Clinical Case Report

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Pyoderma gangrenosum after cesarean section treated with skin graft

A case report

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Abstract

Rationale: Pyoderma gangrenosum (PG) is a rare skin disease. Pregnancy is a unique physiological condition. Here we report a rare case of PG after cesarean section.

Patient concerns: A 32-year-old female presented with wound breakdown 1 day after cesarean section, with progression to a skin ulcer and no response to antibiotic therapy.

Diagnoses: We experienced a case of PG after cesarean section. This was initially misdiagnosed as a wound infection, with fever and wound redness as clinical manifestations.

Interventions: The patient was initially treated with antibiotics, followed by glucocorticoid and human immunoglobulin therapy. Wound debridement, vacuum sealing negative pressure drainage, skin grafting, and hyperbaric oxygen therapy were also performed.

Outcomes: The wound healed without adverse reactions.

Lessons: When a surgical incision infection does not respond to antibiotic treatment and the culture is negative, PG should be considered.

Abbreviations: CRP = C-reactive protein, IL = interleukin, PCT = procalcitonin, PG = pyoderma gangrenosum, TNF = tumor necrosis factor.

Keywords: caesarean section, pyoderma gangrenosum, skin graft

1. Introduction

Pyoderma gangrenosum (PG) is a type of dermatitis with a very low incidence, and is characterized by dermal neutrophilic infiltration and destruction.[1] The cause is still unclear, but the disease may be associated with neutrophil dysfunction, release of inflammatory mediators, or genetic susceptibility.[2] PG is usually characterized by scattered lesions in the limbs, with pustules and ulceration after lesion enlargement. PG forms a clear, insidious, blue-edged painful ulcer, with satellite-like purple papules, and usually presents without fever. PG lesions can be ulcerative, pustular, bullous, or proliferative.[3] The pathological damage in the skin presents as necrosis and ulceration in the central epidermis and dermis, with dense infiltration of various inflammatory cells around the ulcer; however, the pathological manifestations are not characteristic. PG may be associated with a variety of systemic diseases, including inflammatory bowel disease, rheumatoid arthritis, and hematological malignancies.

Pregnancy is an immunosuppressed state, and pregnant women are susceptible to infection. The incidence of PG in pregnancy is extremely low, and the occurrence of PG after cesarean section is even rarer, with only 17 cases reported worldwide between 1996 and 2019,[4] among which only one was treated with surgery. We report a case of PG after cesarean section. Treatment included glucocorticoid therapy and surgery.

2. Case

A 32-year-old G_8P_1 female with no significant medical history was admitted to a hospital in Changsha for "lower abdominal pain more than 1 day" on September 12, 2017, at >7 months of gestation. Premature rupture of membranes occurred. Ultrasound showed "placental abruption," and emergency cesarean section was performed. On postoperative day 2, the patient developed a fever to 42°C. Local swelling and redness developed, with gradual progression to skin ulceration at the incision site. Wound secretion culture was negative for group B *Streptococcus*. The postoperative placental pathological diagnosis was stage I acute chorioamnionitis. Cefoperazone sulbactam, doxycycline, roxithromycin, imipenem, vancomycin, ornidazole, and other antibiotics were successively given for infection. However, the patient's condition did not improve.

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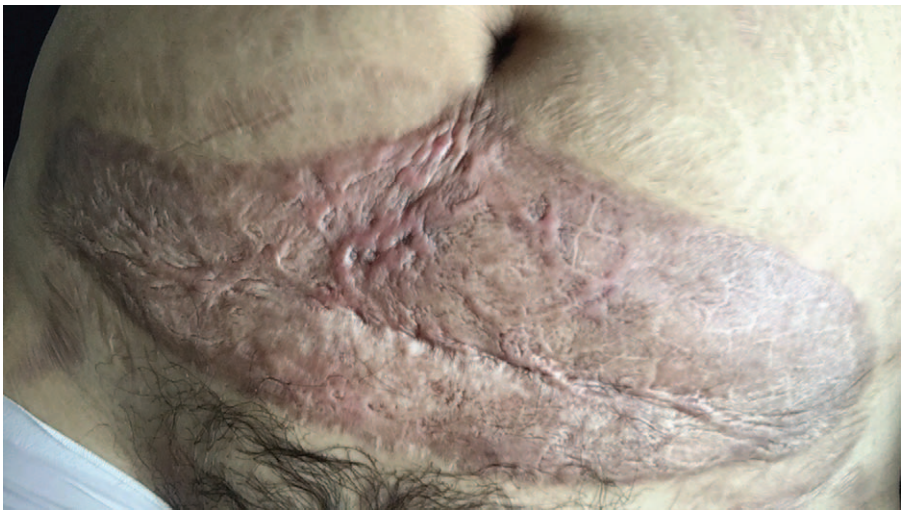

Figure 1. Pyoderma gangrenosum after cesarean section treated with skin graft 14 months later.

