVHD typically follows the erythematous or morbilliform component that heralds the disease.

Accurate differentiation of acute GVHD from SSSS requires histologic examination. Whereas GVHD demonstrates vacuolar degeneration of the basal layer and satellite cell necrosis, SSSS is characterized by acantholysis and intraepidermal splitting. Rapid diagnosis of SSSS may also be achieved with frozen-sectioning of a skin biopsy specimen demonstrating granular layer cleavage.4 Given our patient’s medication regimen, drug hypersensitivity reactions were also considered. However, the facial and palmar involvement, history of diarrhea, and skin biopsy findings strongly suggested acute GVHD and coexisting SSSS.5

Although 1 other case of SSSS in a patient with a history of cutaneous GVHD exists,6 to our knowledge, ours is the first reported case of acute GVHD and coexistent SSSS. Despite the clinical similarities, the 2 conditions have unique histologic features, and skin biopsy should be performed in HSCT patients to delineate the diagnosis when appropriate.

Cristina Thomas, BA
Pedram Yazdan, MD
Jonathan A. Cotliar, MD

Author Affiliations: Department of Dermatology, Northwestern University Feinberg School of Medicine, Chicago, Illinois.

Corresponding Author: Jonathan A. Cotliar, MD, Robert H. Lurie Comprehensive Cancer Center, Department of Dermatology, Northwestern University Feinberg School of Medicine, 676 N St Clair St, Ste 1600, Chicago, IL 60611 (j-cotliar@northwestern.edu).

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Cyclosporine in the Management of Poststreptococcal Pustulosis

Poststreptococcal pustulosis (PSP) is a rare neutrophilic disease occurring after a streptococcal pharyngitis. In our report, we describe a mother and daughter who developed PSP and were successfully treated with low-dose cyclosporine.

Report of a Case | A woman in her 50s and her daughter, in her 30s, presented simultaneously with painful pustules on the palms (Figure, A) and a few on the soles. The eruption began 5 days after culture-proven group A streptococcal pharyngitis in the daughter and tonsillitis in the mother. Both were systemically well with no fever, arthropathy, or mucosal lesions. Both patients had already received a week of oral cephalexin therapy because pustules continued to develop. There was no medical or family history of psoriasis. The mother had type 2 diabetes mellitus.

Laboratory investigations revealed leukocytosis in the mother (leukocytes, $13.5 \times 10^9/L$; neutrophils, $9.1 \times 10^9/L$; eosinophils, $0.3 \times 10^9/L$) and daughter (leukocytes, $12.2 \times 10^9/L$; neutrophils, $7.2 \times 10^9/L$; eosinophils, $0.3 \times 10^9/L$) and daughter (leukocytes, $12.2 \times 10^9/L$; neutrophils, $7.2 \times 10^9/L$; eosinophils, $0.3 \times 10^9/L$) (normal leukocyte upper limit, $10.5 \times 10^9/L$). (To convert leukocytes, neutrophils, and eosinophils to cells per microliter, divide by 0.001.) Cultures of the pustules were sterile. There were no signs of renal involvement: urinalysis findings and serum creatinine levels were normal. Human leukocyte antigen typing and biopsy were not performed.

We elected to treat both patients with cyclosporine as an alternative to prednisone. This decision was based on the rapid action of cyclosporine, its direct suppressive effect on cytokines that influence neutrophils, and no hyperglycemic adverse effects when compared with corticosteroids. The patients were prescribed oral cyclosporine, 50 mg, twice daily for 3 days (approximately 1 mg/kg/d), then 25 mg by mouth twice daily for 3 days. Both patients reported marked reduction in pain within 48 hours and dramatic improvement of the lesions within 1 week (Figure, B). Because the lesions responded rapidly, we discontinued cyclosporine treatment after the initial course. There were no reported adverse effects of cyclosporine and no recurrences after 1 year of follow-up.

Discussion | Poststreptococcal pustulosis, aka *pustulosis acuta generalisata*, is a rare postinfectious disorder associated with streptococcal pharyngitis. To our knowledge, only 25 cases have been described worldwide. It typically presents with a symmetric eruption of sterile pustules predominantly on the hands and feet, though they can occur elsewhere. Laboratory abnormalities include leukocytosis and/or elevated acute-phase reactants. Both arthropathy and glomerulonephritis have been reported. Histopathologic examination reveals subcorneal collections of neutrophils.

Poststreptococcal pustulosis can resemble palmoplantar pustulosis, pustular psoriasis, acute generalized exanthematous pustulosis, pustular vasculitis, and subcorneal pustular dermatosis. These and other neutrophilic disorders have historically been treated with prednisone or dapsone. Our cases suggest a role for a short course of low-dose cyclosporine as an alternative to systemic corticosteroids for PSP and possibly related neutrophilic disorders. In a recent systematic review of chronic palmoplantar pustulosis, cyclosporine was effective in 48% of patients receiving 1 mg/kg/d compared with 19% receiving placebo ($n = 58; P < .001$) and 89% of patients receiving 2.5 mg/kg/d compared with 21% patients receiving placebo ($n = 40; P < .001$). While these results are promising, we cannot exclude spontaneous resolution.

Two published reports have found an association of HLA-B35 and HLA-A2; HLA-B35 has also been linked with pustular psoriasis. In addition, deficiency of the anti-inflammatory cytokine interleukin (IL)-36 receptor antagonist (gene, IL-36RN) may also be associated with PSP.

![Figure. Poststreptococcal Pustulosis Before and After Cyclosporine Treatment](http://archderm.jamanetwork.com/pdфacess.aspx?url=/data/journals/derm/933272/ on 05/01/2017)