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CASE REPORT

Refractory pyoderma gangrenosum in Caucasian adolescent with Takayasu arteritis and life-threatening infections

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Abstract

Pyoderma gangrenosum (PG) in Caucasians with Takayasu's arteritis (TA) is uncommon. We described a case of refractory PG in an 18-year-old Caucasian man with TA since the age of 10 and was treated with corticosteroids, methotrexate, anti-TNF therapy (adalimumab), anti-CD20 therapy (rituximab), cyclophosphamide and most latterly tocilizumab and leflunomide. He has vascular stenosis complicated with renovascular hypertension and is steroid-dependent. He presented with a 6-week history of a left cheek rapidly enlarging lesion associated with pain, bleeding and purulent discharge not responding to flucloxacillin. Incisional biopsy suggested PG. He later developed similar lesions on the volar aspect of the right hand and at venepuncture sites. Despite topical immunosuppressive medication and high-dose pulsed intravenous methylprednisolone, the left cheek lesion continued to grow rapidly. These painful, unsightly ulcers caused significant psychosocial stress and limited his daily life. Following a multidisciplinary team (MDT) discussion, tocilizumab was switched to abrocitinib. While initial improvement of lesions was observed, he subsequently developed an acneiform eruption which evolved into PG and became superinfected with herpes zoster virus and *Staphylococcus aureus*, requiring hospitalisation for intravenous (IV) acyclovir and antibiotics. Following several MDT discussions, abrocitinib was discontinued and a new regimen consisting of ciclosporin, dapsone and enhanced frequency IV immunoglobulin (IVIg) every 2 weeks was initiated, effectively stabilising his PG. This case highlights the rare association of PG and TA in Caucasians, the complexities of managing PG complicated by severe infections and underlying immunodeficiency, and the significant psychosocial burden of PG.

KEYWORDS
Caucasian, immunodeficiency, pyoderma gangrenosum, Takayasu's arteritis

Ting Fong Yeo and Sofia Labbouz contributed equally to this study.

INTRODUCTION

Pyoderma gangrenosum (PG) is a noninfectious, inflammatory, neutrophilic dermatosis that causes painful, necrotic, cutaneous ulcers. Steroids and immunosuppression remain the mainstay of treatment.

CASE REPORT

This 18-year-old Caucasian teenager presented with a 6-week-old lesion on his left cheek that started as a small, crusted papule enlarging rapidly, associated with pain, bleeding and purulent discharge. Examination revealed a

