Effectiveness of 4% Disodium Cromoglycate in the Treatment of Disseminated Pyoderma Gangrenosum

Sir,
The clinical features of pyoderma gangrenosum were first described in 1930 by Brunsting et al. (1). Pyoderma gangrenosum is an ulcerative process of the skin, defined clinically by a raised, purple, tender, undermined border and an irregular, purulent necrotic base. It may be painful, can involve subcutaneous tissues and usually heals with a criviform scar. The lesions are solitary or multiple and present either as a merely cutaneous disorder or in association with systemic diseases, including ulcerative colitis and Crohn's disease, paraproteinemia, polyarthritis, chronic active hepatitis, leukemia and other conditions. Treatment differs and is often unsatisfactory. Therapeutic agents include corticosteroids, dapsone, sulfasalazine, azathioprine, cyclosporine, doloazine (2) and, most recently, 4% disodium cromoglycate (3–7). We report another successful case in the treatment of pyoderma gangrenosum with 4% disodium cromoglycate.

CASE REPORT
In June 1995, a 57-year-old woman with a 5-month history of pyoderma gangrenosum was admitted to the Department of Dermatology, University of Regensburg (Germany).

The lesions had started on the left tibial region increasing rapidly in size. Further ulcers had developed, affecting also the right thigh and lower leg and both elbows. Treatment with topical antibiotic agents had been unsuccessful.

There were no symptoms and no history of inflammatory bowel disease. With the exception of splenectomy at the age of 9, a gastric ulcer in 1982 and an adenoma of the thyroid gland, the patient was in good health.

Physical examination revealed on both legs (Fig. 1) and elbows multiple ulcers with a boggy, necrotic base with dark-red, undermined, irregular and painful borders.

Histopathologically, the corium showed necrosis, thrombosis and fibrinoid necrosis of small vessels with leukocytoctasia and a dense infiltrate of neutrophils, lymphocytes, plasma cells and histiocytes. In clinically normal, adjacent skin histological signs of necrotizing vasculitis were present.

Laboratory tests revealed leucocytosis (11.16 × 10⁹/l), thrombocytosis (1.013 × 10⁹/l), an elevated level of rheumatoid antibody (72.5 mg/l) and an increased erythrocyte sedimentation rate (65/120). There was a slightly elevated IgA level (487 mg/dl), which was considered insignificant, and the antinuclear antibody-titer was 1:320. The serum chemistry profile, rheumatoid factor and serum protein electrophoresis were normal. Bacterial cultures for aerobic and anaerobic organisms were negative. An abdominal sonography showed a hepatomegaly, all other clinical investigations including chest-ray were not pathological.

The patient was treated with topical application of 4% disodium cromoglycate in aqua conservans four times a day to the ulcers. Disodium cromoglycate, cromolyn sodium and sodium cromoglycate are synonyms for the disodium salt of cromoglycic acid (7).

Within 3 days the ulcers started to reepithelialize, and within 16 days after the start of treatment, 90% of the ulcers had healed (Fig. 2).

Two months later, however, there was a recurrence when the patient stopped using disodium cromoglycate. After the patient had responded well to the therapy with 4% disodium cromoglycate four times a day, and 18 days later healing was complete, leaving pink scars.

DISCUSSION
Pyoderma gangrenosum has been treated empirically with a variety of medications with inconsistent results (2). Other authors reported encouraging results with 4% cromolyn solution in the management of pyoderma gangrenosum in a total of 11 patients, of which 3 had no associated treatments, with healing within 2–3 weeks (3–7).

In our patient, pyoderma gangrenosum had been present for 5 months and was progressive in size and number. After 3 days of treatment with 4% disodium cromoglycate four times a day the lesions started to reepithelialize, and after 16 days the ulcers had almost healed. The effect of topical cromolyn was prompt, suggesting that the response was directly related to the cromolyn application and not the result of spontaneous healing. Furthermore, 2 months later when the treatment with disodium cromoglycate was interrupted by the patient, there was a recurrence of pyoderma gangrenosum. After the therapy with disodium cromoglycate was resumed, the ulcers healed within 18 days. In the literature, concentrations of disodium cromoglycate for the therapy of pyoderma gangrenosum range from 1% to 4% (3–7). Whether a higher concentration might be more beneficial is speculative.

