Clinical Medicine: Dermatology

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CASE REPORT

Pyoderma Gangraenosum after Cesarean Delivery

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Abstract

Objective: Presentation of pyoderma gangraenosum (PG) as an important differential diagnosis for wound healing disorders after cesarian section. Adequate therapeutic regimens are discussed.

Case report: A 39-year-old woman developed a PG after cesarean section. A treatment with prednisolone and cyclosporine A was started. Within three days of treatment, the inflammatory process was significantly reduced. Serological inflammatory markers and fever dropped to normal levels. Due to the development of a pronounced arterial hypertension, dapsone was additionally applied to reduce glucocorticoids and cyclosporine A doses.
Rapid normalisation of blood pressure without aggravation. Modern wound dressings helped to rapidly establish granulation and reepithelialization. The immense ulceration completely healed after six months of therapy.

Conclusion: PG is a potentially lethal disease and must be considered as an important differential diagnosis after abdominal surgery and cesarean section. Modern systemic and topical treatments help to treat PG successfully.

Keywords: pyoderma gangraenosum, cesarean section, wound healing disorder, immunosuppressive therapy, cyclosporine A, dapsone

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Introduction

Pyoderma gangraenosum (PG) is a non- infectious, inflammatory disease of unknown etiology. It occurs idiopathically or associated with systemic diseases such as inflammatory bowel disease, collagen vascular diseases, hematological malignancies, or infectious diseases like active hepatitis or HIV.

The clinical condition may develop spontaneously on intact skin or after minimal trauma or surgery. This far, only a few cases of PG have been reported after cesarean section. In addition, PG is a very rare but dangerous event during pregnancy.

The initial lesion commonly occurs as an extremely painful papule or pustule, rapidly enlarging with a progressive necrosis. Active ulcera exhibit a characteristic morphology with an intense livid-red inflammatory edge. Pustular or bullous lesions may appear indicating aggravation of the disease. Frequently, PG is misdiagnosed as a pyogenic wound infection.

Commonly, first-line treatments with antibiotics are ineffective and repeated blood cultures or wound swabs show no evidence of bacterial or fungoid infections. Surgical wound debridement may even result in a rapid enlargement of the ulceration. Of note, new lesions can appear as a result of the pathergic phenomenon leading to a potentially life-threatening clinical condition.

Due to the lack of indicative laboratory parameters, the diagnosis of PG is based on clinical. Histopathological findings are not specific, either. However, an early clinical diagnosis of PG is crucial in order to inhibit the inflammatory process and thus preventing massive tissue destruction, superinfection, or necrotic fasciitis.

Therapies of PG include immunosuppressive treatments with systemic glucocorticosteroids, cyclosporine A, dapsone, clofazimine, azathioprine, mycophenolate mofetil, tacrolimus, thalidomide or immunglobulins. Different available biologics blocking TNF-α function have also been demonstrated to be effective in treatment of PG associated with inflammatory bowel disease. If a surgical intervention is unavoidable, a sufficient prophylactic perioperative immunosuppressive therapy is demanded.

Case Report

A previously healthy 39-year old woman, gravida 1, para 1 underwent an uncomplicated cesarean delivery at 36 weeks of gestation after developing fever associated with pathological cardiotocography findings (fetal tachycardia). An amniotic infection was assumed. After cesarean section, the fever persisted under diverse intravenous antibiotic regimens. Investigations revealed no evidence of an infections focus. Six days postpartum, the patient developed a small red papule, followed by a painful necrotic ulceration at the incision site of the abdomen within 24 hours. The patient underwent several wound resections and debridements worsening the ulceration. CRP levels raised up to 313 mg/l (normal range: 0–5), the white blood count raised up to 73 10^3/µl (normal range: 4.0–10.0 10^3/µl) and the platelet count rose up to 728 10^3/µl (normal range: 150–350 10^3/µl). Additionally, a proteinuria was observed. Several blood cultures and wound swabs were negative for any bacterial or fungoid infection. The ulceration extended and involved a large area of the anterior abdominal wall and the upper right extremity (Fig. 1). Many blisters occurred at and around the livid-red border of the ulceration. Furthermore, the patient developed a massive lymphoedema of the right leg. Recurrent computer tomography (CT) investigations showed no signs of a diffuse abscess or phlegmonous cellulitis.

