A case report of atypical presentation of pyoderma gangrenosum with ulcerative colitis: successful treatment with prednisolone and mesalazine therapy

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Summary

Introduction. Pyoderma gangrenosum (PG) manifests as recurrent deep ulceration of the skin and PG is often associated with a variety of systemic diseases, such as inflammatory bowel disease (IBD), rheumatoid arthritis, paraproteinaemia, hematologic malignancies and hepatitis. Approximately 30% of the cases of PG develop in patients with inflammatory bowel disease. There has been neither laboratory finding nor histological feature diagnostic of PG, and diagnosis of PG is mainly made based on the exclusion criteria.

Patient and methods. We report here a male patient 21 years old, complained of rectal bleeding of 3 weeks duration. He presented with a large, painful and rapidly progressive cutaneous ulcer in the right flank. Laboratory and microbiological investigations, colonoscopic biopsy and a skin biopsy from the ulcer were performed.

Results. An atypical presentation of PG with ulcerative colitis (UC) was diagnosed. The PG rapidly resolved after beginning of prednisolone and mesalazine therapy and the ulcer healed with scar. After successful treatment the patient suddenly stopped all his treatment and he came back again with rectal bleeding and a rounded, painful and rapidly progressive cutaneous ulcer in each cheek. One month after starting prednisolone and mesalazine treatment, complete healing of both ulcers with scars has occurred.

Conclusion. A rare atypical presentation of PG with risk of misdiagnosis and the unusual rapid healing of PG with combination of prednisolone and mesalazine therapy were concluded.

KEY WORDS: pyoderma gangrenosum; ulcerative colitis; prednisolone; mesalazine.

Introduction

Pyoderma gangrenosum (PG) is a rare inflammatory, non-infective and non-neoplastic ulcerative cutaneous disease associated with a variety of systemic diseases including inflammatory bowel disease (IBD), arthritis, haematological malignancies, paraproteinaemia and hepatitis (1-5). No laboratory findings or histological features are diagnostic of PG, and diagnosis of PG is mainly established by exclusion criteria (6). We reported here an adult male patient with ulcerative colitis (UC) who manifested with atypical presentation of PG in the right flank and both cheeks. After diagnosis, a rapid healing of the skin ulcers was obtained by prednisolone and mesalazine therapy.

Case report

A male patient 21 years old was referred and admitted to the department of dermatology, Assiut University Hospital. He was presented with a large, painful and rapidly progressive cutaneous ulcer in the right flank. The condition was associated with rectal bleeding of 3 weeks duration. Two weeks before a lesion appeared in the same skin area presenting as a small red plaque with surrounding erythema. The lesion rapidly progressed to a large and painful cutaneous ulceration. Antibiotic treatment with amoxicillin and ciprofloxacin was ineffective and the patient received paracetamol every 6 hours for pain relief.

On examination, the patient had pallor and mild hyperthermia (37.5-38°C). He complained of 3-5 daily episodes of diarrhoea with rectal bleeding. No lymphadenopathy was observed. A large, oval, painful and rapidly progressive cutaneous ulcer of 15 x 12 cm in diameters was over the right flank. The edges were well-defined, undermined and presented with granulated tissues, crusts, and purulent exudates (Figure 1). The lesion was very tender. A swab and microbio-
logical examination of the specimen from the ulcer was negative for bacteria and fungi. Routine laboratory investigations were done, complete blood count revealed white cell count of 15 × 10⁹/L leucocytosis with neutrophilia, reactive thrombocytosis platelet count of 868 × 10⁹/L and microcytic hypochromic anaemia his haemoglobin was 7.6 g/dl. He received blood transfusion and his haemoglobin became 9 g/dl. The erythrocyte sedimentation rate was 32 mm/h.

Stool analysis was reddish in colour, alkaline in reaction, showed positive blood and mucus with pus cells 75-80/HPF, RBC over 100/HPF and positive entameba histolytica. Liver and kidney function tests, anticoagulation panel were normal. Venereal Disease Research Laboratory (VDRL) test, HIV test, anti-neutrophilic cytoplasmic, antinuclear and anti-DNA antibodies, rheumatoid factor and LE test were all negative. Venous and arterial functional studies, and chest X-ray, were normal. The findings of the MRI of the posterior abdominal wall were highly suggestive of malignant ulcerating cutaneous and subcutaneous mass lesion with deep extension down till the fascial coverings of the underlying back muscles. No detected abdominal findings inside the abdominal cavity.

A skin biopsy from the ulcer was performed under local anaesthesia and stained with H&E. Histopathological analysis showed central necrotizing supplicative inflammation with ulceration (Figure 2A), and heavy neutrophilic supplicative inflammatory reaction with fibrin deposition (Figure 2B). The histopathological changes were consistent with pyoderma gangrenosum.

Colonoscopic biopsy was performed under general anaesthesia and stained with H&E. Histopathological analysis showed marked mucosal architectural distor-

Figure 1 - A large oval and painful cutaneous ulcer over the right flank. The edges were undermined. Granulated tissues and purulent exudates were evident.

Figure 2 - Skin biopsy of PG. A) Central necrotizing supplicative inflammation with ulceration (H&E, 40x). B) Heavy neutrophilic supplicative inflammatory reaction with fibrin deposition (H&E, 400x).
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Inflammation (chronic colitis), shallow ulceration and pseudopolyps (Figure 3A), with neutrophilic infiltrate of crypts (cryptitis) and lamina propria (Figure 3B, C). The histopathological changes were consistent with ulcerative colitis.

