Correspondence to: Dr F L Dumoulin; dumoulin@uni-bonn.de

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Combined therapy for pyoderma gangrenosum

A P Rozin, A Balbir-Gurman, L Gilead, D Slodownik

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We report a case of successful combined therapy for rapidly progressive pyoderma gangrenosum (PG). A 78 year old woman was admitted to the department of rheumatology with large right leg skin ulcers affecting the anterior and mediolateral lower shin region (fig 1A). The lesions had developed from small pustules to a focus of large painful skin damage during the past month. Her past history was free of any skin disease. Arterial hypertension, depression, and osteoporosis were controlled with permanent treatment. Her laboratory findings were unremarkable, including negative hepatitis B surface antigen and hepatitis C virus and normal liver function.

A marginal biopsy was performed, which highlighted a massive neutrophil infiltrate invading subcutaneous fat with necrotic debris associated with PG, with no evidence of vasculitis, malignancy, or infection. The patient had had seropositive rheumatoid arthritis for 32 years and her joint disease was controlled with long term treatment with azathioprine 150 mg/day. Despite the large rapidly progressive skin lesion and threat of leg amputation we decided to stop azathioprine and to begin combined therapy. This treatment included intravenous monthly cyclophosphamide pulse therapy 1000 mg (20 mg/kg), oral cyclosporin A 100 mg/day (2 mg/kg), a moderate dose of prednisone 30 mg/day (0.6 mg/kg) with tapering to 20 mg/day after 2 months, and a local treatment. To achieve a clean wound, she underwent one session of maggot debridement treatment (MDT). After confirming a normal ankle brachial index by duplex we started to apply two layer pressure dressings with occasional granulation tissue promoters. After 3 months of the treatment the wound healed completely (fig 1B). Three additional monthly pulses of cyclophosphamide were given. The patient's present treatment comprises cyclosporin A 2 mg/kg and prednisone 10 mg/day. She is well, has normal daily living, and no active arthritis.

DISCUSSION

PG is a non-infectious neutrophilic dermatosis that usually starts with sterile pustules, which rapidly progress to painful ulcer with undermined violaceous borders. In 17–74% cases, PG is associated with an underlying disease, most commonly inflammatory bowel disease, rheumatological or haematological disease, or malignancy. Diagnosis of PG is based on a history of an underlying disease, typical clinical presentation,

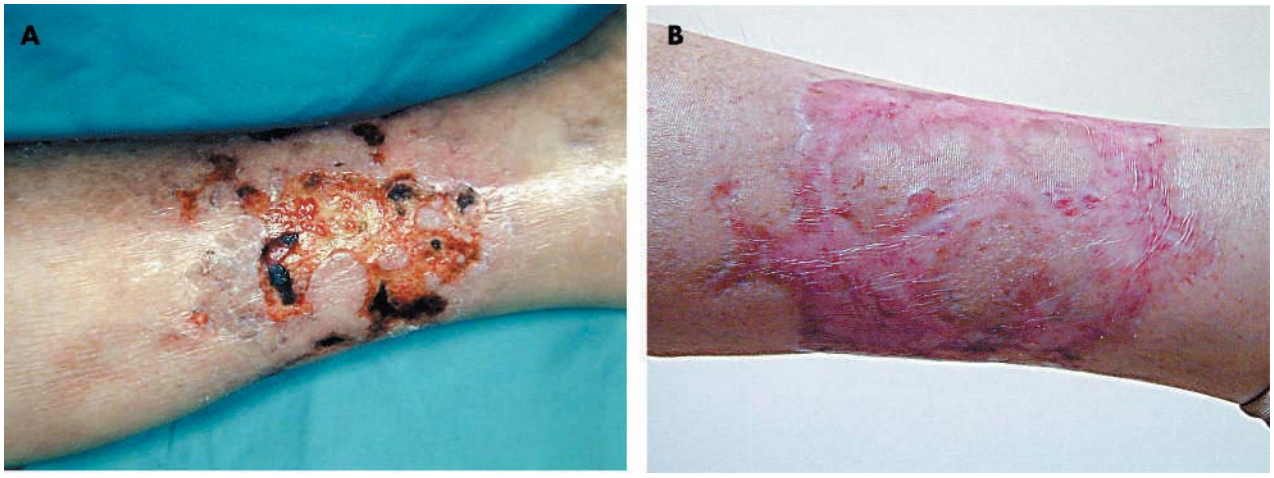

Figure 1 (A) Large ulcers of pyoderma gangrenosum with an irregular, well defined, undermined, partially raised violaceous border on admission. (B) Complete healing of the wound after combined prednisone-cyclosporin A-pulse cyclophosphamide therapy and local maggot debridement 3 months later.