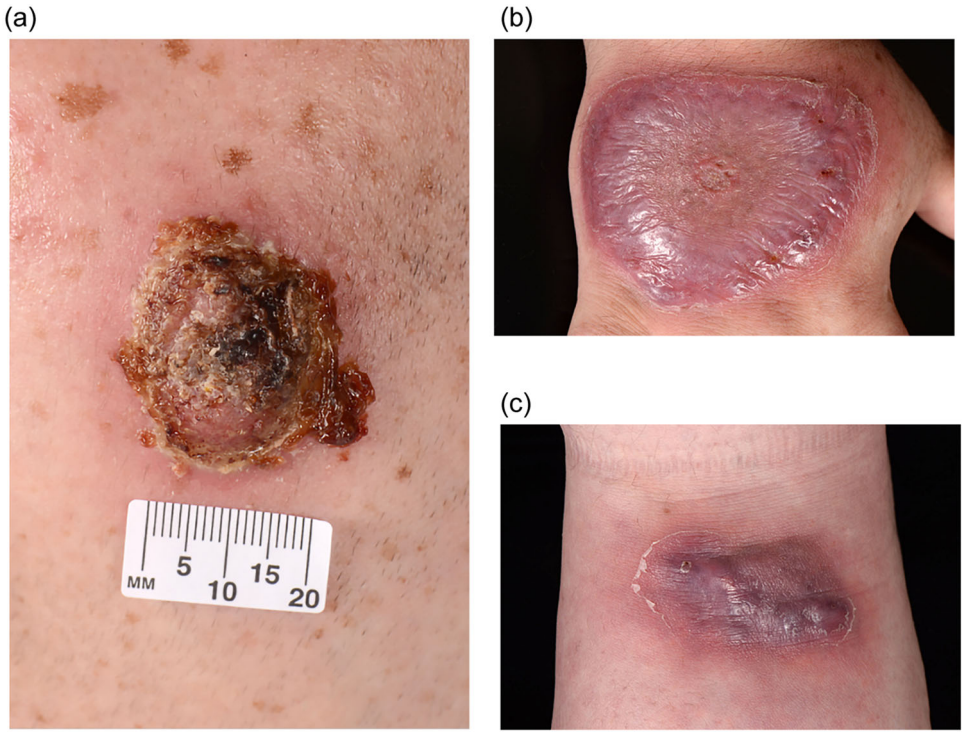

FIGURE 1 (a) 3 cm × 2 cm plaque on the left cheek with haemorrhagic crust and inflamed border. (b) Initial lesion on the dorsum of the right hand. (c) New lesion after minor trauma to the left foot dorsum.

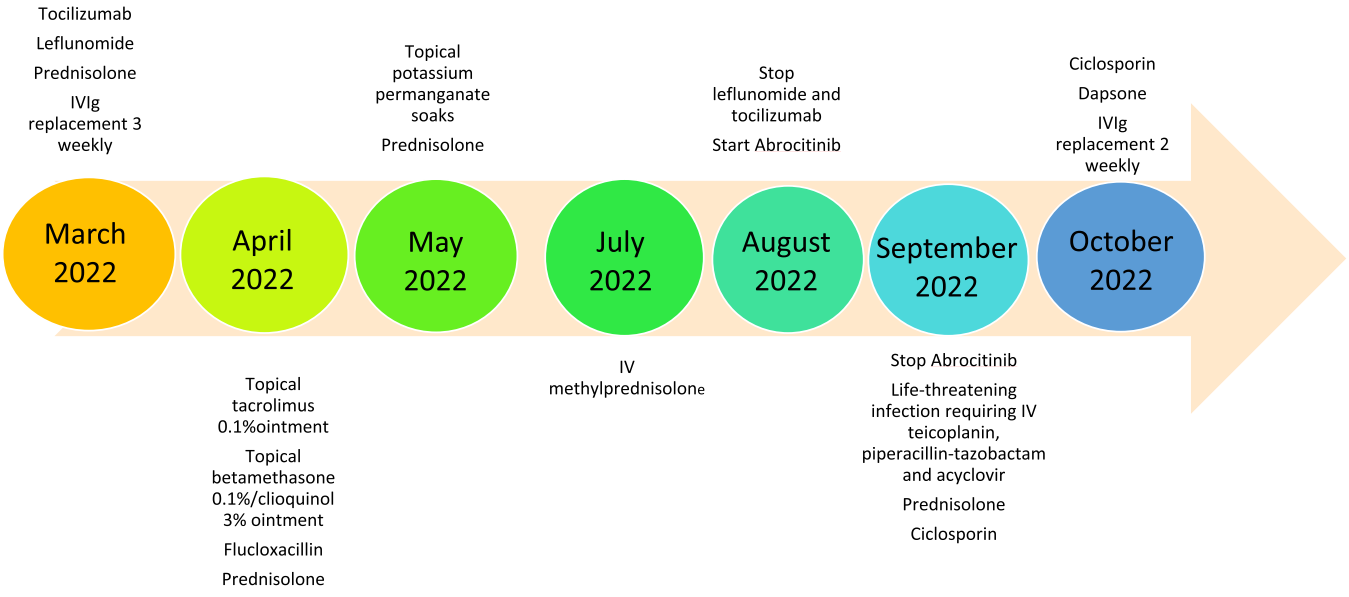

FIGURE 2 Treatment summary.

3 cm × 2 cm plaque with a haemorrhagic crust and inflamed border (Figure 1a). Initial treatment with 2% fusidic acid cream and a course of oral flucloxacillin (Figure 2) in primary care had no effect. He developed similar enlarging lesions on the dorsum of the right hand (Figure 1b) and dorsum of the left foot (Figure 1c) secondary to minor trauma.

