# Ecthyma gangrenosum: a manifestation of *Pseudomonas* sepsis in three paediatric patients

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## ABSTRACT

***Pseudomonas aeruginosa* sepsis rarely occurs in healthy children. In immunocompromised children, it usually carries a high mortality rate. Ecthyma gangrenosum is a known cutaneous manifestation of *Pseudomonas* septicaemia. Three paediatric cases of *Pseudomonas aeruginosa* septicaemia with ecthyma gangrenosum were retrospectively reviewed. The three patients were aged seven years, seven months, and five months, respectively. An underlying disease of hypogammaglobulinaemia was present in the oldest patient. Blood cultures grew *Pseudomonas aeruginosa* in all three patients. All underwent repeated wound debridement and received intravenous ceftazidime and an aminoglycoside for a minimum of two weeks. One needed colostomy and subsequent posterior sagittal anorectoplasty as a result of complete obliteration of the anal canal from the ecthyma. There was no mortality. In conclusion, *Pseudomonas aeruginosa* sepsis should be treated early. Recognition of ecthyma gangrenosum as a manifestation of this problem can allow early institution of the appropriate antibiotics before culture results.**


**Keywords: ecthyma gangrenosum, hypogammaglobulinaemia, immunocompromised children, *Pseudomonas aeruginosa***

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## INTRODUCTION

*Pseudomonas aeruginosa* is an aerobic Gram-negative bacterium which can cause opportunistic infections in the immunocompromised, carrying with it high mortality. It is a well-known opportunistic pathogen. It thrives well in soil and water, resists extremes of temperature and even antiseptics, enabling it to survive well even in the hospital, making it a common nosocomial pathogen. Colonisation starts in the gastrointestinal tract and spreads to moist cutaneous sites such as the axilla and perineum. Community-acquired *Pseudomonas* infection in healthy patients is uncommon.

Ecthyma gangrenosum is a well-recognised manifestation of *Pseudomonas* infection with or without septicaemia[1-6, 8-10]. It usually first presents as a painless macule that enlarges to become an elevated papule. It then evolves into a haemorrhagic bulla that ruptures, forming a gangrenous ulcer with a grey-black eschar surrounded by an erythematous halo[4]. They represent dermal necrosis resulting from arterial and venous thrombosis secondary to bacterial multiplication in the wall of the vessels[7]. They can occur singly or at multiple sites, commonly the axilla and perineal regions. Hence, early recognition is important for early institution of appropriate antimicrobial therapy.

Other causative agents of ecthyma gangrenosum or ecthyma gangrenosum-like lesions include *Staphylococcus aureus, Serratia marcescens, Klebsiella* species, *Escherichia coli, Neisseria meningitidis, Aeromonas hydrophila, Sternotrophomonas maltophilia* and fungal organisms such as *Aspergillus, Candida, Fusarium* and *Rhizopus* species[11-23]. We reviewed three paediatric cases of *Pseudomonas* septicaemia with ecthyma gangrenosum.

## CASE REPORTS

### Case 1

A previously-healthy five-month-old Chinese girl presented with a six-day history of fever associated with four days of diarrhoea. On the day of admission, she developed a "blister" on her back. Assessment on admission revealed a lethargic child with 10% dehydration. Her vital signs were: axillary temperature 37.8°C, pulse rate 175 per minute, respiratory rate 50 per minute, and blood pressure 107/54 mmHg. There was a deep anal ulcer at the six o'clock position and a 1 cm ulcer with surrounding erythema at the

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interscapular area. More lesions typical of ecthyma gangrenosum developed over the next 24 hours on both her thighs and her left cheek. The lesion on her left thigh got progressively bigger (Fig. 1). She also had hepatomegaly of 3 cm and splenomegaly of 1 cm.

