Treatment of Pyoderma Gangrenosum with Placental Membrane in a Patient with Graft vs. Host Disease

Kanika Kochhar, DPM[1]; Alton R. Johnson Jr., DPM, CWSP[2]

Michigan Medicine. University of Michigan

[1]Podiatry Fellow at University of Michigan Medicine. [2]Attending Physician at University of Michigan Medicine.

Introduction

Pyoderma gangrenosum (PG) is an inflammatory, destructive neutrophilic dermatosis which is often extremely painful for patients. It predominantly affects adults and is most frequently seen in the lower legs. The pathophysiology is unclear; however, it is known that there is a nonspecific finding of neutrophilic infiltration. There are no pathognomonic markers. PG can be chronic and last for months or even years. Fifty percent of pyoderma cases have been associated with other systemic autoimmune disease such as ulcerative colitis, Crohn's disease, rheumatoid arthritis and inflammatory bowel disease. Lesions secondary to PG may be precipitated by minor trauma; this phenomenon is known as pathergy.

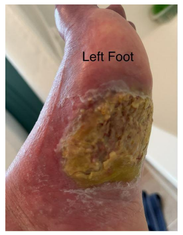
Mainstay treatment for PG includes immunosuppression. Examples include a variety of topical and systemic agents utilized in conjunction with local wound care. The hallmark systemic treatment for PG includes potent topical corticosteroids, cyclosporin or tacrolimus topical ointment. Intralesional injections of corticosteroid into an erythematous, active border may also be considered. Negative pressure wound therapy has been shown to improve the rate of healing in PG. In severe cases, systemic therapy with oral corticosteroids (prednisolone) are appropriate.

Graft vs. Host Disease (GVHD) is a major cause of morbidity and mortality following either an allogenic hematopoietic stem cell transplantation or a bone marrow transplant for many leukemias, lymphomas, and immunodeficiency disorders. GVHD occurs in 25% to 70% of these patients. The condition is an exaggerated manifestation of a normal inflammatory mechanism. It entails donor lymphocytes encountering foreign antigens and thus fostering inflammation. GVHD occurs within the first 100 days post transplant. Factors which predispose to the development of acute GVHD include HLA disparity, sex mismatching, multiple donor pregnancies and age. Primary target organs are skin, liver, and GI tract. Clinically, GVHD may present as pruritic, maculopapular, morbilliform rash, or lichenoid in nature. There are various degrees of erythema, patchy hypo and hyper pigmentation, and poikiloderma. Treatment for GVHD includes combinations of methotrexate, cyclosporine and corticosteroids.

Case

The patient is a 69-year-old female with past medical history of type 2 diabetes, peripheral neuropathy, and chronic GVHD. Of note, the patient had mantle cell lymphoma and received an allogenic bone marrow transplant from her brother in 2009. She has now been in remission for over thirteen years. She presented to the comprehensive wound care clinic with previously diagnosed pyoderma gangrenosum to the plantar left foot. She had been seeing a dermatologist for management and wanted a second opinion. The lesion started in August 2022 and had gradually gotten larger. She has had multiple punch biopsies.

She was admitted to the hospital in September 2022 for concern for infection to the foot. Here she received a six-week course of IV meropenem (1g IV q8 hours) and daptomycin 500mg IV daily. Additionally, she was treated with posaconazol to prevent fungal infections as well as acyclovir to cover for potential viral etiologies. She also received IVIG and prednisone. Lastly, a left foot MRI was ordered which showed superficial focal soft tissue process involving the plantar midfoot.



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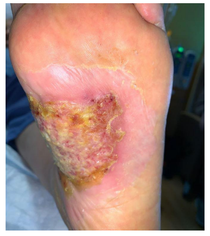

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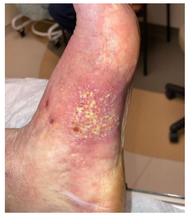
While inpatient, dermatology performed a biopsy for tissue culture and hematoxylin and eosin (H&E) staining. Aerobic organisms, tissue cultures, acid-fast bacilli (AFB) and fungal culture all showed no growth. The biopsy results read an “ulcer with dense suppurative and granulomatous inflammation.” At this time, these findings were found to be consistent with a neutrophilic dermatosis such as pyoderma gangrenosum. However, as there was also evidence of necrosis to the wound, the patient was also treated for infection and was discharged on oral Bactrim.

The patient followed up in the comprehensive wound care center on 11/17/23. On this day she received her first application of placental membrane. She was instructed to remain non-weightbearing. She went on to receive an additional five applications of placental membrane every 2-3 weeks for the next two months.

With each graft application, there was noted to be a significant decrease in non-viable tissue. The wound was noted to be fully healed on 1/26/23, approximately ten weeks after her first graft.



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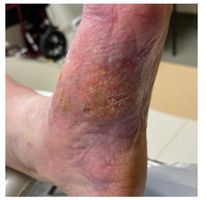

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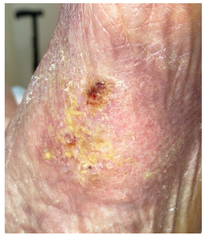

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Discussion

No clinical practice guidelines are available currently for the treatment of PG. The primary goal in management of this condition includes controlling systemic inflammatory processes and local wound care. Debridement should be avoided in the active phase as it may result in enlargement to the ulcer (pathergy). The main purpose of biopsy is to exclude other causes of ulceration. Specimens should be sent for bacterial, mycobacterial and fungal cultures. The biopsy should include the active border of the ulcer and penetrate to the level of the subcutaneous tissues

Additionally, this case demonstrates that human placental membrane is an effective treatment modality for wounds secondary to PG, including in immunocompromised patients. It is important for providers to be aware of this condition and to consider pyoderma gangrenosum when assessing patients with ulcers. Appropriate and prompt treatment at an early stage of the disease may avoid the complications of prolonged systemic treatment, delayed wound healing and scarring.

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