Twenty-two days post partum the patient was referred to our department for dermatologic examination. The clinical history and the typical clinical signs led to the diagnosis of pyoderma gangraenosum.

Immediately, a systemic treatment with high doses of prednisolone was started (3 mg/kg/b.w. once daily, first intravenously, later orally). On day 3, a combination therapy with prednisolone (2 mg/kg/b.w.) and cyclosporine A (CyA) was started at a dose of 5 mg/kg/b.w. because of a rather slow regress of the skin lesions. As a topical treatment

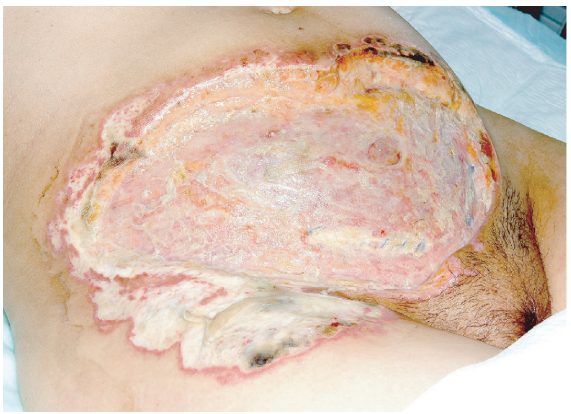

Figure 1. PG before therapy.

droplets of cyclosporine A (CyA, 100 mg/ml in olive oil (1:1) were applied on the wound edges.

Within three days of treatment, the inflammatory process was significantly reduced and the patient's temperature dropped to normal levels, as well as the CRP levels and the leukocyte count. The lymphoedema disappeared continously.

Two weeks later, a systemic treatment with dapsone at a dose of 150 mg per day was added in order to reduce the prednisolone dosis because of a therapy- resistant arterial hypertension. Along with a reduction of the prednisolone (1 mg/kg/b.w.) and cyclosporine A (1 mg/kg/b.w.) doses, the blood pressure rapidly dropped to normal levels and wound healing continuously improved (Fig. 2).

The patient was discharged from hospital ten weeks after delivery by cesarean section and seven weeks after diagnosis of a PG with stable wound conditions and without any inflammatory signs. The prednisolone treatment could be continuously reduced, followed by discontinuation of CyA and dapsone. A regular wound healing process was observed that was controlled regularly in our day care clinic (Fig. 3).

Discussion

PG is a non-infectious disease of unknown etiology. As a cutaneous form of vasculitis, it is suggested that defects of humoral as well as cellular immunitiy play a role in PG.[1] Because of a similar pathologic spectrum of the inflammatory process, PG is classified in the subgroup of the neutrophilic dermatoses, next to the sweet`s syndrome, subcorneal pustular dermatosis, and erythema elevatum et diutinum.[2] In general, PG is rare and frequently associated with systemic diseases

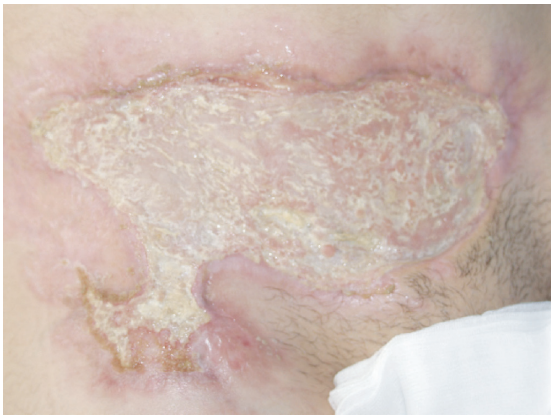

Figure 2. PG after 6 weeks of therapy.