She was resuscitated with 10 ml/kg of intravenous normal saline and empirically started on intravenous cloxacillin, metronidazole and ceftriaxone. Investigation results were: full blood count (FBC) on Day 1: white blood cell count (WBC) $2.35 \times 10^9$/L, haemoglobin (Hb) 8.8 g/dL, platelets $116 \times 10^9$/L, absolute neutrophil count (ANC) $0.7 \times 10^9$/L; C-reactive protein 209 mg/L; prothrombin time (PT) 15.4 s, partial thromboplastin time (PTT) 44 s; liver function test (LFT): protein 50 g/L, albumin 25 g/L, bilirubin 20 $\mu$mol/L, alanine aminotransferase (ALT) 18 U/L, aspartate aminotransferase (AST) 43 U/L, alkaline phosphatase (ALP) 54 U/L. Repeated FBC on Day 3: WBC $7.61 \times 10^9$/L, ANC $6.32 \times 10^9$/L (without granulocyte colony stimulating factor (GCSF)/granulocyte-macrophage colony stimulating factor (GM-CSF) treatment). Blood cultures and tissue cultures grew *P. aeruginosa* sensitive to ceftazidime and gentamicin.

Work-up for immune deficiency: Nitroblue tetrazolium test (NBT) 100%; IgG 12.9 g/L, IgA 0.84 g/L, IgM 1.52 g/L, IgE 151 IU/L; flow cytometry: normal. She was converted to intravenous ceftazidime and gentamicin on Day 2 when Gram-stain showed Gram-negative bacilli and evolution of the rash raised the suspicion of ecthyma gangrenosum. She was continued on ceftazidime and gentamicin for a total of 14 days. She also required debridement of the anal and back ulcers with creation of a defunctioning colostomy for better wound healing. Posterior sagittal anorectoplasty was performed later.

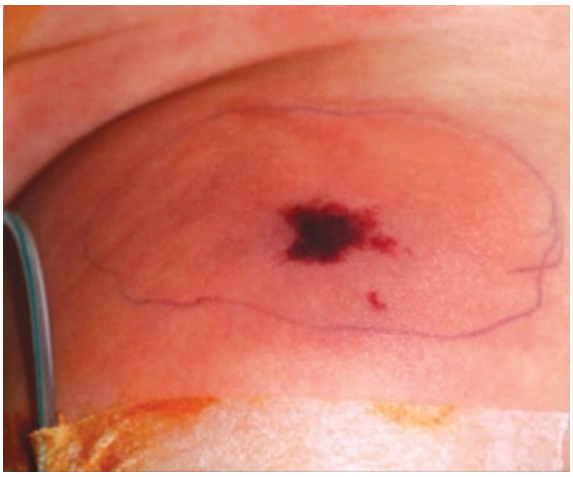

**Fig. 1** Photograph of ecthyma gangrenosum shows a dark necrotic centre with surrounding halo. The circular pen marking, made a few hours before the photograph was taken, showed the progression of the lesion.

**Case 2**

A seven-year-old Chinese boy, a known case of congenital hypogammaglobulinaemia, presented with four days of fever and skin lesions. He was found to be lethargic and tachycardic with a pulse rate of 190 per minute. Vital signs were: axillary temperature 39°C, respiratory rate 70 per minute, and blood pressure 76/36 mmHg. There was a 7 cm $\times$ 5 cm necrotic ulcer on his upper chest and multiple nodular erythematous lesions with bluish cores over all four limbs. The latter subsequently developed into haemorrhagic bullae and necrosis.

Investigation results were: FBC (Day 1): WBC $0.24 \times 10^9$/L, platelets $212 \times 10^9$/L; C-reactive protein 224 mg/L; PT 15.9 s, PTT 34.1 s; LFT: protein 35 g/L, albumin 18 g/L, bilirubin 85 $\mu$mol/L, ALP 39 U/L, ALT 311 U/L, AST 105 U/L; Repeat FBC (Day 9): WBC 9.15 $\times$ 109/L, ANC $2.01 \times 10^9$/L (without GCSF/ GM-CSF treatment).

