

CASE REPORT:

Pyoderma gangrenosum associated with melanoma

Pyoderma gangrenosum – a rare, neutrophilic dermatosis – is associated with diseases including inflammatory bowel disease, arthritis and haematologic disease. This case story describes an unusual association between pyoderma gangrenosum and malignant melanoma. Clinicians should consider malignant melanoma in all patients with pyoderma gangrenosum.



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P pyoderma gangrenosum (PG) is a rare, non-infectious, ulcerating, neutrophilic dermatosis, that most frequently affects the lower extremities of adults aged 25–54 years.^[1,2]

There are four main clinical types of PG: (i) ulcerative; (ii) pustular; (iii) bullous; and (iv) vegetative (2). In addition, peristomal PG is known.^[2,3] These variants of PG can be linked to specific associated conditions in approximately 50% of patients.^[2] The most common associated diseases are inflammatory bowel disease (IBD), arthritis and haematologic disease.^[1,4,5]

In the present case, we describe a female patient with PG associated with malignant melanoma as an unusual clinical presentation. We emphasize the importance of diagnosing the PG-associated diseases in time and initiating the necessary treatment.

CASE REPORT

In June 2010 a 59-year-old woman was referred to the authors' institution with a 14-day history of spontaneously developed, large, exuding wounds on her legs. The patient reported a sore, slightly elevated bruising on the left lower leg as the initial area of concern. A couple of days later, she developed similar bruising over her right hip. During the days that followed, these two areas deteriorated into large, exuding wounds: a 10 cm x 10 cm ulcer, sharply defined with a red–purple edge on the left lower leg [FIGURE 1]; and a 12 cm x 10 cm ulcer on the right hip – similar in appearance to the one on the lower leg, but more necrotic.

On presentation to the authors' institution, thorough physical examination of the patient

revealed no pathological findings, beyond the described skin changes.

The ulcers were clinically suggestive of PG. After blood samples and a skin biopsy were taken, treatment with prednisolone (40 mg per day) and painkillers was commenced. Wound care with local steroids, foam dressings, and absorbent bandages (changed daily) was also undertaken.

Laboratory tests included complete differential blood count, electrolytes, liver enzymes, Wassermann reaction, antinuclear antibody, rheumatoid factor, antineutrophil cytoplasmic antibodies, immunoglobulines, and urine analysis. The aberrant blood samples showed elevated C-reactive protein (CRP) of 126 mg/L, and erythrocyte sedimentation rate of 68 mm/hour, thrombocytes of 622 x 10⁹/L, leukocytes of 22 x 10⁹/L with a predominance of neutrophils of 19 x 10⁹/L, and microcytic anaemia with a haemoglobin level of 6.2 mmol/L.



Figure 1. Pyoderma gangrenosum on the patient's left lower leg (10 cm x 10 cm) at presentation. Note the sharply defined, red–purple wound edge.

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A 6-mm punch biopsy taken from the edge of the lower-leg ulcer showed necrosis and inflammatory dermal infiltrates composed of mature neutrophils, compatible with PG. A computed tomography scan of the chest-abdomen-pelvic and bone marrow biopsy revealed no underlying disease.

Two days after presentation, the ulcer on the lower leg had increased in size to 13 cm x 10 cm. There were no signs of infection in either wound. CRP had decreased to 22 mg/L, erythrocyte sedimentation rate to 33 mm/hour, and leukocytes to 16.6 x 10⁹/L. A week after commencement of treatment no further reduction in ulcer size had been achieved on either the lower leg or hip. Local treatment of the wound was betamethasone cream with chionoform cream with a nonadherent, absorbent dressing.

In July 2010, 5 weeks after the first presentation to the authors' institution, treatment with azathioprine (dose escalation to 200 mg per day) was commenced, phasing out prednisolone and within a couple of months and the wounds showed marked improvement. The wounds were treated locally with a zinc ointment to the periwound area and a foam dressing. Granulation began and there was an initial epithelialization.

In March 2011, the patient presented to her GP with skin alteration on the back and swelling in the armpit. After excision, she was diagnosed with malignant melanoma. She was confused and magnetic resonance imaging revealed cerebral metastases. Treatment with azathioprine was discontinued and intravenous steroids commenced.

The patient died in May 2011.

DISCUSSION

PG lesions are described as painful, sharply outlined, necrotic ulcers, creating haemorrhagic or purulent exudates, and with undermined, violaceous borders and a surrounding zone of erythema.^[6] PG is a clinical diagnosis; there is no specific histological or serological marker for the condition that can alone provide the diagnosis.^[5] However, histologically, PG is characterised by the presence of inflammatory dermal infiltrates with a predominance of mature neutrophils.^[7]

Local wound care of PG is important to improve conditions for healing and prevent secondary bacterial infection. The ulcers should be cleansed daily and application of potassium permanganate solution or silver sulphadiazine cream can be helpful.

