Ecthyma gangrenosum, a skin manifestation of *Pseudomonas aeruginosa* sepsis in a previously healthy child
A case report
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Abstract

Rationale: Ecthyma gangrenosum (Eg) is a necrotic lesion that is mostly seen in immunocompromised patients. It reflects a severe sepsis, possibly caused by *Pseudomonas aeruginosa* (Pa).

Patient concerns: A healthy 3-year-old girl admitted to the Pediatric Emergency Department presented a sepsis-associated purpura with neurological and respiratory distress.

Interventions: An empiric antibiotherapy (anti-meningococcal) was prescribed.

Diagnoses: Forty-eight hours after admission, blood and wound cultures were positive for *Pa*. As a result, the decision was made to change the antibiotic therapy.

Unfortunately, on day 3, the patient died. Exhaustive immunologic tests are presently being carried out.

Outcomes: Eg caused by *Pa* is uncommon in healthy children, and purpura sepsis is usually caused by *Neisseria meningitides* infection.

Lessons: Eg should be recognized rapidly so that the appropriate treatment can be prescribed as quickly as possible.

Abbreviations: Eg = ecthyma gangrenosum, HIV = human immunodeficiency virus, IV = intravenous, Pa = *Pseudomonas aeruginosa*.

Keywords: children, ecthyma gangrenosum, *Pseudomonas aeruginosa*, sepsis

1. Introduction

Ecthyma gangrenosum (Eg) is a rare but typical skin manifestation, most commonly caused by *Pseudomonas aeruginosa* (Pa), an aerobic Gram-negative opportunistic pathogen that has a high risk of associated mortality in cases where the infection is systemic.[1,2] Although rare, the presence of Eg is indicative of a severe systemic infection with a potentially fatal prognosis.[3] These skin lesions may be seen on admission or can develop later. The recognition of Eg lesions permits the earliest possible introduction of the most effective antimicrobial therapy, which is a key prognostic factor for survival. Eg with *Pa* is rare in healthy children, and empiric antibiotic regimens used in sepsis are generally not effective.

2. Patient presentation

A 3-year-old girl was admitted to the emergency department with a 4-day history of fever, lethargy, impaired consciousness, and multiple necrotic lesions that began the day before admission. She had no recent history of contact with contagious diseases or foreign travel, no familial medical problems. She was not on any medication and had received the appropriate immunizations.

On arrival, she was in a poor condition. Blood pressure and oxygen saturation were undetectable. She was lethargic, with cyanosis of the extremities, and her capillary refill time was more than 4 seconds. Many purple necrotic lesions were visible on her legs, thorax, face, and genital areas. The largest was a 5-centimeter necrotic lesion surrounded by an intense erythematous ring (Fig. 1).

Initial resuscitation included 100mg/kg intravenous (IV) ceftriaxone injection, 3 boluses of 20mL/kg IV normal saline, and oxygen via a face mask.

Laboratory tests indicated leukopenia (1200 white blood cells/mm³) with an absolute neutrophil count of 200 cells/mm³, anemia (5g/dL hemoglobin), and thrombocytopenia (9000 platelets/mm³) associated with a coagulation disorder with no sign of disseminated intravascular coagulation. An uncompen-
sated metabolic acidosis, hyponatremia, renal failure, and increased liver enzyme levels were observed. The inflammatory markers, C-reactive protein and procalcitonin, were markedly raised, at 231 mg/L and 217 ng/mL, respectively. Chest x-ray revealed pulmonary edema. Blood and wound cultures were sent for laboratory analysis.

The patient was transferred to the Pediatric Intensive Care Unit with a diagnosis of meningococcal septic shock. As her respiratory distress worsened, she was intubated. Inotropic support was started to combat low blood pressure despite refilling and cardiac failure. One unit of packed blood cells and 3 units of packed platelets were transfused. During the first 2 days, she received 200 mg/kg/day cefotaxime IV, with the hypothesis of a *Neisseria meningitidis* infection. She was stable for the first 24 hours.

On day 3, *Pa* was identified in the blood and the skin lesion cultures, and the antibiotic regimen was immediately changed to 200 mg/kg/day ceftazidime IV. The skin lesions became more necrotic and spread further. The patient suffered from a brutal deterioration, with multiple organ failure, which necessitated hemodialysis, inotropic support, fresh frozen plasma transfusion, and intensive care management.

By day 4, severe skin lesions had spread even further and were necrotic and hemorrhagic, with blisters and ulcers underneath (Figs. 2 and 3). Despite an aggressive resuscitation, progression was rapidly fatal (Fig. 4).

*Pa* was isolated from 1 blood sample, 3 necrotic skin lesions, and a cerebrospinal fluid sample. The *Pa* identified in cerebrospinal fluid was resistant to ceftazidime; conversely, the blood and wound cultures were ceftazidime sensitive. Bone marrow aspiration was not performed. HIV serology was negative. Quantitative immunoglobulin levels revealed normal immunoglobulins (G, A, D, and M).

### 3. Discussion

*Pa* is an opportunistic bacterium, which can be found on the skin, in the nose and throat, and in the stools. It generally causes infection in immunocompromised patients with conditions such as neutropenia, immunodeficiency, and hypogammaglobulinem-
mia. The presence of *Pa* infection in healthy subjects is very uncommon.

In some reported cases of *Pa* sepsis in previously healthy children, most patients were male and less than 1 year old. Fever, diarrhea, pneumonia, skin lesions (50%), and shock are the most relevant associated symptoms. The reported overall mortality rate associated with *Pa* sepsis in children is variable, ranging from 20% to more than 50%. Antibiotic treatments have been based mainly on anti-pseudomonas beta-lactam antibiotics and aminoglycosides, either alone or in association.