At age 10, he was diagnosed with Takayasu's arteritis (TA) with resultant vascular stenosis and renovascular hypertension, treated with various therapies, including anti-TNF factor inhibition (adalimumab), anti-CD20 therapy (rituximab), cyclophosphamide and methotrexate. At the time of presentation, he was on prednisolone 10 mg daily, tocilizumab 162 mg weekly and leflunomide 10 mg daily (Figure 2). He had secondary hypogammaglobulinemia following previous rituximab treatment and was receiving IVIg replacement therapy every 3 weeks.

Left cheek biopsy showed inflammation surrounding neighbouring folliculitis (Figure 3a), suggesting PG with the PARACELSUS score of 12.[1] Despite topical treatment (tacrolimus 0.1% ointment, betamethasone 0.1%/

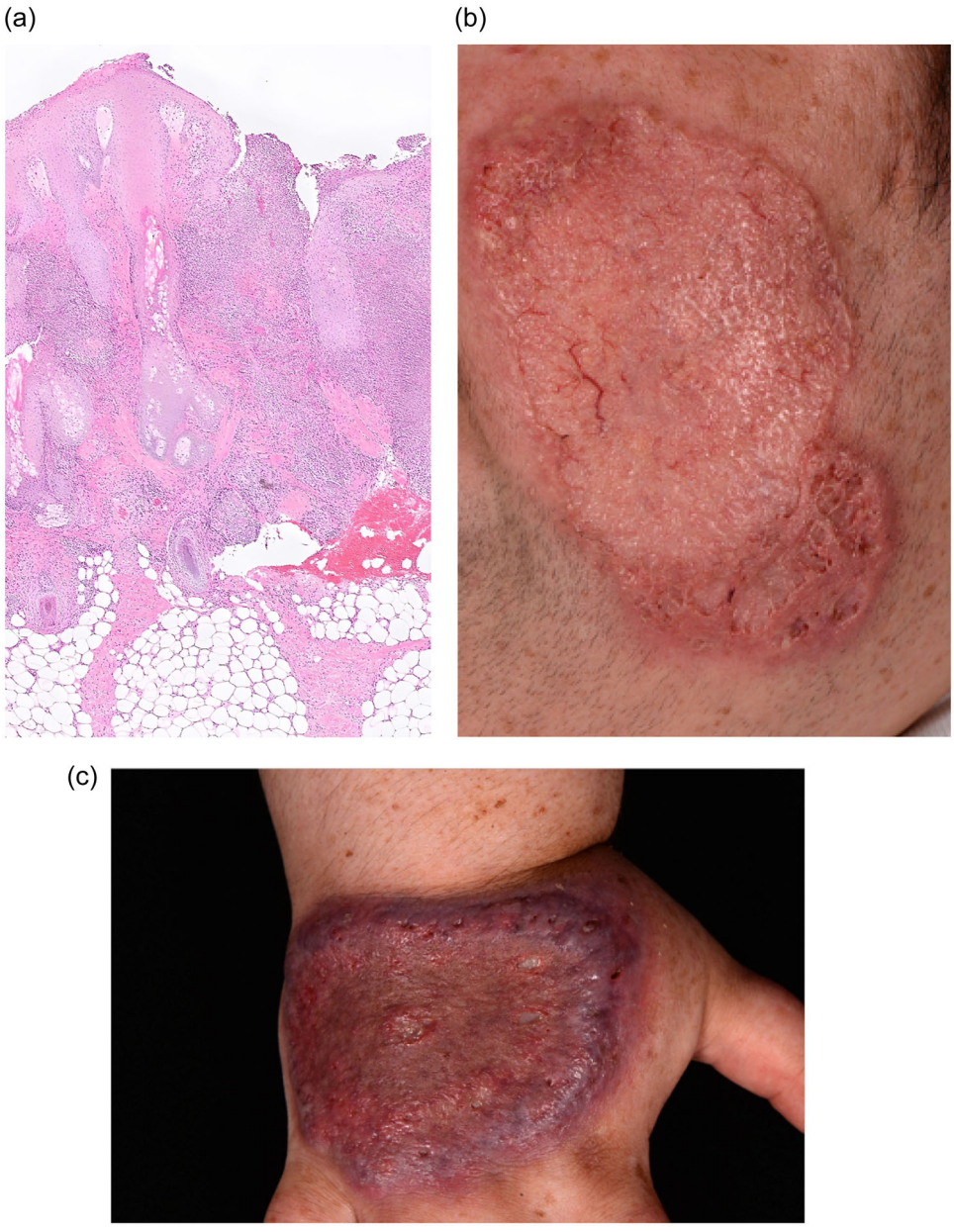

FIGURE 3 (a) Incisional biopsy of left cheek lesion. An ulcer occupies the entire thickness of the dermis and inflammation is centred around neighbouring follicles. The dermis shows predominantly neutrophilic infiltrates (haematoxylin and eosin stain, original magnification ×2). (b) Left cheek PG increasing in size. (c) Right-hand dorsum PG worsened with an inflamed border. PG, pyoderma gangrenosum.

clioquinol 3% ointment), increased dose of prednisolone 20 mg daily and IV methylprednisolone, the left cheek PG grew to 11 cm × 6 cm (Figure 3b) and the lesion on the right hand worsened, measuring 9 cm × 6.5 cm (Figure 3c). This caused significant psychosocial distress as the non-healing wound limited the patient's social life.

Following an MDT discussion between dermatology, rheumatology and immunology teams, tocilizumab (which had been given intravenously latterly) was stopped. Abrocitinib, an oral selective Janus kinase (JAK)-1 inhibitor, was initiated at 100 mg daily (Figure 2) to minimise the risk of developing further pathergy-induced PG