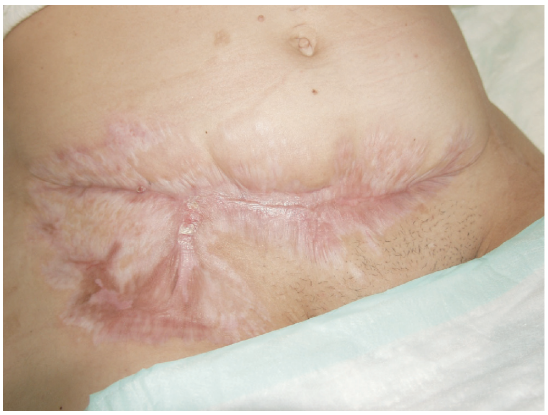

Figure 3. PG after 27 weeks of therapy.

of inflammatory or neoplastic origin. It may be also linked to immunosuppression during infection or chemo(radio)-therapy.[3]

Thus far, only a few cases have been reported after surgery, including cesarean section and during pregnancy.[4–10]

Underlying diseases like inflammatory bowel diseases, rheumatoid arthritis, lupus erythematodes, hematologic malignancies and infectious diseases can be associated with PG,[11,12] however even in these non-surgical patients minor traumata of the skin preceed the development of PG. In our patient, no associated disease was found.

The disease is often misdiagnosed as a pyogenic wound infection as it is often associated with fever, leukocytosis and elevated CRP levels. Additionally, a pyogenic wound infection could be secondarily accompanied by a PG. However, the rapid progression of the inflammation, the dramatic enlargement of the wound, the irresponsiveness to antibiotic therapy, and the progression after surgery or wound debridement support the clinical diagnosis of a PG.[13]

So far, adequate controlled trials are absent and no guidlines or standardized therapies exist for the treatment of a PG. In the literature, the systemic treatment with corticosteroids as a mono-therapy or in combination with cyclosporin A appear to be effective in many cases and should be considered as first-line treatment (Evidence level B). Case reports have also been published demonstrating the therapeutic efficacy of thalidomide, methotrexate, azathioprine, mycophenolate mofetil, tacrolimus, dapsone, clofazimine, minocycline, intravenous immunoglobulins, etanercept and infliximab.[5,14–18]

A combined systemic therapy of prednisolone (2 mg/kg/b.w.) and cyclosporine A (5 mg/kg/b.w.)

resulted in rapid reduction of tissue destruction and stabilisation of the patient's condition which was in a life-threatening state. Of note, a regress of the skin lesions was only observed after the beginning of the combination therapy. The local anti-inflammatory treatment was presumably increased by topical application of cyclosporine A, though effective intralesional drug-levels have not been measured. Due to the development of arterial hypertension, a decrease of cyclosporin A and prednisolone doses was necessary. Alternatively, dapsone (150 mg/d) was added. This treatment revealed to be well tolerated and save.

Dapsone is known for its efficacy in neutrophilic dermatoses. One of the known effects is the inhibition of neutrophil chemotaxis. A few case reports have shown a successful treatment of PG by a dapsone monotherapy. Commonly, dapsone is combined with corticosteroids.[15]

In severe states of PG, a combination of glucocorticoids with either cyclosporine A or other immunosuppressors should be favoured in order to rigorously inhibit the inflammatory activity of the PG. Glucocorticoids should be applied in one single dose in the early morning. In this case, a triple therapy of glucocorticoids (1 mg/kg/b.w.), CyA (3 mg/kg/b.w.) and dapsone (150 mg/d) was as effective as a therapy with high dose glucocorticoids (2 mg/kg/b.w.) and CyA (5 mg/kg/b.w.). Despite of the large ulcerated area, we noticed a good secondary wound healing process under the modified treatment, without any further complications.

In summary, PG must be recalled to be an important differential diagnosis after cesarean and abdominal surgery that may appear as a sustained wound infection resistant to antibiotic therapy. An early diagnosis and treatment is important to avoid life-threatening complications based on a PG. A rapid response to adequate systemic immunosuppressive therapy supports the diagnosis of a PG.

Disclosure

The authors report no conflicts of interest.

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