Therefore, the patient received treatment in the form of prednisolone (40 mg/day) and mesalazine therapy (4 gm/day) to control PG and UC. His bowel symptoms and skin lesion both gradually improved 2 weeks after starting treatment (Figure 4A). The prednisolone was tapered gradually according to the clinical improvement. Mesalazine administration was continued. The PG completely resolved 30 days after beginning of therapy, although the ulcer healed with scar (Figure 4B).

Two months after successful treatment with prednisolone and mesalazine, the patient felt that he is completely cured, he suddenly stopped all his treatment, and then he came back again with rectal bleeding. He presented with 2 rounded, painful and rapidly progressive cutaneous ulcerations, the first one in his right cheek and the second one in his left cheek of 5 days duration. The ulcers started as small red plaques with surrounding erythema, and then rapidly progressed to painful cutaneous ulcerations. On examination, the patient revealed 2 rounded, painful and rapidly progressive cutaneous ulcers, the first one central in his right cheek about 5x5 cm in diameter (Figure 5A), and the second one in the upper part of his left cheek about 3x3 cm in diameter (Figure 5B). The edges were undermined and presented with granulated tissues, crusts, and purulent exudates. The lesions were very tender. A skin biopsy from the ulcer of the right cheek was performed under local anaesthesia, to confirm again the diagnosis of pyoderma gangrenosum. Immediately we started the treatment with prednisolone and mesalazine with the same therapeutic doses. Two weeks later, the rectal bleeding gradually stopped and his skin ulcers on both cheeks were improved (Figure 6A, B). One month after starting treatment, complete healing of both ulcers with scars has occurred (Figure 7A, B). We advised the patient that he should be carefully followed-up, and gradually tapered his treatment according to the clinical improvement. Patient consent to publish his personal health information was obtained.

Figure 3 - Colonoscopic biopsy of UC. A) Marked mucosal architectural distortion (chronic colitis), shallow ulceration and pseudopolyps (H&E, 100x). B) Chronic colitis (architectural distortion) with neutrophilic infiltrate of crypts (cryptitis) and lamina propria (B, C).
Figure 4 - A) Improvement of the skin ulcer in the right flank of the patient started 2 weeks of treatment. B) Complete healing of the skin ulcer with scar after 30 days.

Figure 5 - A) Cutaneous ulcer central in the right cheek of the patient. B) Another cutaneous ulcer in the upper part of his left cheek. The edges were undermined and presented with granulated tissues, crusts, and purulent exudates.

Figure 6 - A) Improvement of the skin ulcer in the right cheek 2 weeks after starting treatment. B) Left cheek of the patient with improvement of the skin ulcer.
Discussion

Brunsting et al. (7) in 1930 first described five patients with rapidly progressive and painful suppurative skin ulceration with necrotic and undermined borders that were called PG. This lesion is a neutrophilic dermatosis associated with a variety of systemic diseases, such as paraproteinemia, arthritis, and myeloproliferative diseases, and IBD. In about 50% of the cases, UC is the underlying condition and PG may parallel the severity of the disease (1, 8, 9).

The relationship between the clinical course of PG and UC remains controversial. To clarify the uncertain relationship between PG and UC, an understanding the pathogenic relationship is important. There are some previous reports suggesting that UC and PG, at least in part, share a common pathogenic immune-mechanism. For example, one report proposed that the skin merely reflected the primary pathogenic process in the colon as a Shwartzman phenomenon. Another report suggested that immune complexes from inflamed intestinal mucosa caused cutaneous lesions (10, 11). Furthermore, other reports suggest that IL-15 and IL-8 play an important role in the relationship of PG and UC (12, 13).

PG can occur at any site but it is more common on the legs, in perineal, vulvar and penile regions. Atypical presentations may occurred at other sites such the arms or the trunk. Therefore, PG is an excluded diagnosis on the basis of laboratory findings and histopathology, associated with a high rate of clinical suspicion, its misdiagnosis can result in serious clinical consequences. The good clinical response to systemic steroids associated with other immunosuppressive therapy such as cyclosporine, azathioprine and cyclophosphamide is also important criteria (6).

In our patient the bowel symptoms and the skin lesion both gradually improved 2 weeks after starting treatment with prednisolone and mesalazine therapy. The PG resolved 30 days after beginning of therapy, and the ulcers healed with scar. The rapid healing of such rapidly progressive, painful skin ulcerations is unusual. In previous studies, some patients refractory to steroid treatment can benefit from the combination of systemic steroid with cyclosporine (14, 15).

Mesalazine is the standard first line treatment for mild to moderate UC, and is thought be anti-inflammatory through induction of peroxisome proliferator-activated receptor-gamma (PPAR-γ) gene expression and nuclear factor kappa-B (NFκB) activation, as well as inhibiting prostaglandin and interleukin-1 synthesis (16). However, no studies have yet been published on PPAR-γ gene expression, NFκB activation or prostaglandin and interleukin-1 synthesis in PG. Moreover, in consideration of possible association between PG and UC, the improvement of PG might be secondary to improvement of the UC (17). A case of successfully treated PG with topical mesalazine cream was reported previously (18), and the authors suggested that leukocytes' motility and cytotoxicity were suppressed by mesalazine in PG. Another study suggested that mesalazine play a direct role for the treatment of PG (17).

Conclusion

Combination of systemic steroid and mesalazine therapy can be an effective option for treatment of PG, especially when associated with UC, and can lead to rapid healing.

References