lesions through injections. His skin lesions improved significantly (Figure 4a–c). However, after a month, he developed an acneiform eruption, a likely side effect of abrocitinib, and more PG lesions across the face, neck and torso requiring hospital admission. Abrocitinib was discontinued, and IV teicoplanin, piperacillin-tazobactam and aciclovir (Figure 2) were started empirically. Following multiple MDT discussions, leflunomide was stopped with topical potassium permanganate soaks added. Ciclosporin 50 mg twice a day, dapsone 100 mg once a day and enhanced replacement IVIg (Figure 2) every 2 weeks were initiated and stabilised his PG.

DISCUSSION

TA is a rare, chronic granulomatous large vessel vasculitis of unknown aetiology that predominantly affects females and involves the aorta, its branches and pulmonary artery.[2] Skin manifestations occur in up to 28% of people with TA, with erythema nodosum more common in Caucasians[3] and PG more common in Asians.[4] There have been three reported cases of TA and PG in Caucasian women who developed PG before a diagnosis of TA,[2,5,6] but this is the first reported case of a male Caucasian teenager developing PG 10 years after a TA diagnosis. PG can occur at any time with TA, but it is more common when the vasculitis becomes more occlusive.[3]

PG can be challenging to treat and there are no standardised regimens for refractory cases. Some of the cytokines involved in the autoinflammatory process in PG act through the JAK/STAT pathway,[7] therefore JAK inhibitors (JAKi) may have a role in therapy-resistant PG. Tofacitinib (JAK-1/3 inhibitor), ruxolitinib (JAK-1/2 inhibitor) and baricitinib (JAK-1/2 inhibitor) have demonstrated promising results in previously published cases.[8–10] Abrocitinib with JAK-1 selectivity may provide a better safety profile.[11] JAKi have also shown