Blood cultures and wound cultures (Day 1) grew *P. aeruginosa* sensitive to ceftazidime, gentamicin and amikacin. Wound culture (Day 9) grew *P. aeruginosa* sensitive to imipenem, gentamicin and amikacin, and resistant to ceftazidime and netilmicin. Wound culture (Day 26) grew *P. aeruginosa* sensitive to ciprofloxacin, resistant to ceftazidime, imipenem and gentamicin, and intermediate to amikacin and netilmicin. Wound culture (Day 36) grew *P. aeruginosa* sensitive to imipenem, amikacin, polymyxin B and ciprofloxacin, and resistant to ceftazidime and gentamicin; and *Klebsiella sp.* sensitive to ciprofloxacin and polymyxin B, and resistant to imipenem and amikacin. Wound culture (Day 50) grew *P. aeruginosa* sensitive to ceftazidime, gentamicin and amikacin; *Acinetobacter baumannii* sensitive to ceftazidime, imipenem, gentamicin and amikacin; and *S. aureus* sensitive to erythromycin and cloxacillin. Wound culture (Day 60) grew *S. aureus* sensitive to erythromycin and cloxacillin. NBT was 93%.

He was given initial fluid resuscitation with normal saline and fresh frozen plasma as well as inotropic support with intravenous adrenaline, dopamine and dobutamine. Antibiotic cover was started on admission with intravenous ceftazidime (D1-11, D56-62) and amikacin (D1-28), gentamicin (D56-62). Intravenous imipenem (D11-32) and oral ciprofloxacin (D31-44) were subsequently started because of emergence of resistant strains of *Pseudomonas*. Oral erythromycin (D57-70) was also given for superimposed *S. aureus* wound infection as he was allergic to penicillins. Intravenous immunoglobulin (900 mg/kg) was given on admission and subsequently every three weeks, in view of the underlying hypogammaglobulinaemia.

Wound management was with chlorhexidine wash and paraffin dressing as well as topical polymixin B wash. Wound desloughing was needed on Day 34. Split skin graft was successfully done on Week 7 with good graft take.

**Case 3**

A five-month-old Malay girl presented with five days of fever and diarrhoea as well as skin lesions for one day. On examination, she was ill with erythematous lesions and central necrosis over her right calf, left cheek, left shin and left forearm. There was also an anal ulcer with slough extending 2-3 cm deep. Her abdomen was distended with generalised guarding. Investigation results were: FBC (Day 1): WBC $1.95 \times 10^9$/L, Hb 8.3 g/dL, platelets $236 \times 10^9$/L, ANC $0.95 \times 10^9$/L; FBC (Day 3): WBC $11.4 \times 10^9$/L, ANC $8.44 \times 10^9$/L; C-reactive protein 218 mg/L; LFT: protein 40 g/L, albumin 20 g/L, ALP 46 U/L, AST 28 U/L, GGT 9 U/L.

Blood culture grew *P. aeruginosa* sensitive to ceftazidime, gentamicin, amikacin, meropenem and piperacillin; tissue culture from the anus grew *P. aeruginosa* (same antibiotic sensitivity); wound culture from skin lesions and anal ulcer grew *P. aeruginosa* (same antibiotic sensitivity); and tissue biopsy from the perianal tissue and right calf lesion showed gangrene. Antibody testing for human immunodeficiency virus was negative; and IgG level was 2.3 g/L. Tests repeated one month later were: 14.8 g/L; IgM, IgG and IgE levels: normal; C3, C4 normal.