Topical potent corticosteroids are useful to reduce the irritation in the skin surrounding the ulcer. Nonadherent foam dressing are recommended.^[3]

The systemic diseases associated with PG are seen in approximately 50% of the overall cases of PG, but in patients with the ulcerative type of PG they occur in >70% of patients.^[2]

Ahronowitz et al^[5] report IBD to be the most common PG-associated disease, followed by arthritis, haematologic abnormalities, and haematologic malignancies. Other associations listed as rare or questionable include hidradenitis suppurativa, pyogenic arthritis–pyoderma gangrenosum–acne syndrome, pulmonary disease, systemic lupus erythematosus, thyroid disease, solid organ malignancy, autoimmune hepatitis, and sarcoidosis.^[5] The most common malignant disease associated with PG is haematologic malignancy,^[5] this is seen in up to 7% of PG cases – predominantly acute myeloid leukemia, which has a 1- year mortality rate as high as 75%.^[8]

In the present case, the authors describe PG in association with malignant melanoma. The global incidence of cutaneous melanoma is increasing.^[9,10] Melanoma, which commonly spreads via the central nervous system (CNS), is challenging to treat due to the lack of active systemic agents and the limited CNS penetration of available agents. Consequently, a poor prognosis is associated with CNS metastasis from malignant melanoma.^[11]

This patient with PG reported here subsequently developed cancer and died of metastatic disease. The presence of both these diseases concomitantly may be unrelated. However it could be postulated that there is a link and it may be worth thinking about malignancy, when a patient develops PG with no other related systemic disease. It is suggested that immunosuppressive treatment increases the risk of skin cancer, however this is usually related to non-melanoma skin cancer and the long-term administration of immunosuppressive treatment in transplant patients.^[12]

CONCLUSION

This case describes an unusual and worrying clinical scenario that suggests underlying malignancy should be considered in PG cases. The increasing incidence of cutaneous melanoma means that presentations associated with PG may become more common and clinicians should be vigilant. ■

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Expert commentary

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Ppyoderma gangrenosum is an ulcerative, cutaneous condition that usually occurs on the legs. Ulcers initially look like small insect bites or papules, progress to become larger wounds, and frequently become chronic. Patients of any age may be affected by the condition, but it predominantly occurs in the fourth and fifth decades of life. Though mortality is rare and the prognosis generally good, pyoderma gangrenosum causes pain, scarring, and often recurs.

Pyoderma gangrenosum does not have characteristic serologic or histologic features. Thus, all other potential causes of similar lesions must be excluded prior to making a diagnosis of pyoderma gangrenosum. Other causes of cutaneous ulceration that is similar in appearance to pyoderma gangrenosum include infection, malignancy, vasculitis, collagen vascular diseases, diabetes, and trauma.

The aetiology of pyoderma gangrenosum is still vague, but dysregulation of the immune system is suspected to be a major feature and the condition is associated with underlying systemic diseases in half of cases.^[1] Ascertaining the underlying systemic condition associated with a given case of pyoderma gangrenosum can be clinically challenging.

There is no consensus on the treatment of pyoderma gangrenosum, due in part to the rarity of the condition itself. Systemic medications that have been successfully used in treatment include corticosteroids, sulfasalazine, dapsone, thalidomide, minocycline, clofazamine, mycophenolate mofetil, cyclosporine, intravenous immunoglobulin, cyclophosphamide, and biologic medications.^[2] To date, only one controlled, clinical trial has been published that reports the safety and efficacy of infliximab – an antitumor necrosis factor monoclonal antibody – for the treatment of pyoderma gangrenosum.^[3]

Although there are some reports of successful flap coverage, sites of pyoderma gangrenosum-induced ulceration are not generally considered good candidates for skin grafts. Further skin breakdown at the harvest site is also a clue to diagnosis, and pathology is often seen.

Given these limitations, the current treatment strategy for pyoderma gangrenosum is to:

1. Reduce inflammation by multiple modalities, and
2. Optimise wound healing by conservative methods.

The case report provided here by Carøe and Fogh demonstrates the difficulties of treating pyoderma gangrenosum. The diagnostic approach and treatment strategy used were in accordance with currently accepted strategies. Although it is difficult to determine whether the malignant melanoma played a role in the formation or aggravation of the ulcer in this case, malignancy should be evaluated as a possible underlying cause of pyoderma gangrenosum.

The authors should be congratulated for their efforts in treating this difficult condition, and for their vigorous search for the underlying cause. ■

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