

Pyoderma Gangrenosum Associated with Osteomyelitis in a Paediatric Patient

A Case Report

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ABSTRACT

Pyoderma gangrenosum is a rare ulcerative skin disorder mainly occurring in adults. It is seen less frequently in children. The cause is unknown but it may occur in association with several disorders. Osteomyelitis is a very rare association. We report a case of pyoderma gangrenosum associated with osteomyelitis in a two-year-old girl.

Pioderma Gangrenoso Asociado con Osteomielitis en un Paciente Pediátrico

Reporte de Caso

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RESUMEN

El pioderma gangrenoso es un raro trastorno cutáneo ulcerativo que se produce principalmente en adultos. Se observa con menos frecuencia en los niños. La causa es desconocida, pero puede ocurrir en asociación con varios desórdenes. Su asociación con la osteomielitis es rara. Reportamos un caso de pioderma gangrenoso asociado con osteomielitis en una niña de dos años de edad.

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INTRODUCTION

Pyoderma gangrenosum is a rare destructive inflammatory skin disorder usually seen in adults between the third and fifth decade of life. It occurs even more rarely in children. Lesions may be solitary or multiple and usually start as painful nodules or pustules which ulcerate to form a progressively enlarging ulcer with tender, raised, undermined, sometimes bluish edge. It is associated with various autoimmune diseases and responds to immunosuppressive therapy suggesting an immune-mediated pathogenesis. However, the aetiology is unknown and the pathogenesis remains unclear. Pyoderma gangrenosum may present in the absence of any apparent underlying disorder or in association with systemic disease. It is most commonly associated with arthritis, inflammatory bowel disease, haematological malignancies, monoclonal gammopathy and myeloma. Sterile chronic recurrent multifocal osteomyelitis is a rare association of neutrophilic dermatoses, which include pyoderma gangrenosum

and Sweet syndrome (1). We present a case of pyoderma gangrenosum associated with osteomyelitis in a two-year-old girl.

CASE HISTORY

A girl aged two years and eight months was referred for admission to hospital with a history of 'sores' on the limbs and scalp which ruptured to form rapidly enlarging, painful ulcers. Numerous doctors had been consulted and she had been treated with ketoconazole suspension, various oral and topical antibiotics and topical gentian violet with no improvement.

On examination, she was anxious, febrile with pale mucosae and bilateral cervical and inguinal lymphadenopathy. Significant findings were in the skin where she had multiple cutaneous ulcers ranging in size from 2 x 3 to 6 x 12 centimetres on the upper and lower limbs (Fig. 1) and a solitary lesion on the occipital scalp (Fig. 2). The edges were undermined and ragged and the bases were composed of granulation tissue, crusts and purulent exudate.

Routine laboratory investigations revealed that the patient had anaemia with a haemoglobin of 10g/dl and leukocytosis with white cell count of $12.2 \times 10^6/L$ with neutrophilia. The erythrocyte sedimentation rate was elevated at 33mm/hour (Westergren). Blood film showed moderate hypochromasia with mild microcytosis. Haemoglobin electrophoresis demonstrated haemoglobin A + A₂ and Venereal

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Fig. 1: Ulcer on right leg. Purple areas are due to gentian violet applied prior to admission

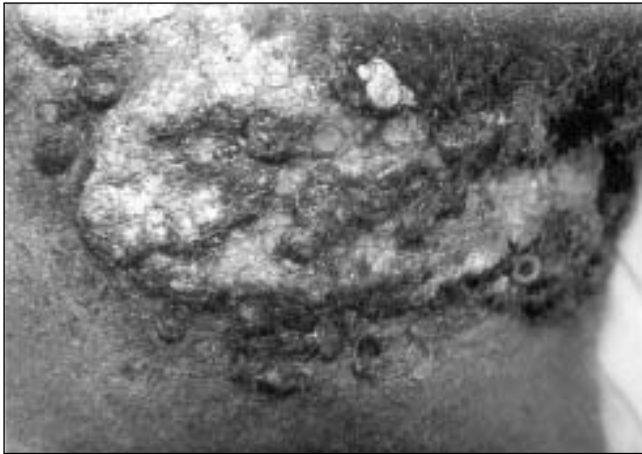


Fig. 2: Ulcer on occipital scalp.

Disease Research Laboratory (VDRL) test, antinuclear and rheumatoid factors were negative. Tests for the human immunodeficiency virus (HIV) and human T-cell lymphotropic virus type-1 (HTLV-1) infection were negative. Blood cultures showed no growth but bacterial swabs from the ulcers showed "a light growth of *Staphylococcus aureus*, *Klebsiella pneumoniae* and group D streptococcus", all sensitive to cefuroxime. Fungal cultures of samples from the ulcers were negative. Serum immunoglobulins, abdominal ultrasound, barium enema, barium meal and follow-through and chest roentgenogram were normal. Colonoscopy with mucosal biopsy was also normal.