and histopathology, and exclusion of other diseases that would lead to a similar appearance. Despite recent advances in treatment, the prognosis of PG remains unpredictable.[1] The optimal treatment of PG includes a combination of local wound care and systemic treatment. Often, it is difficult to control aggressive cases, necessitating administration of a combination of systemic treatments.[2] We followed this way and administered first line treatment of high dose corticosteroids and cyclosporin A[3] along with monthly pulses of cyclophosphamide.[4 5] MDT was first introduced in America in 1931. Sterile maggots of the green bottle fly *Lucilia (Phacnicia) scricata* are used for MDT. Up to 1000 maggots are introduced into the wound and left for 1–3 days. One of the major advantages of MDT is that the maggots separate the necrotic tissue from the living tissue. In 80–95% of cases a complete or significant debridement of the wound is achieved. An immediate amputation can be prevented as a result of MDT.[6] In another study 21 ambulatory patients with non-healing wounds were treated with MDT.[7] Of the eight patients who were advised to undergo amputation or major surgical debridement, only three required surgical resection (amputation) after MDT. Eleven healed without any additional surgical procedures.[7] It is a simple, efficient, well tolerated, and cost effective tool for the treatment of wounds and ulcers which do not response to conventional treatment.[6] We used it as first line treatment together with systemic treatment and achieved a rapid and complete effect.

Authors' affiliations
A P Rozin, A Balbir-Gurman, B Shine Department of Rheumatology, Rambam Medical Centre and B Rappaport Faculty of Medicine, Israel-Technion Institute of Technology, Haifa, Israel
L Gilead, D Slodownik, Department of Dermatology, Hadassah Medical Centre, Jerusalem, Israel

Correspondence to: Dr A P Rozin, Bat Galim, Rambam Medical Centre, PO Box 9602 Haifa, Israel, 31096; a_rozin@rambam.health.gov.il

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Benefit of immunosuppression for severe Takayasu's arteritis and coincident primary biliary cirrhosis

E Feist, K G A Hermann, S Filimonow, R I Rückert, T Dörner, F Hiepe

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Takayasu's arteritis and primary biliary cirrhosis (PBC) are two unrelated autoimmune diseases without a so far reported coincidence, probably because they occur at different ages.[1 2] As a systemic vasculitis, Takayasu's arteritis affects predominantly the aorta and its branches in female patients before the age of 40 years. The clinical manifestations are variable and severe anatomical lesions can lead to life threatening ischaemia. We report an unusual case, where, after the initial diagnosis of a coincident severe Takayasu's arteritis with PBC, subsequent immunosuppressive treatment led to a striking clinical improvement of vasculitic symptoms in an elderly woman.

CASE REPORT

A 70 year old woman was referred to our hospital with generalised weakness and disseminated painful cutaneous, erythematous nodules on the extensor sites of both lower legs. A rheumatic disorder had been suspected since 1960 because of remittent nausea, attacks of fulminant headaches, and an erythema nodosum. Clinical examination showed a diminished bilateral radial and an absent carotid pulse as well as hypotensive blood pressure on both arms (85/60 and 90/60 mm Hg). No focal neurological and no pathological musculoskeletal findings were present.

In laboratory analysis, a raised erythrocyte sedimentation rate of 52 mm within the first hour as well as a C reactive protein of 14 mg/l (normal <8) were detected. Liver enzymes and measures of cholestasis were moderately raised. Antinuclear antibodies were positive at a titre of 1/1280, with a dense granular nucleoplasmic pattern and cytoplasmic staining suggesting antimitochondrial antibodies (AMA). AMA were confirmed in immunofluorescence on rat kidney cells at a positive titre of 1/32, and in AMA-M2 enzyme linked immunosorbent assay (ELISA; >500 U/ml, normal <10).

In Doppler sonography, occlusion of both common carotid arteries (CCA) and of both internal carotid arteries (ICA) as well as of the left subclavian artery was detected. The filiforme external carotid arteries showed an antegrade flow on the right and a retrograde flow on the left side. Along the right subclavian artery, examination showed a post-stenotic signal. Perfusion of the brain was ensured by two hypertrophic vertebral arteries with a suspected stenosis on the right side. These severe anatomical changes were confirmed by digital subtraction angiography (fig 1A). Ultrasound examination of the abdomen showed no signs of involvement of abdominal vessels, but a chronic alteration of liver tissue.

Despite the age of our patient, Takayasu's arteritis was diagnosed with the assumption of a disease duration of four decades. Moreover, the remittent attacks of headaches and nausea, the skin involvement, and raised inflammatory parameters were consistent with an active vasculitis. A coincident PBC was supported by high positive AMA, raised measures of cholestasis, and morphological liver changes.[3] Therefore, a therapeutic approach with corticosteroids (initially 50 mg a day) in combination with a cyclophosphamide bolus (700 mg) was justified. Immediately, a clear