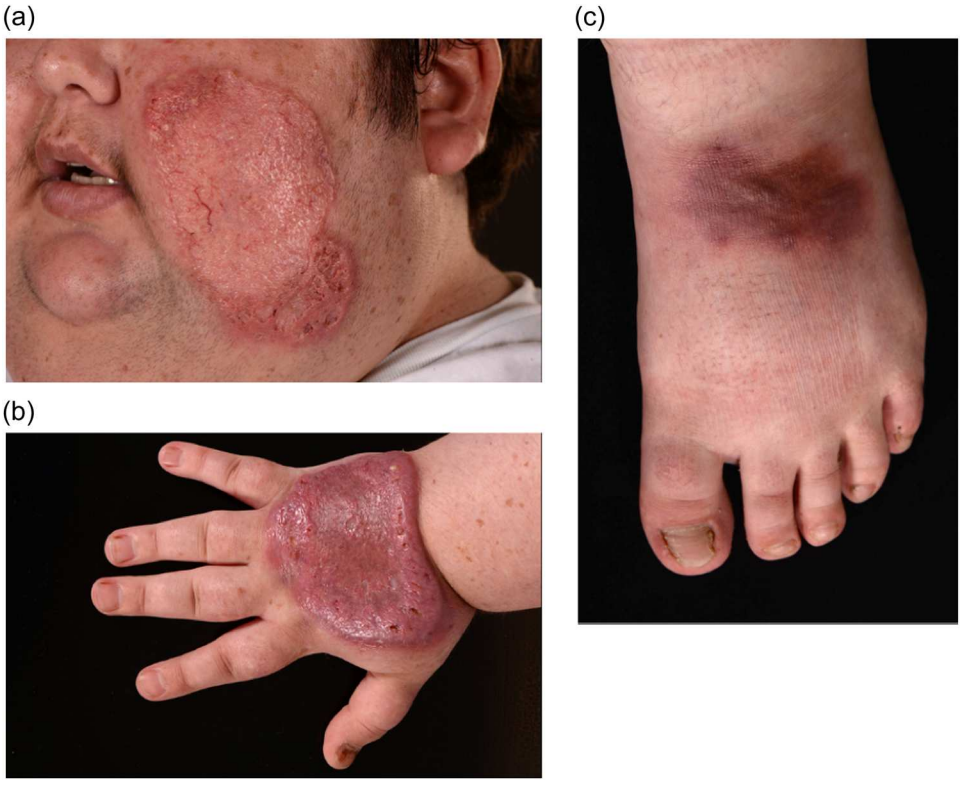

FIGURE 4 Significant improvement after the use of abrocitinib. (a) Left cheek PG decreased in size. (b) Right-hand PG with improving inflammation. (c) Left foot PG with good healing. PG, pyoderma gangrenosum.

effectiveness in treating refractory TA.[8–10] A recent study[12] demonstrated significant improvement in PG treatment with abrocitinib combined with cyclosporine. The combined use of ciclosporin,[13] oral dapsone[14] and enhanced IVIg replacement, which demonstrated effectiveness in previous studies, stabilised the progression of PG in our severely immunodeficient patient.

PG is a chronic, painful and unsightly dermatological disease that can significantly decrease quality of life (QoL). However, there is limited research on the QoL of patients with PG. The stigma associated with these skin lesions may lead to social isolation and diminished self-esteem. A higher prevalence of depression was demonstrated among PG patients than in the general population.[15] Effective treatment for PG should address the psychosocial consequences of the condition.[15]

In summary, we present a male Caucasian teenager with a rare association of PG and TA. Multiple treatment strategies were attempted to control his refractory PG and treat life-threatening infections. This case broadens the therapeutic options for refractory PG and stimulates further research on the role of JAKi in PG treatment. This case also emphasises the significant psychological impact of PG, highlighting the importance of further research assessing QoL in PG patients and developing a PG-specific QoL assessment tool.

AUTHOR CONTRIBUTIONS

Ting Yeo and Sofia Labbouz were responsible for the drafting of the text, sourcing and editing of clinical images, investigation results, drawing original diagrams and critical revision for important intellectual content. Nicholas Lawrance, Hemalatha Bhuvanai Sitaraaman, Rachel S. Tattersall and Michael J. Cork were responsible for the critical revision for important intellectual content. Rachel S. Tattersall and Michael J. Cork gave final approval of the manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data sets generated from the current study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

All patients in this manuscript have given written informed consent for participation in the study and the use of their deidentified, anonymised, aggregated data and their case details (including photographs) for publication. Ethical approval: Not applicable

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