Rare disease

Pyoderma gangrenosum

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Summary

A 3.5-year-old girl presented with skin lesions beginning as a small pustule that progressed to very painful large ulcer with rolled up edges and irregular borders. At presentation, active ulcers were present over the left elbow. There were healed ulcers with scarring present on the chest, back, both thighs and abdominal wall.

This child had negative antinuclear antibody, cytoplasmic antinuclear cytoplasmic antibody, antiphospholipid antibodies and tests for hepatitis B and C. She did not have any symptoms to suggest ulcerative colitis. Her colonoscopy was absolutely normal. Histopathology from her skin lesion was consistent with pyoderma gangrenosum.

BACKGROUND

Pyoderma gangrenosum (PG) presents usually in adults and is secondary to an underlying disease in >50% of cases. It is very rare in children. We present a 3.5-year-old girl who had clinical features of PG and an associated underlying disease was excluded by appropriate investigations.

CASE PRESENTATION

A 3.5-year-old girl presented with skin lesions and scarring over the chest and leg for a period of 1 year. She was apparently well a year back when she developed a pustule over the back and upper part of the chest that ruptured spontaneously forming an ulcer, which was extremely painful. She was treated by a local practitioner in her village, with local applications (details of treatment not available) without any response. Ulcer gradually increased in size and in due course healed with scarring. She had developed more such lesions in various parts of her body. The patient was then admitted to a hospital for 4 months as a case of non-healing ulcer, and a split skin graft was planned for her but could not be done for some reasons.

There was a history of appearance of new lesions on trivial trauma. There was no history of drug intake prior to the onset of her illness. Family histories were unremarkable.

Examination revealed an anaemic child with all anthropometric data below the third percentile. All vital parameters were within normal limits.

There were large scars present over the chest (figure 1), back, abdominal wall and thighs. She had ulcers over the left elbow (figure 2). The ulcers were large with irregular borders and rolled up edges. The base of the ulcer was covered with necrotic material. During her stay with us, she developed a small pustule over the dorsum of the right foot (figure 3). There were no joint swellings.

Systemic examination was unremarkable.

INVESTIGATIONS

Complete blood count showed increased total white blood cell count with neutrophilic response and the red cell indices were suggestive of iron deficiency anaemia.

Antinuclear antibody, cytoplasmic antinuclear cytoplasmic antibody (c-ANCA), antiphospholipid antibody, hepatitis surface antigen and anti-hepatitis C virus were negative. Enzyme-linked immunosorbent assay for HIV I and II was negative. Liver profile was normal.

Urinalysis and chest x-ray were also normal and so was colonoscopy.

Skin biopsy showed chronic suppurative inflammation. A moderately dense superficial and deep lymphoplasmocytic infiltrate was present around the vessels. Overlying epidermis showed psoriasiform hyperplasia. Abundant fibroplasia was present in the dermis. A few loci of suppuration were also present especially around a hyperplastic follicular infundibulum.

In view of the clinical features, these findings were consistent with PG (figure 4).

DIFFERENTIAL DIAGNOSIS

PG is a diagnosis of exclusion. The misdiagnosis of PG can have serious consequences. Treatment directed at PG with high-dose prednisone or other immunosuppressive medications may be contraindicated in patients with any of several diseases that may produce ulceration resembling that of PG, such as infectious or malignant processes.

The differential diagnosis of PG includes vasculitis, thrombophilic conditions, malignancies, other inflammatory diseases and infections.¹ The forms of systemic vasculitis most likely to cause skin ulcers are polyarteritis nodosa, the types of vasculitis associated with ANCA and mixed cryoglobulinemia² (usually associated with hepatitis C). Thrombophilic states that can be confused with PG include livedoid vasculitis (atrophie blanche) and the antiphospholipid syndrome.

Figure 1 Healing with cribriform scarring.

TREATMENT

Besides local wound care and topical applications, this child was started on prednisolone in the doses of 2 mg/kg body weight. Since the family could not afford steroid-sparing drugs, they were not added.

The child showed good response to treatment and within 4 days the ulcer on the left elbow started to heal (figure 5) and the lesion that appeared during her hospital stay (figure 3) did not progress to ulceration.

DISCUSSION

PG is rare in children and more so in infants younger than 1 year.³ The cause of PG is unknown, but some studies have

suggested that abnormal neutrophil chemotaxis is the primary process.⁴

We report PG in a 3.5-year-old girl without any associated disorders, which was well controlled with oral prednisone. This entity in children usually presents with multiple lesions, mainly located on the face, buttocks, thighs and extremities, which, in some instances, are associated with pathergy. PG in infants has a good response to therapy and healing is usually achieved.

PG is an inflammatory condition of the skin first described by Brunsting and colleagues in 1930.⁵ PG begins as a pustule or vesiculopustule that progresses to an ulcer or deep erosion with violaceous overhanging or undermined borders.

Figure 2 Typical ulcer.

Figure 3 Skin lesion beginning as a pustule.

