

# Suspected Induction of a Pyoderma Gangrenosum–Like Eruption Due to Sulpiride Treatment

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*A case of a pyoderma gangrenosum (PG)–like eruption due to the antipsychotic drug sulpiride, a form of risperidone, is described. The contribution of sulpiride to the etiology of the PG-like lesion is based on the reduction and healing of the ulcer upon cessation of the drug and the formation of a bulla following the drug's re-administration. The literature on drug-induced PG or PG-like eruptions is discussed. The selectivity of sulpiride for dopamine receptors and its limited effect on other neuronal pathways differentiates sulpiride from other types of antipsychotic drugs commonly used in Israel, including phenothiazine, butyrophenone, and thioxanthenes. Adverse systemic and cutaneous reactions to sulpiride and to risperidone are described. To our knowledge, this is the first report of a PG-like eruption due to the former.*

**P**oderma gangrenosum (PG) was described 71 years ago as a secondary cutaneous gangrene to streptococcal infection.<sup>1</sup> Although the cause of PG remains obscure, the number of associated conditions has markedly increased in recent years.

Sulpiride, an antipsychotic drug, is a form of the widely used drug risperidone, which has been associated with numerous cutaneous side effects.<sup>2</sup> To our knowledge, this is the first report of a PG-like eruption due to sulpiride.

## Case Report

A 48-year-old white, schizophrenic, obese male presented with a 15×20 cm ulcer on his left leg of 2 weeks duration. He had been diagnosed with



**Figure 1.** A large ulcer, 15×20 cm, with well-defined undermined borders surrounded by a halo of erythema.

schizophrenia 30 years earlier and, for the last 5 years, was treated with sulpiride, with good psychiatric results. The patient denied any trauma or pruritus prior to the ulcer, which he described as developing over a period of a few days.

Physical examination revealed a well-defined ulcer with undermined borders surrounded by an intense halo of erythema (Figure 1). The ulcer was covered with yellow-green necrotic crusts with a

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**Figure 2.** A large hemorrhagic bulla at the borders of the ulcer.

bad odor. A clinical diagnosis of PG was made. In addition to schizophrenia, the patient was morbidly obese and allergic to roxithromycin, a macrolide antibiotic. The patient had no symptoms of inflammatory bowel disease. Tests for anti-DNA, rheumatoid factor, anti-Ro (Sjögren's syndrome A), anti-La (Sjögren's syndrome B), C<sub>3</sub>, and C<sub>4</sub> were negative. Fluorescent antinuclear antibody, which was examined in a 1:80 titer, demonstrated positive results. In our case, the positive fluorescence was graded 2 (using a 4-point scale). Complete blood cell count, blood smear, liver and kidney function tests, antiphospholipid, and VDRL test were also negative. Serum protein immunoelectrophoresis demonstrated a mild increase in IgA and IgG. Chest x-rays and venous and arterial doppler examinations were normal. There were no signs of arterial or venous insufficiency. An x-ray and bone scan of the leg showed no osteomyelitis. A purified protein derivative test for tuberculosis was negative. Repeated bacterial cultures taken from the ulcer revealed *Enterococcus*, *Proteus mirabilis*, *Proteus penneri*, group A streptococci, and *Proteus morganii*. Patch test and migration inhibitory factor test to sulpiride were negative.

A biopsy specimen from the erythematous border of the ulcer showed a large ulceration, with scar granulation tissue at its base. No microscopic organisms were present, and no vasculitis was detected. An angiocentric inflammatory infiltrate consisting mostly of neutrophils was found, as well as the formation of new blood vessels. Direct immunofluorescence was negative.

The ulcer was treated conservatively with 1% cromolyn sodium wet compresses and systemic antibiotics sensitive to the bacteria demonstrated in cultures taken from the ulcer. The antipsychotic drug haloperidol was given, and a slight decrease in the size of the ulcer was observed. The patient's psychiatric condition deteriorated 2 weeks after discontinuation of sulpiride, and the drug was re-introduced. Eight days later, a large hemorrhagic bulla appeared at the border of the ulcer (Figure 2). Sulpiride was immediately stopped because of a suspected connection between the development of the bulla, the ulcer, and the medication. Haloperidol was re-introduced, and treatment continued with topical 1% cromolyn sodium cromoglycate carbonate odor absorbing dressing (Smith & Nephew Medical, Ltd, London, United Kingdom). When the patient was discharged, the ulcer was about one third its original size.

### Comment

PG or PG-like eruption due to drug reactions is rare. During the last decade, 3 cases of PG due to isotretinoin were published<sup>3,5</sup> and, in each case, discontinuation of the drug and introduction or continuation of topical and systemic treatment resulted in healing of the ulcers. PG induced by granulocyte colony-stimulating factor was reported in a patient with small cell lung carcinoma. In this case, discontinuation of the drug and continuation of topical treatment also resulted in resolution of the ulcer.<sup>6</sup>

Sulpiride is a benzamide substitute and is chemically unrelated to other dopamine receptor antagonists of the phenothiazine, butyrophenone, or thioxanthene groups of antipsychotic drugs commonly used in Israel.<sup>7</sup> As an antipsychotic agent, it shares some common properties with the classical neuroleptics haloperidol and chlorpromazine. It differs from them in several fundamental respects, in particular its selectivity for dopamine receptors and its relatively limited interference with other neuronal pathways. Adverse reactions to the drug, as well as to risperidone, include dyskinesia, extrapyramidal syndromes, sedation, reversible galactorrhea, and amenorrhea due to elevated prolactin levels.<sup>7</sup>

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Gastrointestinal disturbances, tachycardia, and moderate drops in blood pressure also have been reported.<sup>7</sup> Cutaneous drug reactions to risperidone were reported by the author<sup>7</sup> and other investigators<sup>8</sup>: acneform eruption, bullous eruption, exfoliative dermatitis, furunculosis, hypo- and hyperhidrosis, as well as lichenoid eruption, photosensitivity, pigmentation, and psoriatic and seborrheic eruptions. To our knowledge, our patient is the first reported case of PG due to sulpiride treatment. The patient had been treated with the drug for 5 years prior to the appearance of the ulcer, which developed quickly and reached a very large size. Reduction and healing of the ulcer upon cessation of the drug and continuation of topical and systemic treatment and the formation of a bulla on the border of the ulcer following re-administration of the drug led us to conclude that sulpiride was the main cause of PG in this patient.

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