An outside consultation was requested. By September 21, the patient had developed an incisional skin defect of about 25 × 15 cm, extending deep to the anterior sheath of the rectus abdominis, with extensive yellow-white necrotic tissue and liquefied adipose tissue visible on the wound surface; there was extensive redness, swelling, and blistering of skin around the wound, with scattered purulent areas. PG was considered and the patient was treated with intravenous methylprednisolone 80 mg and human immunoglobulin 10,000 mg. After 1 day of glucocorticoid treatment, the patient's fever decreased and the wound showed no further deterioration.

Due to a "large abdominal skin lesion," the patient was admitted to the burn unit of our hospital on September 22. Blood tests after admission showed a white blood cell (WBC) count of 23.4×10^9/L (neutrophils, 95.2%); red blood cell (RBC) count of 3.33×10^{12}/L; hemoglobin of 96.0 g/L; platelet count of 286.0×10^9/L; and albumin of 33.1 g/L, but no renal function abnormalities. The patient was treated with linezolid combined with levofloxacin and metronidazole. Continuous methylprednisolone, immunoglobulin, and other immune therapy were administered. Wound debridement was performed and vacuum sealing negative pressure drainage (VSD) was initiated on September 22.

On September 23, blood tests were as follows: WBC, 18.7×10^9/L (neutrophils, 90.8%); RBC, 3.07×10^{12}/L; hemoglobin, 90.0 g/L; platelets, 343.0×10^9/L; procalcitonin (PCT), 0.21 ng/mL; C-reactive protein (CRP), 76.0 mg/L; and albumin, 28.9 g/L. The antibiotic treatment regimen was adjusted, with substitution of minocycline. After 2 days of glucocorticoid therapy, the infection index began to decrease and the wound surface showed no further expansion. Blood tests on September 25 were as follows: WBC, 10.1×10^9/L (neutrophils, 75.8%); RBC, 3.4×10^{12}/L; hemoglobin, 100.0 g/L; platelets, 365.0×10^9/L; PCT, <0.05 ng/mL; CRP, 19.3 mg/L; interleukin (IL)-1β, 41.0 pg/mL; tumor necrosis factor (TNF)-α, 26.2 pg/mL; IL-6, 10.6 pg/mL; and IL-10, 12.0 pg/mL. No bacterial growth was observed on wound tissue culture. Human immunoglobulin was discontinued and cyclosporine A was added on September 26. Incision debridement and VSD were repeated on September 26.

Further debridement and skin grafting were performed on October 9. Histopathological analysis of debrided tissue (abdominal incision) showed suppurative inflammation with necrosis, but no clear evidence of fungal infection. Periodic acid-Schiff (PAS) and PAS-diastase staining was negative. The patient was discharged on October 19, 2017, with the following results: IL-1β, 52.7 pg/m; TNF-α, 2.0 pg/mL; IL-6, 2 pg/mL; and IL-10, <5.00 pg. Routine blood tests, CRP, PCT, and other infection indicators gradually returned to normal, the necrotic wound tissue receded, and the cesarean section wound healed.

After discharge, the patient regularly returned to the dermatology clinic for treatment. She continued prednisone 40 mg daily and cyclosporine 50 mg 3 times a day, and gradually reduced the dosage; treatment was stopped in October 2018, and the wound completely healed (Fig. 1).

3. Discussion

Among reported PG cases during pregnancy,[5–12] including the gestational and postpartum periods, >50% had occurred at the cesarean section incision. Some case reports described PG lesions on the limbs, the abdomen, and the axilla during pregnancy, with resolution in 2 cases after cesarean section. Postoperative follow-up revealed no lesions at the cesarean section incision. This result may be due to glucocorticoid and cyclosporine treatment.

