

Pyoderma Gangrenosum Associated with Sarcoidosis

G. Kontochristopoulos^{1*}, E. Saxioni¹, G. Doulaveri-Gherasim¹, G. Politis² and N. Zakopoulou¹

¹Second Department of Dermatology, "A. Syngros" Hospital, 5, I. Dragoumi Street, GR-161 21 Athens, Greece, and ²Sixth Department of Chest Hospital of Athens, Athens, Greece. *E-mail: hcvd@compulink.gr
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Sir,

Pyoderma gangrenosum (PG) is a rare, destructive, inflammatory skin disease of unknown aetiology which belongs to the group of neutrophilic dermatoses (1–3). In about 50% of patients, an underlying disease will be found, such as inflammatory bowel disease and haematological malignancies. In others, the diagnosis of idiopathic PG is reluctantly made. We report here a case of PG associated with systemic sarcoidosis.

A 53-year-old man was admitted to our hospital in September 2001 with a pretibial ulcer on the right leg of 7 months' duration. Initially, the ulcer presented as a bulla that later ulcerated and progressively expanded laterally. Examination disclosed a large, 6 × 8 cm, relatively flat ulcer, with a swollen necrotic base and a raised violaceous border (Fig. 1a). The patient had a 30-month history of generalized lymphadenitis. Laboratory tests revealed hypergammaglobulinaemia (2.1 g/dl, normal 0.7–1.6) as well as elevated ACE (angiotensin converting enzyme) (60 mg/dl, normal <52). A chest X-ray showed bilateral hilar lymphadenopathy. Infections, such as tuberculosis and malignancies had been excluded. A biopsy specimen of an inguinal lymph node showed granulomatous infiltration and led to the diagnosis of sarcoidosis. Histological examination of a skin biopsy from the border of the ulcer revealed necrotizing inflammation with perivascular infiltration of neutrophils, consistent with the diagnosis of PG. The patient was treated with prednisolone at a dose of 75 mg/day, which resulted in resolution of lymphadenopathy over the next 8 weeks, but only partial control of PG. The addition of colchicine at a dose of 2 mg/day led to rapid healing of the skin ulcer. The prednisolone dosage was gradually reduced, and finally stopped. The patient continued therapy with colchicine and no relapse occurred during a follow-up period of 6 months (Fig. 1b).

DISCUSSION

PG is a chronic, non-infective, cutaneous necrosis, presenting as a painful nodule, pustule or haemorrhagic



Fig. 1. (a) Pyoderma gangrenosum on the lower right leg before treatment and (b) healing with scarring 6 months after treatment with prednisolone and colchicine.

bullae, which then breaks down to form a progressively enlarging ulcer (1, 2). The histopathologic changes are not pathognomonic, but show features of a large sterile abscess formation, capillary thrombosis, haemorrhagic necrosis and massive cell infiltration consisting of the predominant cells of PG, the neutrophils.

PG is usually associated with underlying diseases, including ulcerative colitis, Crohn's disease, arthritis (rheumatoid arthritis, Felty's syndrome, osteoarthritis), immunological diseases (congenital and acquired hypogammaglobulinaemia, selective IgA deficiency), haematological malignancies (leukaemia, multiple myeloma, lymphoma) and, less frequently, with chronic active hepatitis, thyroid gland diseases, chronic obstructive pulmonary diseases, atrophic gastritis, systemic lupus erythematosus and Takayasu's arteritis.

The coexistence of PG and sarcoidosis is rare: excluding our case, only 3 similar cases have been reported in the literature (4, 5). The frequent association of PG with immunological diseases and the numerous humoral and cell-mediated defects reported in association with PG, such as the increased TNF- α production, abnormal T-cell regulation and failure of phagocytosis by monocytes, provide evidence of an altered immunological reactivity as a pathogenetic factor of the disease (1, 2). Additionally, in sarcoidosis, there is a large number of immunological disturbances such as CD8 T-cell dysregulation with an abnormal CD4/CD8 ratio, abnormalities of monocytes, macrophages and increased adherence of T-lymphocytes to fibroblasts (5–7). Abnormal chemotaxis and phagocytosis, cutaneous anergy and T-cell abnormalities as well as the development of new lesions following trivial trauma are common features in both entities, and offer a possible explanation for the coexistence of the two diseases.

Drugs of choice for the treatment of PG are systemic corticosteroids, which are usually administered in relatively high doses (prednisone 60–80 mg daily) (1, 2, 4). However, low-dose administration of corticosteroids in patients with sarcoidosis may contribute to the appearance of PG, as this has been reported in 2 out of 3 cases in the literature (4). Cyclosporine is often dramatically effective in the treatment of PG, but we did not use this agent since there are reports that cyclosporine may worsen the underlying sarcoidosis

(3). Colchicine is an alternative therapy for PG (8) providing satisfactory results, as in our case. Colchicine has also been used in the treatment of sarcoidosis (9). Colchicine inhibits microtubule synthesis during cell activation and decreases phagocytosis and neutrophil chemotaxis. Moreover, this agent affects the production, intracellular transport and secretion of cytokines in lymphocytes and macrophages, down-regulates TNF receptors and prevents the migration of inflammatory cells into damaged tissues (8–10).

In conclusion, our case suggests a possible relation between PG and sarcoidosis. Although steroids are the mainstay of systemic therapy in PG, colchicine is worth considering for refractory cases.

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