Pyoderma Gangrenosum With Pathergy in a Pregnant Patient Without Associated Systemic Disease

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Pyoderma gangrenosum (PG) is a rare chronic ulcerative skin condition often associated with systemic disease. PG associated with pregnancy is an extremely rare presentation; only 9 other cases have been reported in the literature. We present PG in a pregnant patient (third trimester) with pathergy. No associated systemic disease was identified. Histology was consistent with PG and the lesions responded to intralesional triamcinolone therapy.

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Case Report

A 36-year-old woman presented at 37 weeks' gestation with a chief complaint of severe lumbar pain attributed to benign pregnancy-related lumbar pain from mechanical stress. Multiple prior pregnancies were uncomplicated. Because of her lumbar pain, the treating obstetrician decided to induce labor, which was then delayed because multiple skin lesions were observed over the left lateral malleolus, left anterior ankle, and right lower back. The patient's prior medical history was notable for recurrent deep vein thromboses, gastric bypass surgery, and hidradenitis suppurativa (HS). The patient reported that the lesion on her left ankle appeared 3 weeks prior to this admission. Individual lesions began as red bumps that drained yellow fluid and became crusted. In the ensuing 24 to 48 hours, similar lesions appeared on her right arm, right ankle, and left lower back. The patient was admitted to the obstetrics service approximately 2 days following this series of events. The lesions were occasionally symptomatic with some pain and itching, particularly around the left ankle, which she admittedly would manipulate with a pen. The patient denied additional symptoms. Physical examination (Figure 1) revealed a 2×3-cm erythematous plaque on her left lateral malleolus studded with several pustules and papules, some with central umbilication and crust. Similar lesions were noted on her right lower back, right wrist, and right ankle. The affected areas were mildly tender to palpation. Bacterial and viral cultures as well as a bedside Tzanck smear were unremarkable. The initial differential diagnosis included resolving lesions of herpes simplex and impetiginized folliculitis. The patient was instructed to apply mupirocin cream to the lesions. Labor was induced and the patient delivered a healthy newborn. She was discharged and returned home on hospital day 5.

Less than 24 hours after discharge, the patient was readmitted for worsening skin lesions. On examination, all of the lesions had dramatically changed, including the lesions on the left ankle, which presented with several ulcerated nodules draining pus with a prominent raised border. The patient reported having scratched many of the lesions prior to them worsening. In addition, the patient had developed an erythematous pustule at the site where intravenous access had been obtained on the right wrist (Figure 2). The results of a biopsy of the left ankle and right wrist lesions showed an ulcer with a neutrophilic infiltrate (Figure 3). Bacterial and fungal stains were unremarkable. There was no evidence of mycobacteria and polariscopic examination was negative. The working diagnosis was pyoderma gangrenosum (PG) with pathergy at the intravenous access site. Tissue samples also were obtained for bacterial and fungal culture, which remained negative

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The authors report no conflict of interest.

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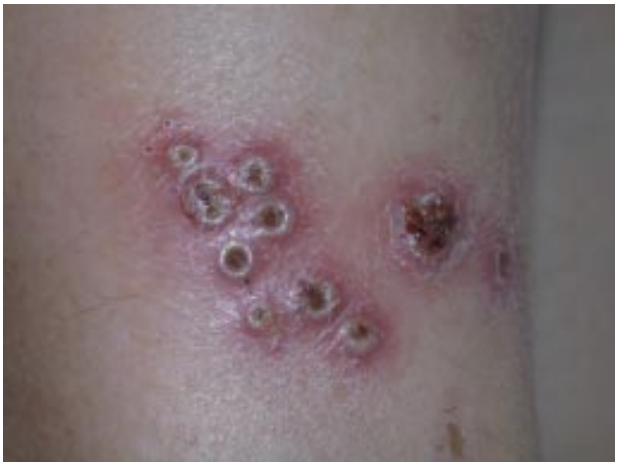

Figure 1. Multiple, tender, umbilicated pustules and papules forming a large plaque measuring 2×3 cm on the left lateral malleolus.