Fig. 2. Healed lesions after a total of 34 days of topical disodium cromoglycate treatment.

Fig. 1. Pyoderma gangrenosum on lower leg prior to therapy.
The mechanism by which disodium cromoglycate may promote healing of pyoderma gangrenosum is unknown. It has been used extensively for the treatment of allergic rhinitis and for asthma. Disodium cromoglycate is known to inhibit degranulation of sensitized mast cells and thus decreases the release of histamine and slow-reacting substance of anaphylaxis. Furthermore Kay et al. (8) described the inhibition of enhancement of neutrophils, eosinophils and monocytes by disodium cromoglycate in a time- and dose-dependent fashion.

An additional consideration is that disodium cromoglycate may under certain circumstances inhibit type III (Arthus) reactions, which are themselves capable of causing tissue damage in the lungs (9).

The beneficial effect of disodium cromoglycate in pyoderma gangrenosum may not be specific for that condition, but it is safe and effective in the management of pyoderma gangrenosum. In our opinion 4% disodium cromoglycate should therefore be considered for initial topical therapy of pyoderma gangrenosum, which may be combined with any systemic treatment. Nevertheless, a multicenter trial of cromoglycate treatment would be of interest.

REFERENCES


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Gianotti-Crosti Syndrome in an Adult Patient Following a Recently Acquired Epstein-Barr Virus Infection

Sir,

Gianotti-Crosti syndrome (GCS) is a self-limiting papulovesicular acrodermatitis with underlying viral infection, up to now predominantly diagnosed in children.

Patients with the clinical finding of GCS have been described to develop a distinctive self-limiting papular or papulovesicular skin eruption with a predominant localization of the acral regions such as cheeks, buttocks and extremities in association with underlying viral diseases (1, 2).

Originally, hepatitis B virus was reported to be associated with the elaboration of GCS, although its causative role could not be established in all patients (3). In recent reports a variety of viral infections have been reported to be linked to the finding of GCS, including Epstein-Barr virus, cytomegalovirus (CMV), enteroviruses, adenoviruses and human immunodeficiency virus (HIV) (3–9).

Following a study by Caputo and co-workers the term GCS is used for description of acral papular eruptions of childhood with underlying viral disease, regardless of further specification (9).

Occurrence of GCS in adult patients is a very rare finding, which has been described only occasionally in the medical literature and predominately in association with hepatitis B infection (10). Very recently elaboration of GCS after a preceding vaccination against influenza virus was reported, although association to a positive anti-hepatitis B titer could not be completely ruled out (11).

We here call attention to onset of GCS following a recently acquired Epstein-Barr virus infection in an adult patient who had an otherwise unremarkable medical history.

CASE REPORT

A 26-year-old Caucasian female patient presented at our hospital with acute exanthematic macular drug reaction to oral administration of amoxicillin, which had been prescribed for a 2-week history of persistent pharyngeal inflammation. Therapy with intravenous prednisolone rapidly improved the skin symptoms, and the patient was free of skin eruptions 4 days after admission.

At this point, viral titers positive for anti-EBV-IgM antibodies with slight elevation of anti-EBV-IgG were obtained, results indicative of recent EBV infection. Further immunological specification showed anti-EBV-Ca IgG > 1:40, anti-EBV-Ca-IgM > 1:12 (capsular antigen) and negative results for anti-EBV-EA-IgG and anti-EBV-NA (nuclear antigen). Titers for hepatitis A, B, C as well as anti-HIV 1/2 and a battery of other viruses were negative.

Two days later the patient presented again with new skin lesions differing from the previous ones in terms of morphology and localization. Succulent, inflammatory, non-itching papular to partly papulovesicular-appearing lesions, approximately 3–5 mm in diameter, were now seen, located predominantly at the acral regions. The eruptions were symmetrically distributed on the neck, upper and lower limbs as well as on the buttocks (Fig. 1). Lesions were not painful. Involvement of mucous membranes was not seen. Koebner's phenomenon was absent. Ultrasound examination of spleen and liver showed no patho-