Pyoderma gangrenosum is a rare, chronic ulcerative skin disease. It is a diagnosis of exclusion, after ruling out other causes of cutaneous ulceration. The etiology of pyoderma gangrenosum is poorly understood but is likely multifactorial. We describe 2 families affected by ulcerative pyoderma gangrenosum. This familial clustering suggests a possible genetic role in the development of pyoderma gangrenosum in some cases.

Pyoderma gangrenosum is a rare, chronic ulcerative skin disease. No specific laboratory or histologic tests confirm the diagnosis. Pyoderma gangrenosum is a diagnosis of exclusion, after ruling out other etiologies of cutaneous ulceration such as infectious, malignant, vasculitic, and factitial. Four distinct clinical variants of pyoderma gangrenosum have been described: ulcerative (classic), pustular, bullous, and vegetative.1 Ulcerative pyoderma gangrenosum characteristically presents on the lower extremities or trunk, often in sites of previous trauma (pathergy). The earliest lesion is a pustule that typically persists and develops into a large painful ulcer, with erythematous-to-violaceous undermined, rolled borders. Satellite violaceous papules or pustules may fuse with the ulcer as it expands. Although pyoderma gangrenosum has been reported in otherwise healthy people, 50% of the cases are associated with underlying hematologic, gastrointestinal, and arthritic disorders.2-4 To our knowledge, 3 families with pyoderma gangrenosum, which was not associated with underlying systemic disorders, have been reported previously.5-7 We describe 2 additional families affected by idiopathic ulcerative pyoderma gangrenosum.

Case Reports

Patient 1—In 1993, a healthy 23-year-old white man injured his right shin with a tow truck motor. The initial superficial injury subsequently ulcerated. Before presentation at our clinic, the patient had received multiple unsuccessful treatments, including tetracycline, dapsone, prednisone, and isoniazid. A split-thickness skin graft in August 1997 failed. The patient reported a history of minor trauma precipitating small ulcers before healing but denied a history of inflammatory bowel disease or arthritis. Additionally, there was no family history of inflammatory bowel disease, connective tissue diseases, or diabetes mellitus. However, family history was significant for pyoderma gangrenosum, occurring in his brother, maternal uncle, and maternal great uncle (Figure 1). On presentation in June 1998, an 11×10-cm dry ulcer with a rolled violaceous border was present on the right medial calf (Figure 2). The findings from antinuclear antibody (ANA), rapid plasma reagin, and hepatitis profile were normal. Results from complete blood cell count, serum chemistries, protein C, α1-antitrypsin, CH50, and serum protein electrophoresis were within normal limits. A culture of the ulcer grew coagulase-negative Staphylococcus. Despite aggressive treatment (eg, multiple skin grafts, various intravenous and oral courses of antibiotics [dicloxacillin, levofloxacin, tetracycline, and rifampin], multiple immunomodulating medications [colchicine, cyclosporine, azathioprine, cyclophosphamide, mycophenolate, high-dose pulse steroids, thalidomide, leflunomide, and infliximab]), the ulcer on the patient’s right medial calf persists.

Patient 2—In 1994, the otherwise healthy 22-year-old brother of patient 1 developed nonhealing ulcers on his lower extremities. The patient denied any trauma at the involved sites. During the next 3 months, the ulcer on the right lower extremity healed spontaneously, but the left leg ulcer persisted. The patient reported a history of stable vitiligo on his hands and feet since 9 years of age but denied a history of hematologic,
gastrointestinal, or arthritic disease. The findings from the physical examination in March 1996 revealed a 4×4.5-cm ulcer with violaceous border and surrounding erythema on the left medial shin (Figure 2). Biopsy results of the ulcer demonstrated epidermal ulceration with an inflammatory infiltrate of neutrophils and mononuclear cells. Cultures of the biopsy specimen demonstrated moderate growth of coagulase-positive *Staphylococcus*. Cultures tested negative for acid-fast bacilli and fungus. Results from the hepatitis profile and ANA were normal. Also, complete blood cell count, complement, and immunoglobulin levels were within normal limits. During the next 3 years, the patient improved minimally with therapies including doxycycline, cephalosporin, erythromycin, systemic steroids, topical antibiotics, and multiple split-thickness skin grafts.