Criteria for the diagnosis of PG

Major criteria

- ▶ Rapid progression of a painful necrolytic cutaneous ulcer with an irregular, violaceous and undermined border

- ▶ Exclusion of other causes of cutaneous ulceration.⁶

Minor criteria

- ▶ History suggestive of pathergy or clinical finding of cribiform scarring

Figure 4 Skin biopsy showing changes consistent with PG.

Figure 5 Ulcer showing healing.

- ▶ Systemic diseases associated with PG
- ▶ Histopathologic findings (sterile dermal neutrophilia ±mixed inflammation ±lymphocytic vasculitis)
- ▶ Treatment response (rapid response to systemic glucocorticoid treatment).

The histopathologic findings in PG are not specific and the biopsy cannot be diagnostic (in and of itself) of PG. The principal importance of biopsy, which should not be deferred because of concerns of potentially extending lesions through pathology, is to exclude other diseases. Although vascular inflammation in lesions of PG is not uncommon, the histology is not that of a true vasculitis.⁷

There is currently no gold standard of treatment or published algorithm for choice of therapy. The majority of data come from case studies that lack a standard protocol not only for treatment administration but also for the objective

assessment of lesion response to a specific therapy.⁸ Once diagnosed, treatment should be directed first towards the underlying disease that is present (inflammatory bowel disease, especially ulcerative colitis, haematologic malignancy or paraproteinemia, Behçet disease, hepatitis, HIV, systemic lupus erythematosus).

Treatment strategies include pain control, local wound care, topical applications and systemic drugs.

Ulcerative PG is often treated initially with high-dose corticosteroids (prednisone 1–2 mg/kg/d), because of the rapidity of response in 2–3 days. Some ulcers may require months to years to fully resolve and/or are unresponsive to corticosteroids; other immunomodulators have been used. The next most commonly used agent, cyclosporine, can help act as a corticosteroid-sparing therapy. However, cyclosporine has its own side-effect profile that includes

renal toxicity with prolonged use. Its use should be restricted to patients with idiopathic disease. Given the side effects of immunosuppressants, intravenous immunoglobulin has also been tried in severe cases, though its cost becomes a major drawback.⁹

More recently, tumour necrosis factor- α blockers and other injectable biologics have been used with some success. Infliximab is the only biologic demonstrated to be efficacious in classic PG in a randomized, double-blind, placebo-controlled trial.¹⁰

A host of other biological agents, like etanercept, efalizumab, adalimumab and alefacept, have also been tried. The majority of data come from case studies that lack a standard protocol for either treatment administration or the objective assessment of lesion response to a specific therapy.

Learning points

- ▶ PG is a rare disorder. The lesions begin as pustule, progress to large painful ulcers and heal by scarring.
- ▶ In 50% of cases, underlying systemic disorder is associated. Ulcerative colitis, vasculitis and haematological malignancies are the common underlying disorders that should be excluded by appropriate tests.
- ▶ Skin biopsy should be done to exclude other causes.
- ▶ Treatment strategies include pain management, local care, topical applications and use of immunosuppressants.
- ▶ Biological agents have been recently used. Only infliximab has been tried in a well-controlled study.

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Competing interests None.

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REFERENCES

1. **Trent JT**, Kirsner RS. Diagnosing pyoderma gangrenosum. *Adv Skin Wound Care* 2001;**14**:151–3.
2. **Adachi Y**, Kindzelskii AL, Cookingham G, *et al*. Aberrant neutrophil trafficking and metabolic oscillations in severe pyoderma gangrenosum. *J Invest Dermatol* 1998;**111**:259–68.
3. **Schmid MH**, Hary C, Marstaller B, *et al*. Pyoderma gangrenosum associated with the secondary antiphospholipid syndrome. *Eur J Dermatol* 1998;**8**:45–7.
4. **Torrel A**, Colmenero I, Serrano C, *et al*. Pyoderma gangrenosum in an infant. *Pediatr Dermatol* 2006;**23**:338–41.
5. **Brunsting LA**, Goeckerman WH, O'Leary PA. Pyoderma gangrenosum: clinical and experimental observations in five cases occurring in adults. *Arch Derm Syphilol* 1930;**22**:655–680.
6. **Su WP**, Davis MD, Weenig RH, *et al*. Pyoderma gangrenosum: clinicopathologic correlation and proposed diagnostic criteria. *Int J Dermatol* 2004;**43**:790–800.
7. **Callen JP**, Jackson JM. Pyoderma gangrenosum: an update. *Rheum Dis Clin N Am* 2007;**33**:787–80.
8. **Miller J**, Yentzer BA, Clark A, *et al*. Pyoderma gangrenosum: A review and update on new therapies. *J Am Acad Dermatol* 2010;**62**:646–54.
9. **Cummins DL**, Anhalt GJ, Monahan T, *et al*. Treatment of pyoderma gangrenosum with intravenous immunoglobulin. *Br J Dermatol* 2007;**157**:1235–9.
10. **Brooklyn TN**, Dunnill MG, Shetty A, *et al*. Infliximab for the treatment of pyoderma gangrenosum: a randomised, double blind, placebo controlled trial. *Gut* 2006;**55**:505–9.

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