Response of Atypical Bullous Pyoderma Gangrenosum to Oral Minocycline Hydrochloride and Topical Steroids

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An 80-year-old Caucasian female with rheumatoid arthritis and recurrent atypical bullous pyoderma gangrenosum is described. There was no evidence of any underlying myeloproliferative disorder. Rapid healing occurred in response to oral minocycline hydrochloride and topical clobetasol propionate.

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Pyoderma gangrenosum (PG) is a necrotising non-infective ulcerating skin disease of unknown cause. A number of clinical sub-types have been described, including atypical bullous PG and superficial granulomatous pyoderma. The established treatment for PG is oral corticosteroids, but their use has been associated with significant morbidity and mortality. Hence a wide variety of alternative therapeutic regimes have been explored (1). Successful treatment of PG with oral minocycline hydrochloride has been reported (2,3,4). In this Department we have seen several patients with PG who have responded to the use of potent topical steroids alone (unpublished observations). In particular, the superficial, localized, granulomatous form of PG frequently heals without systemic steroid therapy (5). We report here a case of atypical bullous PG which responded to minocycline hydrochloride and topical clobetasol propionate 0.05% (Dermovate®).

CASE REPORT

An 80-year-old Caucasian female, with long-standing but quiescent seropositive rheumatoid arthritis presented in November 1984 with a 3-month history of an enlarging painful ulcer on the right lower leg, initiated by minor trauma, and which had been unresponsive to topical treatment. blistering lesions had appeared on the left leg 2 weeks previously and on the left middle finger one week prior to admission. On examination there was a large, deep, necrotic ulcer over the right malleolus which extended around much of the lower leg, with surrounding erythema and induration. Three haemorrhagic bullous and eroded plaques were present over the left lower leg with a further de-roofed lesion on the dorsum of the left middle finger, the latter being erythematous, swollen and tender. There were features of rheumatoid arthritis but general examination was otherwise unremarkable.

Laboratory investigations showed haemoglobin, 9.7 g/dl; white blood cell count, 9.4 x 10^9/1; platelet count, 978 x 10^9/1, and plasma viscosity, 1.94 cp (normal range 1.5-1.72 cp). Serum ferritin, protein electrophoresis and complement studies were all normal. Bone marrow trephine showed a normally cellular marrow with normal haemopoiesis; the megakaryocytes were increased in number but showed normal morphology. Platelet function tests were normal. Histological examination of an eroded plaque on the left lower leg revealed ulceration of the epidermis, with an underlying neutrophilic abscess in the upper dermis. There was a moderate lymphocytic infiltrate around the vessels in the lower dermis, but no evidence of a true vasculitis. Direct and indirect immunofluorescence studies proved negative.

The clinical and histological features were consistent with a diagnosis of bullous PG and prednisolone 40 mg daily and azathioprine 100 mg daily were introduced, with subsequent healing of the bullous lesions and improvement of the leg ulcer. Two months later, however, our patient suffered upper gastrointestinal bleeding from an endoscopically and histologically proven benign gastric ulcer. The immunosuppressive therapy was therefore rapidly tapered off and stopped. The leg ulcer was subsequently slow to heal, requiring several months in-patient therapy and pinch grafting.

Our patient re-presented in June 1986 with a 4-month history of blistering lesions affecting several fingers. On examination the index and middle fingers of the right hand and the middle and ring finger of the left hand were diffusely swollen, dusky in colour and tender. Haemorrhagic bullae and erythematous plaques were present on several fingers (Fig. 1). The area of previous leg ulceration remained healed. Relevant laboratory investigations included complement studies which showed evidence of circulating immune complexes, and skin swabs which showed no growth. Histological examination of an erythematous lesion on the left thumb showed numerous small abscesses in the upper dermis composed predominantly of neutrophils and foamy macrophages. Plump reactive vascular endothelium was present but there was no evidence of a necrotizing vasculitis. Special stains for bacteria and fungi were negative. These histological findings supported the clinical diagnosis of recurrent bullous PG and in view of the previous upper gastrointestinal haemorrhage, systemic steroids were avoided and minocycline 100 mg twice daily and topical clobetasol propionate 0.05% were commenced. The patient showed an excellent response, with complete healing of all lesions within one week. Minocycline was continued for a further 2 weeks and then stopped. On review 6 months later the lesions had remained healed and fol-
DISCUSSION

Atypical bullous PG is a variant of PG which is frequently associated with myeloproliferative disorders (6). The low haemoglobin level in our patient was accounted for by gastrointestinal blood loss and an anaemia of chronic disease. Other haematological investigations suggested a reactive thrombocytosis but there was no evidence of any serious underlying haematological disorder.

The development of a gastric ulcer leading to an upper gastrointestinal haemorrhage, in this case, illustrates one of the hazards of high-dose systemic steroid therapy. The evidence suggesting a protective effect from the prophylactic use of H2 blockers with systemic steroids is by no means conclusive and systemic steroids were therefore avoided during the treatment of the second episode of our patient’s atypical bullous PG. The rapid response and healing in response to minocycline hydrochloride and topical clobetasol propionate strongly suggests a causative role for one or both of these drugs in the healing process. While any proposed mechanism of action of minocycline remains speculative, the known anti-inflammatory (7) and immuno-suppressive (8) actions of tetracycline may be important.

REFERENCES