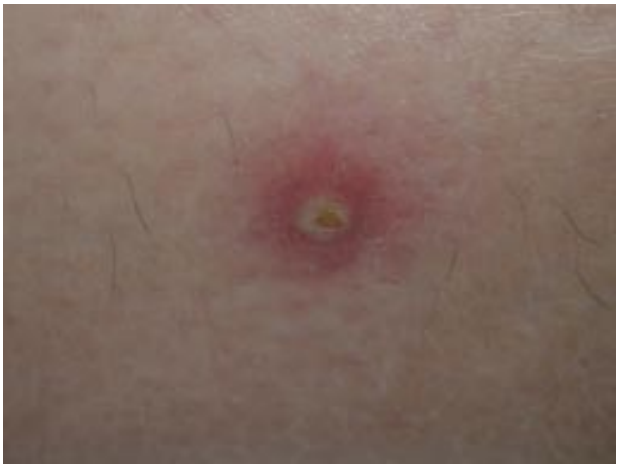

Figure 2. Development of a pustule on the right wrist at the intravenous access site, consistent with pathergy.

at 8 weeks after obtaining the specimen. The patient had recent negative test results for syphilis, hepatitis B, and hepatitis C, with no relevant abnormalities on peripheral blood count. An investigation for associated autoimmune disorders, such as systemic lupus erythematosus, rheumatoid arthritis, and cryoglobulinemia, was unremarkable. A colonoscopy and an upper endoscopy were notable for several benign polyps in the ascending colon; however, there was no evidence of inflammatory bowel disease. Because an infectious etiology was adequately ruled out, the large tender plaque on the left ankle was injected with intralesional triamcinolone (20 mg/mL) to prevent further growth, and the patient was discharged and returned home with wound dressings.

On follow-up in the dermatology clinic 4 days later, the patient noted substantial improvement in both the degree of pain and the size and appearance of the lesions. The patient was seen in regular follow-up every 2 weeks for a month and then on a monthly basis; by the fifth visit, she had complete resolution of the lesions, with residual hyperpigmentation and scarring.

Comment

Fifty percent of patients with PG have an underlying systemic disease.[1] It has been reported most often with inflammatory bowel disease, followed by arthritis and hematologic malignancy.[2] Rarely, chronic active hepatitis, collagen vascular disease, and other diseases have been associated with PG. More than one third of cases are idiopathic. The 4 most common clinical variants of PG are ulcerative, pustular, bullous, and vegetative PG. Additionally, there is a Sweet syndrome overlap entity termed *bullous Sweet syndrome*, usually found in patients with leukemia. Ulcerative, or classic, PG presents as a pustule that ulcerates, forming a large painful lesion with violaceous undermined borders, and is most commonly seen on the lower extremities and trunk. Pustular PG presents as multiple painful pustules on an extremity that can ulcerate and is frequently seen in association with ulcerative colitis. Clinically, bullous PG is a superficial blistering variant that can resemble impetigo and often is associated with concomitant leukemia. Vegetative PG is the most superficial variant, occurring on the trunk, and is infrequently associated with underlying systemic disease. PG has been reported to occur in association with pregnancy in only 9 cases.[3-11] Although PG itself appears to have little influence on the course of pregnancy, the diagnosis should prompt a search for an associated disease that may impact the health of the mother or fetus, and appropriate treatment should be instituted.

Our patient had a colonoscopy, as well as an upper endoscopy, which did not reveal changes consistent with inflammatory bowel disease. Additionally, results of an extensive workup for concomitant diseases known to occur in patients with PG were negative. Pregnancy was the only known concurrent association in our patient.

Our patient had a history of HS managed with the intermittent use of antibiotics, though she did not experience a flare during pregnancy or in follow-up. Upon review of the literature, it is interesting to note the reports of co-occurrence of PG and HS. In a review of 86 patients with PG, 4 patients (5%) had a history of HS, which was thought to be coincidental rather than a true association.[12] A more recent case series of 6 patients with both PG and HS did not show a correlation in disease activity.[13] The high estrogen state in pregnancy has

