SIR, Pyoderma gangrenosum (PG) is an ulcerative skin disease simulating pyoderma gangrenosum. Necrotizing vasculitis secondary to disseminated histoplasmosis could be neither grown nor demonstrated histologically in the lesions.

Histoplasma capsulatum is a dimorphic fungus that causes histoplasmosis, a systemic infection characterized by pulmonary and cutaneous manifestations. Histoplasmosis is a common opportunistic infection in patients with immunosuppression, such as those with HIV infection or organ transplantation.

The definitive diagnosis of DH should be performed by classical microbiological methodology comprising direct examination, culture and serology. However, Toranzo et al. [9] recently described a molecular method based on the PCR technique where diagnosis of histoplasmosis could be neither grown nor demonstrated histologically in the lesions.

**Fig. 1** Large ulcer with irregular borders and violet pigmentation with necrohaemorrhagic background supports the diagnosis of PG.
was evaluated using whole blood targeting a portion of the gene HcP100. The method showed 89% sensitivity and 96% specificity for the diagnosis of histoplasmosis.

Similar to the case described by Small et al. [8], evidence for infection by H. capsulatum came in our case only from isolation of the fungus from a remote site (blood), but not from the lesion itself. The response to specific antifungal therapy with itraconazole strongly supported the diagnosis of IPG in this case. Our experience suggests that any PG-like lesion without adequate response to antibiotic treatment and a failing corticosteroid trial should alert the physician to consider the anatomic location, make a detailed and thorough assessment of the pathology with staining for non-bacterial infections (considering atypical forms of vasculitis as the case) and systematically perform isolation studies of deep mycosis. We believe that the PCR technique for Histoplasma, despite not being validated through multicentre studies where a large number of samples could determine its specificity, can be useful in cases where the classical methodology (direct examination, culture and serology) produces inconclusive results.

**Rheumatology key message**

- Atypical pathogens should be suspected in vasculitic ulcer unresponsive to corticosteroid and antibiotic therapy.

**Disclosure statement:** The authors have declared no conflicts of interest.

**Supplementary data**

Supplementary data are available at Rheumatology Online.

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**References**


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**Successful desensitization to low-dose methotrexate**

Sir, A 57-year-old woman with RA was initially treated with prednisone for 4 months before MTX was commenced as a disease-modifying agent. After 5 weeks of MTX therapy, she developed an immediate reaction following a 20 mg dose which was characterized by generalized urticaria, angio-oedema, throat constriction and abdominal cramping. She developed similar reactions to LEF and SSZ. During this period, her dose of prednisone was maintained at 15 mg daily.

A desensitization protocol to MTX was formulated on the basis that it was the preferred disease-modifying agent especially if an approved biologic agent was to be used as part of her therapy. MTX is used as an immuno-suppressive agent in low doses and as an antineoplastic agent in high doses. Anaphylactic reactions are rare and have been reported at various dosing levels.

However, the small number of desensitization protocols to MTX that have been published all target tolerance to high dose levels required in the treatment of malignancy. The initial doses administered in these protocols are usually $\geq 50$ mg [1, 2]. In contrast, desensitization was performed to a low target dose of 25 mg in this patient. As it was not feasible to use oral suspensions of MTX, the protocol involved the slow i.v. administration of incremental doses of MTX (0.025, 0.25, 2.5 and 22.5 mg resulting in a cumulative dose of 25 mg) in the intensive care unit (Table 1). She ingested her daily dose of 15 mg of prednisone prior to the commencement of desensitization. The protocol was completed successfully and the following week she was able to tolerate a 25 mg oral dose of MTX given under medical supervision. She was then able to...