The presence of a viral infection or recent antibiotic therapy had been described as transient risk factors of *Pa* sepsis in immunocompetent children. Chusid and Hillmann postulated that a viral infection may directly alter the mucosal barrier of the gastrointestinal tract, and then reduce host defense. In addition, previous treatment with antibiotics may increase the number of *Pa* in the gastrointestinal tracts.

Furthermore, it is possible that Pseudomonas organisms, by producing toxins, may trigger a transient neutropenic state. These toxins could inhibit granulocyte migration and cause like bone marrow suppression in healthy children. Whether this phenomenon represents a secondary immuno-suppressed state or a predisposition to severe *Pa* infection in previously healthy children needs to be further evaluated. In our patient, neutropenia was probably induced by *Pa* infection rather than being a predisposing factor for the infection.

Clinical presentations of community-acquired *Pa* sepsis show a geographical difference. Fever and diarrhea are the most common presentations in the Eastern world and are called Shanghai fever. However, fever and skin lesions are usually seen in the Western world (North America and Europe). Our European patient presented with Eg skin lesions, but not with diarrhea.

Eg is a well-recognized cutaneous manifestation of *Pa* infection with or without septicemia. It is described as an uncommon vasculitis, affecting the adventitia and media of blood vessels and causing from either hematogenous seeding of a pathogen, or direct inoculation through the skin. Eg appears as painless, erythematous, and purpuric macules in moist areas, which become nodular, bullous, or pustular with an indurated erythematous base and rim. Finally, they form gangrenous ulcers, with a gray-black eschar surrounded by an erythematous halo. The lesions mature within 12 hours and can co-exist at different stages of development. Fifty-seven percent of lesions occur in the gluteal and perineal regions, 30% involve the extremities, 12% the trunk and face. Vaiman et al. analyzed Eg cases described in the literature from 1975 to 2014. Of the 167 published cases, was detected in 123 (73.65%), and other bacterial etiologies were detected in 29 cases (17.35%), including *Escherichia coli*, *Staphylococcus aureus*, *Aeromonas hydrophila*, and *Mucor* species. Of the 123 *Escherichia coli* cases with *Pa* etiology, sepsis was described in 72 cases (58.5%) and an absence of septicemia was reported for 51 cases (41.5%).

The prognosis for children with *Pa* infection is influenced by several risk factors. The first of these is the presence of an unknown immune deficiency. Neutropenia below 500 cells/mm³ can predispose to a severe *Pa* infection, and this seems to be associated with a higher mortality rate, even in previously healthy children. In a study reported by Huang et al., leukopenia was present in 24 (57%) of 43 children evaluated. Of the 10 cases that were fatal, 9 patients had leukopenia on admission. Delay in introducing an appropriate treatment has also been associated with higher mortality. In the study by Huang et al., 90% of the patients who died had not received an optimal antimicrobial treatment. Other risk factors include the presence of multiple Eg lesions and septic shock.

Prognosis in *Pa* infection is highly associated with early institution of optimal antibiotic therapy. Bodey et al. reported an overall cure rate of 67% for patients receiving appropriate antibiotics but only 14% for those receiving inappropriate antibiotics. Moreover, this retrospective analysis of *Pseudomonas* bacteremia cases indicated that in cases where optimal antimicrobial therapy was delayed (24–48 hours), the healing rate decreased from 74% to 46%.

Some authors propose a combination therapy as the preferred mode of treatment, based on synergisms between β-lactams and aminoglycosides, and the emergence of resistant strains with monotherapy.

In our case, we suspect that *Pa* became rapidly resistant to ceftazidime, with the production of an inducible cephalosporinase. This is described in the literature as an increasingly well-recognized *Pa* phenomenon, which explains the importance of the correct application of antipseudomonal therapy. Current recommendations for *Pa* infection are controversial. Bowers et al., from their study, suggested that there is no difference in mortality outcomes associated with the number of appropriate agents administered during initial empirical therapy for *Pa* bacteremia, as long as at least 1 agent is active. The addition of an aminoglycoside to an antipseudomonal beta-lactam penicillin does not improve the clinical efficacy achieved with the beta-lactam penicillin alone. While awaiting bacteriological results, empirical antimicrobial biotherapy should be started with anti-pseudomonal beta-lactam penicillin, and adjusted immediately once the bacterial culture results are known.

A final point is the differentiation of Eg from Purpura fulminans caused by *Neisseria meningitidis*. These 2 skin lesions are different. Purpura fulminans lesions spread faster than Eg lesions and never become bullous. Moreover, antimeningococcoccal antibiotics (such as cefotaxime or ceftriaxone) are not efficient against *Eg* caused by *Pa* infection.

Physicians must be aware of the existence of Eg and should be able to recognize this skin lesion rapidly in order to prescribe the appropriate treatment, generally when the skin lesions become bullous.

4. Conclusion

This case report shows that Eg due to *Pa* infection can occur in a previously healthy child with no other medical issues. The main risk factor found to be connected to the severe *Pa* infection was neutropenia. A clinical picture of Eg in a previously healthy child should suggest a *Pa* infection. Eg is an informative skin lesion for diagnosing *Pa* sepsis and can present before the pathogen is identified. A careful and cautious physical examination is important and should be carried out in order to recognize this lesion. The early institution of the appropriate antimicrobial therapy, anti-pseudomonal beta-lactam penicillin, is important in terms of prognosis. This treatment must be adjusted immediately once bacterial culture results are known. A comprehensive immunologic evaluation should also be conducted.

Acknowledgments

The authors are grateful to Kate Vassaux, PhD, and Mrs Sara Jane Higgins for medical editing.
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