Histology of a skin biopsy showed focal, necrotizing, suppurative inflammation with associated ulceration and peripheral lymphocytic infiltrates extending through the dermis and superficial subcutaneous tissues. Necrotizing vasculitis, however, was not observed. The changes were consistent with pyoderma gangrenosum. The patient was commenced on cefuroxime intravenously and oral prednisone 40

mg on alternate days. The lesions started to show signs of healing and epithelialisation although the edges still appeared active.

On day 15 of admission, an erythematous, firm swelling of the proximal phalanx of the fourth finger of the left hand was noted. A roentgenogram of the left hand showed asymmetric well-organized periosteal thickening of the affected finger with no frank bone destruction (Fig. 3). The



Fig. 3: Roentgenogram of left hand. The proximal phalanx of the fourth digit shows well-organized, periosteal thickening.

findings were compatible with chronic osteomyelitis. Radioisotope bone scan showed increased isotope uptake in the affected digit consistent with acute osteomyelitis. Bacterial and fungal cultures of the aspirate from the left finger showed no growth.

A decision was made to commence oral amoxicillin and clavulanic acid as some bacterial cultures from ulcers were growing *Staphylococcus aureus* sensitive to this antibiotic. Despite eradication of the colonizing bacteria, the ulcer edges remained active and the ulcers progressed. The dose of prednisone was subsequently increased to 60 mg on alternate days. The lesions completely healed, the child became afebrile, began to walk and was no longer agitated. The dose of prednisone was tapered to 40 mg on alternate days and ulcers remained healed at this dose. The patient was discharged after 46 days as an inpatient and the dose of prednisone gradually tapered to 25 mg on alternate days as an outpatient over three weeks. Antibiotics were continued primarily for the osteomyelitis which also improved on this regime.

At clinic review, 21 days after discharge, the lesions were noted to be pruritic and the ulcers were recurring. The patient was re-admitted and the dose of prednisone was increased to 60 mg on alternate days and dapsone was added at a dose of 25 mg. The lesions were dressed with 1% pimecrolimus cream. However, there was no improvement and dapsone was discontinued and sulphasalazine 750 mg per

day was commenced. Progress however remained slow and mercaptopurine 25 mg daily was added to the regime. Healing then progressed at a satisfactory rate. Attempts to decrease and discontinue the sulphasalazine resulted in flaring of the lesions. The patient was discharged on all three drugs and the dose of prednisone has subsequently been tapered to 35 mg on alternate days with no flaring of the lesions. The osteomyelitis has completely resolved.

DISCUSSION

Pyoderma gangrenosum is a diagnosis of exclusion and histology is not diagnostic. Although initial bacterial cultures from the ulcers were positive, it is likely that this was due to secondary infection as the ulcers continued to progress even after they had been rendered sterile. The clinical features, progress and response of the ulcers to anti-inflammatory drugs were consistent with a diagnosis of pyoderma gangrenosum.

Pyoderma gangrenosum is a rare condition, which occurs less frequently in children than in adults. Differences have been noted between adults and children in both clinical presentation and associated disorders. In children, the ulcers usually begin as pustules rather than papules or nodules. In adults the lesions are commonly seen on the lower extremities whereas in children, lesions are also seen on the head, face, buttocks, perianal and genital areas. In adults, pyoderma gangrenosum is most commonly associated with arthritis. In children, it is associated with ulcerative colitis, followed by leukaemia and Crohn's disease (2).

Osteomyelitis is a rare association of pyoderma gangrenosum. Chronic recurrent multifocal osteomyelitis has been reported in association with a number of skin conditions including palmoplantar pustulosis, psoriasis vulgaris and Sweet syndrome (5). The association of chronic recurrent multifocal osteomyelitis with pyoderma gangrenosum has been reported (1, 3–6). Of these cases, four were children and one was an adult. In addition, an adult case of sterile osteomyelitis with a single focus in the sternum after bone marrow puncture for myelodysplastic syndrome has also

been reported (7). In that case, ulceration of the skin overlying the bone marrow puncture occurred and this was subsequently diagnosed as pyoderma gangrenosum.

The skin lesions in this patient responded to prednisone, sulphasalazine and mercaptopurine, which are all considered appropriate drugs for treatment of this condition. Although the patient showed no satisfactory response to dapsone, this drug still remains a useful adjuvant treatment for pyoderma gangrenosum. Refractory lesions have also been successfully treated with the addition of clofazimine, rifampicin, azathioprine, cyclophosphamide or cyclosporin to the steroid regime (2). Satisfactory response has also been reported with topical nicotine, systemic minocycline (in adults), tacrolimus, melphalan, chlorambucil, methotrexate, interferon- α , potassium iodide, thalidomide, infliximab, mycophenolate mofetil and colchicine (8).

Since pyoderma gangrenosum may run a chronic course with significant morbidity, long-term follow-up of this patient is indicated.

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