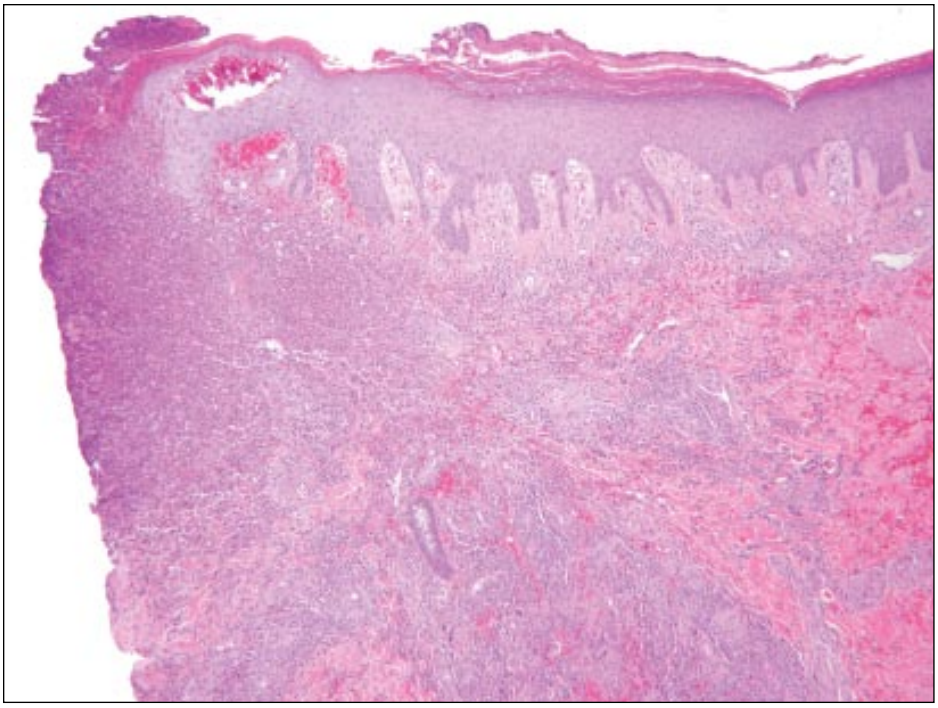

Figure 3. A skin biopsy specimen from the left ankle plaque showed ulceration at the specimen edge, with an underlying diffuse neutrophilic infiltrate (H&E, original magnification ×10). Results of stains for bacteria, fungi, and mycobacteria, as well as polariscopic examination, were unremarkable.

an inconsistent effect on disease activity of HS, though some women report improvement during pregnancy.[14] Histologically, HS is characterized by follicular hyperkeratosis with consequent occlusion and inflammation. Because HS has a predilection for apocrine gland–bearing skin, there can be secondary destruction and inflammation of the apocrine unit with obstruction of the apocrine duct and surrounding structures.[15] Apocrine glands are stimulated by androgen and suppressed by estrogen.[16] In our patient, the high estrogen milieu during her pregnancy may have partially contributed to the suppression of her HS.

Approximately 50% of cases of PG are associated with systemic disease.[1] Pregnancy as the sole trigger of PG rarely has been reported. It is interesting to speculate on the pathogenesis of pregnancy-induced PG. Altered or defective immune system processes are hypothesized to play a role. Pregnancy is associated with immunosuppression, including altered humoral and cell-mediated immunity, inhibition of IL-2 or IL-1 activity, and decreased polymorphonuclear leukocyte chemotaxis and adherence functions.[10] Immune defects, including cell-mediated, humoral, and complement abnormalities; immune complex deposition; and abnormalities in neutrophil chemotaxis, have all been described in cases of PG.[17] However, no single defect has been consistently found in all or a majority of cases. Nonetheless, the frequent association of PG with immune-mediated diseases such as inflammatory bowel disease and rheumatoid arthritis, as well as its response to immunosuppressive agents, suggest an immune etiology for PG,[18] which may explain its association with the immunosuppressed state of pregnancy. Although no definitive link exists between PG and HS, host-defense defects in patients with HS are suspected.[19] Therefore, a defect in the function of neutrophils might be of importance.

Despite its rare association with and minimal impact on the outcome of the pregnancy, PG in pregnancy poses an important therapeutic challenge. A course of oral prednisone, sometimes combined with cyclosporine, is the treatment of choice.[11] This treatment regimen can be especially helpful for patients concurrently diagnosed with PG and HS, as in our patient.[13,20] Because our patient was pregnant, we could not safely use this treatment regimen (ie, systemic prednisone and cyclosporine). Prednisone and cyclosporine should be cautiously used in pregnancy and are not without risk. Local therapies, such as intralesional steroid injections, as used in our patient, help to clear the lesions and often can be sufficient to control extent and progression of lesions without systemic therapy.

Our patient highlights the importance of developing a broad differential diagnosis and considering the possibility of a steroid-responsive condition such as PG when ulcerative lesions present in a pregnant patient.

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