She was given initial fluid resuscitation with normal saline and inotropic support in the intensive care unit. Antibiotic treatment with intravenous meropenem was started on admission. This was converted to intravenous ceftazidime and gentamicin for a total of three weeks from Day 2 when culture results and antibiotic sensitivities were known. Intravenous immunoglobulin was given on Day 2 and Day 16. Urgent examination under anaesthesia of the anal ulcer on day one revealed a depth of 2-3 cm deep with involvement of the entire mucosa layer. Laparotomy showed a perforated appendix with peritoneal soilage. Appendicectomy and defunctioning sigmoid colostomy was performed. The anal ulcer and right calf lesion were debrided at the same setting. She finally underwent a posterior anorectoplasty.

## DISCUSSION

Patients at high risk for this infection include those with malignancies, hypogammaglobulinaemia, steroid therapy, immunodeficiency especially neutropenia and invasive procedures for monitoring and treatment, and respirator therapy. Hence, in the presence of this infection and ecthyma gangrenosum, it is mandatory to look out for immune deficiency states. Several reports of *Pseudomonas aeruginosa* septicaemia associated with ecthyma gangrenosum have been published in children with agammaglobulinaemia[24]. Our patient with hypogammaglobulinaemia presented similarly and required extended course of antibiotics and repeated debridement of the wounds with final skin grafting.

Community-acquired *Pseudomonas* infection can occur in healthy children, especially in young children under one year of age[1-4]. Freud et al and Boisseau et al had described extensive perineal ecthyma gangrenosum in immunocompromised children with *Pseudomonas* septicaemia[25,26]. Our two reported cases with no underlying immune deficiency were both only five and seven months of age, respectively. Both presented with diarrhoea and had extensive lesions involving the perineal region. One of them had underlying appendiceal perforation. Both required defunctioning colostomies to promote wound healing and finally perineal reconstruction. Such gastrointestinal tract involvements are usually seen in the immunocompromised patients below six months of age. Intestinal colonisation with *Pseudomonas* serves as a reservoir for invasive disease. It can result in ulceration of the mucosa, extending into the submucosa and causing localised necrosis. Further invasion into the muscularis and serosa causes perforation, peritonitis and bacteraemia, which significantly increase the mortality[27].

Early institution of antimicrobial therapy is important in reducing the high mortality rate seen in *Pseudomonas* septicaemia. Presence of ecthyma gangrenosum should alert us to the likelihood of *Pseudomonas* sepsis. In vitro synergism between beta-lactams and aminoglycosides and the emergence of resistant strains with monotherapy have made combination therapy a preferred mode. Combination therapy in invasive infections has been shown to decrease mortality in human studies compared with monotherapy[27]. All three cases discussed had community-acquired *Pseudomonas* infection and received combination therapy. All responded well except the boy with hypogammaglobulinaemia who required a protracted course of antibiotics and emergence of resistant strain to aminoglycoside and beta-lactam antibiotics.

Interestingly, all three cases had neutropenia at the time of presentation, which recovered with treatment. Previous studies have reported increased mortality with *Pseudomonas* sepsis in oncology patients with

neutropenia. However, no observation has been made with previously healthy children presenting with transient neutropenia. Whether this phenomenon represents a secondary immunosuppressed state secondary to the infection or a predisposition for severe *Pseudomonas* infection in previously-healthy children need to be further validated. In conclusion, severe *Pseudomonas* septicaemia can be seen in both healthy and immunocompromised children. Early recognition of ecthyma gangrenosum will prompt us to early appropriate therapy.

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**ANNEX**

| Generic name | Brand Name | Manufacturer | City/Country |
|---|---|---|---|
| Imipenam/Cilastatin | Tienam | MSD | New Jersey, USA |
| Amikacin | Likacin | Lisapharma | Italy |
| Erythromycin | Erythromycin Lactobionate | DBL (Mayne Pharma) | Melbourne, Australia |
| Gentamcin | Gentamcin sulfate | Pfizer | Bentley, Australia |
| Ciprofloxacin | Ciprobay | Bayer | Leverkusen, Germany |
| Meropenem | Meronem | AstraZeneca | Cheshire, The United Kingdom |