Case Descriptions

Case 1

We describe the case of a 30-year-old man who presented in November 2003 with multiple lesions, with onset 3 months previously. These initially appeared on the back, later spreading to the rest of the trunk and limbs. The initial lesions consisted of papules and inflammatory nodules that later became abscesses and drained spontaneously (Figure 1). The patient had been treated as an outpatient with various systemic broad-spectrum antibiotics but no improvement was apparent. Initial pathology studies were consistent with furunculosis. Despite treatment with oral sulfone and corticosteroids (oral and intralesional), the patient developed painful ulcerations with irregular violaceous edges (Figure 2) clinically compatible with a
Diagnosis of PG. A new biopsy showed a necrotic and ulcerated epidermis, with pseudopitheliomatous hyperplasia on the edges of the ulcer. Edema was apparent in the dermis, along with a dense infiltrate of neutrophils, lymphocytes, and macrophages (Figure 3), with hemorrhagic areas, edema, and hyalinization of the capillary endothelia.

Disease progression and pathology finally indicated a diagnosis of multiple PG. The patient had no systemic symptoms and tests undertaken to rule out diseases commonly associated with PG proved normal: blood tests (blood count, biochemistry, protein profile, autoantibodies, Sézary cell count, T-cell populations, coagulation, serology for human immunodeficiency virus (HIV), hepatitis C virus, and hepatitis B virus), gastric endoscopy, opaque enema, and bone marrow aspiration. Treatments with oral cyclosporin (5 mg/kg/d), oral methotrexate (15 mg/wk), and topical tacrolimus were unsuccessful.

Later disease progression was atypical, with constant recurrence, general progressive deterioration, and the development of painful ulcers on the legs measuring more than 15 cm across. Finally, whole body computed tomography was performed in the search for an underlying disease. The scan revealed a perforation in the nasal septum and enlarged lateral cervical lymph nodes. The patient admitted to sniffing cocaine over the last 2 years. Following the failure of conventional therapies, treatment with infliximab 5 mg/kg was prescribed in weeks 0, 2, 6, and then every 8 weeks for a year, with associated oral methotrexate 15 mg/wk. The patient was also referred to addiction support services for rehabilitation. A great improvement was seen in the first month and a half, and the lesions had healed by the end of the year in spite of later recurrences coinciding with positive results for cocaine in the urine. Further recurrence occurred after treatment was suspended and 3 months of treatment with etanercept 50 mg/wk made no improvement. Infliximab was prescribed again, but despite improvements during the first 2 months, subsequent complete response was not achieved. Recurrences at the end of each cycle resulted in the drug being administered every 6 weeks. Later relapses in drug use were associated with a worsening of symptoms that were managed with regular injections of corticosteroids.

**Case 2**

The patient was a 30-year-old man who consulted in July 2005. He presented numerous lesions on the back, the upper third of his arms, and a single lesion on the right cheek with onset 4 months previously (Figure 4). These began as inflammatory papules that developed into suppurating nodules and painful exudative ulcers with an irregular granular base and raised violaceous edges. The lesions had been treated with oral antibiotics with no
improvement and the patient presented no systemic symptoms.

Given the clinical similarity to the previous case, in terms of epidemiology, the distribution of lesions, and disease progression, the patient was asked about drug consumption. He admitted sniffing cocaine daily over the last 10 years.

A biopsy was taken, and the pathology study was compatible with a diagnosis of PG. The epidermis showed intraepithelial microabscesses comprised of neutrophils and areas of epidermal necrosis. A dense and diffuse inflammatory infiltrate was seen in the dermis, composed of neutrophils, eosinophils, lymphocytes and macrophages, edema, and extravasated red blood cells. The capillary vessel walls presented edema with fibrinoid deposition.

Tests were performed (complete blood count, renal profile, liver and thyroid function, autoantibodies, protein profile, serology for hepatitis viruses and HIV), Mantoux intradermal test, chest x-ray, and colonoscopy, all with normal or negative results.

Following the failure of conventional therapies and the improvement obtained with infliximab associated with abstinence from cocaine in the previous case, this treatment was chosen as the first alternative, with the addition of topical tacrolimus. There was a rapid reduction in the size of the lesions and suppuration during the first 8 weeks, with progressive epithelialization (Figure 5) and reduced pain.

During the unplanned admissions of the patient to hospital, urine tests were taken and the patient was monitored by addiction support services. The patient presented recurrence of lesions at the end of each cycle of treatment, and so the interval between treatments was reduced to 6 weeks.

Discussion

Most patients (>70%) with ulcerative PG present underlying illnesses like IBD, arthritis, monoclonal gammopathy, or internal neoplasia. PG vegetans is the only form of the disease that tends not to be associated with systemic diseases, but this is characterized by slow-growing painless lesions with more superficial ulceration and less violaceous edges that are not usually purulent.1 Disease progression in our patients is similar to the type of ulcerative PG predominant in the lower limbs. However, in our cases the lesions began with multiple eruptions on the back, later extending to the limbs and, in addition, lacking the associated systemic symptoms.

Certain drugs like sulpiride2 and hematopoietic growth factors can trigger eruptions similar to PG, but no relationship has yet been reported between drug abuse and PG.

Visceral ischemia is commonly associated with cocaine consumption. Endothelial damage can be due to the direct toxic effect, or as a consequence of prolonged vasoconstriction.3 Street cocaine contains impurities used as fillers (for example: quinine, sugar, procaine, and amphetamines) which may also produce distal vascular obstruction or inflammatory reactions.4

There is a broad spectrum of skin lesions produced by various forms of cocaine use (intravenous and subcutaneous injection, and sniffing); they are generally distal and range from simple digital vasospasm and Raynaud syndrome5 to small and medium vessel vasculitis with purpura, urticaria vasculitis,6 ulceration, necrotic livedo,7 and gangrene.8
most serious cases occur when there is intravenous cocaine use and are accompanied by systemic symptoms of fever and visceral toxicity. Direct administration via the skin causes localized necrosis.9 Bullous erythema multiforme lesions have also been described,10 as have infectious bacterial or mycotic complications.

The potent vasoconstrictor effect of sniffed cocaine can produce ischemic necrosis with perforation of the nasal septum, which should be differentiated from other destructive lesions of the midline like Wegener granulomatosis. Two cases have been published of PG complicated by nasal perforation, where examinations found no suggestion of Wegener granulomatosis, and the authors concluded the septal perforation was secondary to mucosal involvement of PG.11 Although the epidemiological characteristics of the progression of the lesions do not agree with those described in our patients, they did not rule out cocaine consumption.

The most effective treatments according to the literature are corticosteroids and cyclosporin and both are considered first line drugs. Infliximab can be considered a first line therapy in this group due to its rapid effectiveness in IBD-associated PG.12 However, it has also been effective in many cases of PG not associated with IBD.13,14 Just as in our cases, rapid improvements are seen in the first month, although minor recurrences in some patients after the tenth week of injections can lead to intervals between infusions being shortened to 6 weeks.15 The combination of infliximab and other immunosuppressants can help maintain effectiveness and extend the duration of remission once treatment has ended.

Finally, while it has been shown that cocaine can produce ischemic skin disorders, our patients are the first reported cases of PG secondary to cocaine use.

Our experience clearly demonstrates the effectiveness of treatment with infliximab associated with abstinence from cocaine use.

Conflicts of Interest
The authors declare no conflicts of interest.