PG involving a cesarean incision typically presents with painful erythema at the incision site. Wound dehiscence can occur or punctate surface ulcers may develop in the erythematous area, eventually coalescing into a deep-seated ulcer running along the wound margin. In contrast with cases unrelated to pregnancy, patients who develop PG after cesarean section often present with fever as the initial symptom. The first symptom in the present case was fever. The intraoperative placental pathological examination suggested chorionic inflammation. The patient had a prolonged course of recurrent fever postoperatively, and the wound ulceration rapidly evolved. Such clinical manifestations can lead to misdiagnosis as a surgery-associated infection.

In some reported cases,[13–15] tests for lupus, immune factors, rheumatoid factor, and anti-double-stranded DNA were all negative, and bacterial growth was not observed in wound culture. Pathological evaluation mostly showed inflammation

and vascular necrosis. The lack of specific diagnostic markers makes early identification of PG in pregnancy difficult. PG remains a diagnosis of exclusion. Neutrophils in patients with skin involvement by PG can also infiltrate the heart, lungs, and digestive tract, leading to multiple organ dysfunctions. Hence, screening for autoimmune disease, aseptic inflammatory disease, and others should be performed.

Pregnancy, as a unique, immunosuppressed pathological state, is characterized by IL-2 inhibition and IL-1 activation, as well as decreased polymorphonuclear leukocyte chemotaxis and adhesion.[16] These changes in maternal immune function may play an important role in the occurrence and development of PG in pregnancy.

In the present case, TNF-α, IL-1, and IL-6 were significantly increased, possibly in association with activation of inflammatory pathways during pregnancy and initiation of labor, or activation of granulocyte colony factors. The reason for neutrophil dysfunction in PG is not clear, but may result from direct or indirect causes, such as enhanced expression of inflammatory factors, including TNF-α, IL-1b, and IL-8.[17] An increase in TNF-α, IL-6, and IL-1 is known to be associated with tumors, autoimmune diseases, severe inflammatory reactions, and graft rejection. TNF-α inhibitors are reportedly effective in treating PG induced by chronic inflammatory bowel disease.[3,18,19] This suggests that TNF-α, IL-1, and IL-6 may be specific markers for PG. When TNF-α, IL-1, and IL-6 continue to increase, and the extent of the increase is not consistent with that of infection-related indicators, a diagnostic trial of glucocorticoid and other immunosuppressive therapies should be considered. This may have important implications for early identification and intervention in PG.

In patients with PG, the wound is painful and fissured, similar to the typical presentation of necrotizing fasciitis. Based on the clinical manifestations, acute wound infection is usually the first diagnosis, but antibiotics used empirically will be ineffective. Therefore, when antibiotics fail to treat the wound, and the wound culture is negative, PG should be considered, with timely adjustment of the treatment plan.

There is currently no standard protocol for the treatment of PG. Treatment methods divided into medications and surgery. Medication is given systemically or topically. As PG can present with systemic involvement, concurrent treatment of the primary disease is necessary. The first-line drug for PG is glucocorticoid, while cyclosporine A, mycophenolate,[20] and TNF inhibitors are second-line drugs. Intravenous immunoglobulin has also been successfully used in the treatment of PG. Cases treated with alefacept, visilizumab, anakinra, and even tacrolimus have been reported.[4] Drug treatment requires assessment of liver and renal function, and cyclosporine A is not recommended in severe renal insufficiency. Surgical treatment is controversial in PG. Local debridement may cause secondary injury, which prevents wound healing and can accelerate the deterioration and expansion of the wound by recruiting neutrophils. One case report[11] discussed flap transplantation for PG that developed in pregnancy, with a satisfactory outcome.

In this case, the patient was hospitalized for 35 days; this duration was less than that reported for similar cases in China and other countries. When the diagnosis of PG is considered, systemic glucocorticoid treatment should be given. After the lesion is effectively controlled, surgical treatment can be scheduled, and greatly enhances the speed of wound healing. Hyperbaric oxygen therapy can then be given to further promote wound healing. Combined drug and surgical treatment can effectively reduce the patient's economic and social burden.

4. Conclusion

Due to the low incidence of PG after cesarean section and the lack of specific diagnostic indicators, the diagnosis is extremely difficult. The misdiagnosis rate is high, and there is still lack of guidance for treatment, requiring multidisciplinary collaboration. Early identification, timely intervention, and long-term management are the keys to therapy in PG after cesarean section.

Author contributions

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