**Patient 3**—A 56-year-old white woman presented in August 1997 with a 10-month history of an ulcer involving the left lower abdominal quadrant. The patient denied any trauma to the site but reported that tape stripping dressings induced adjacent papules to break down and become persistent ulcers. Her medical history was significant for a left total knee replacement, complicated by an infection that required removal of the prosthesis. Her medical history was significant for a left total knee replacement, complicated by an infection that required removal of the prosthesis. The patient denied any medical history of inflammatory bowel disease or connective tissue disease. Of interest, the patient's mother had a history of a nonhealing ulcer in an abdominal scar. On examination, a 3×2-cm ulcer with a violaceous border was observed on the left lower abdominal quadrant. Results of polymerase chain reaction demonstrated the presence of *Chlamydia pneumoniae* in the serum. Despite treatment with rifampin, trimethoprim-sulfamethoxazole, amoxicillin, isoniazid, and aggressive local wound care with alternating topical antibiotics (bacitracin, mupirocin, and metronidazole), the patient's ulcer persists.

**Patient 4**—In 1989, the then 65-year-old mother of patient 3 presented to our clinic complaining of a nonhealing ulcer with an undermining and purplish rolled border at a previous surgical site. Four months previously, the patient underwent an elective abdominal panniculectomy, and the surgical site never completely healed. Therapy with oral tetracycline and local wound care with neomycin and mupirocin were unsuccessful. The patient's medical history was significant for diabetes mellitus, cholecystectomy, and large cell lymphoma of the stomach. The patient's lymphoma was believed to be in remission, after undergoing a partial gastrectomy and completing 4 courses of chemotherapy 13 months before the panniculectomy. The patient denied a history of connective tissue disease.

---

**Figure 1. Genogram of patients 1 and 2.**
tissue or inflammatory bowel disease. Results of the physical examination revealed 2 deep ulcerated areas with rolled violaceous borders and a serosanguinous base. Subcutaneous erythematous nodules measuring 1 to 2 cm in diameter surrounded the ulcers. Results of cultures of the nonhealing wound were negative for bacteria, acid-fast bacilli, and fungus. Results of a biopsy of the ulcer completed at another institution indicated an inflammatory infiltrate with mononuclear cells and neutrophils but no evidence of large cell lymphoma. After surgical excision and oral colchicine therapy, the ulcers finally healed 3 months later.

**Comment**

Each of the patients described above was affected by a chronic ulcerative process clinically and/or histologically compatible with pyoderma gangrenosum. Laboratory data failed to demonstrate other etiologies of cutaneous ulceration or underlying systemic disease. In all 4 cases, the patients exhibited the typical clinical features of pyoderma gangrenosum—a chronic nonhealing ulcer with violaceous rolled border. Three of the 4 cases exhibited pathergy. All 4 patients had an unrelenting course despite aggressive therapy. In particular, the ulcer described in patient 1 persisted despite aggressive use of immunosuppressive agents and various antibiotic regimens.

Pyoderma gangrenosum was described first in 1930 yet remains a poorly understood disease. It appears to be a multifactorial process, with the common finding of immune surveillance abnormalities. Both humoral and cell-mediated defects have been reported in association with pyoderma gangrenosum. Congenital humoral defects include hypogammaglobulinemia, hyper-immunglobulin E syndrome, and autoantibody production against the skin and gastrointestinal tract. In addition, cell-mediated abnormalities described are defective neutrophil function, impaired lymphocyte activity, cutaneous anergy, and congenital deficiency of leukocyte-adherence glycoproteins. Recently, a chronic infection with C pneumoniae has been proposed as a possible etiologic factor in the pathogenesis of some patients with previously idiopathic pyoderma gangrenosum.

Familial clusters of pyoderma gangrenosum-like lesions suggest a possible genetic role in disease development in some patients. Yet to be elucidated, inherited and acquired immune surveillance abnormalities, in combination with persistent infection, may lead to chronic pyoderma gangrenosum-like ulcerations. Study of these kindred and the 3 other families with
pyoderma gangrenosum is needed to clarify its pathogenesis. Our experience has shown that familial ulcerative pyoderma gangrenosum is associated with an aggressive and persistent course.

REFERENCES