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Pseudomonas aeruginosa Sepsis Associated With Ecthyma Gangrenosum in a Previously Healthy Infant: A Case Report and Literature Review

Jing Yin, MS[1], Chong-Wei Li, MS[1], Na Luo, MD, PhD[2], Ji-Jun Ma, MS[1], Li Liu, MS[1], Xiao-Jie Li, MS[1], Xiao-Jie Du, MD[1], and Jian Hu, MD[1]

Introduction

As an opportunistic pathogen, *Pseudomonas aeruginosa* sepsis (PAS) mostly occurs in immunocompromised groups (eg, primary or acquired immunodeficiency, chronic disease, malignancy, or preterm infants). Community-acquired PAS in healthy hosts is uncommon. Ecthyma gangrenosum (EG) is an early characteristic cutaneous manifestation of PAS among a wide range of other clinical features. We report a pediatric case of PAS with EG in a previously healthy 11-month-old boy and review some pertinent literature.

Case Report

A previously healthy 11-month-old boy was admitted to the hospital with an intermittent fever of 39°C for 4 days and diarrhea with a dark-green watery stool. About 1 day prior to hospitalization, an erythematous macula was noted on his foot, which later developed into a hemorrhagic bullae when he arrived at hospital.

A physical examination showed the following features: he was alert, temperature 38°C, heart rate 148 beats per minute, respiratory rate 32 breaths per minute, and blood pressure 90/60 mm Hg. A few erythematous macules were scattered about his face and 4 limbs. A hemorrhagic bulla was present on his right foot. His right lower extremity was obviously swollen with diminished utility. Pulmonary and heart examination were normal. The liver was enlarged to 3 cm below the right costal margin, and the spleen was impalpable. The complete blood count showed a white blood cell count of 8.91×10^9/L with 68% neutrophils, 25% lymphocytes, 12% monocytes, and a platelet count of 191×10^9/L. C-reactive protein was >200 mg/L. Prothrombin time was 14.7 seconds, activated partial thromboplastin time was 28.8 seconds, and the fibrinogen level was 2.858 g/L. The serum immunoglobulin levels were all less than normal: IgG 1730 mg/L, IgA 70 mg/L, IgM 110 mg/L; flow cytometry: CD3, 86%; CD4, 69%; CD8, 7%; CD19, 6%; CD16, 2%. The electrocardiogram and chest radiograph were normal.

On the second day of admission, he suffered a focal seizure in the right upper extremity and entered into a state of lethargy. The rashes rapidly developed into EG. The swelling in the right leg increased with skin redness and high skin temperature. Magnetic resonance imaging revealed an abnormal signal in parietal white matter and right frontal cortex; however, right knee joint cavity effusion, bilateral hip joints, and right ankle joint were normal.

A broad-spectrum antibiotic (imipenem) was administered systemically after admission. In addition, fresh frozen plasma and human serum albumin were administered. On hospital day 3, blood cultures and wound cultures grew *Pseudomonas aeruginosa* that was sensitive to imipenem, meropenen, piperacillin, amikacin, ceftazidime, levofloxacin, and tobramycin. He was continued on imipenem and intravenous levofloxacin was added according to the drug sensitive test. Although his general condition improved after the aforementioned treatment, his temperature fluctuated between 37.5°C and 38.5°C. The skin lesions continued to progress and increased in number. The new subcutaneous indurations rapidly developed into EG and coalesced in areas. Extensive skin necrosis occurred on his right lower extremity including the fourth and fifth toes (Figure 1A). Complete blood counts were repeated for several days and showed a steady increase in the white blood cell counts (reaching up to 53.43×10^9/L), a decrease in

[1]Tianjin Children's Hospital, Tianjin, China
[2]Nankai University, Tianjin, China

Corresponding Author:
Jian Hu, Department of Immunology, Tianjin Children's Hospital, 225, Machang Road, Hexi District, Tianjin 300074, China.
Email: h1957_7591@126.com

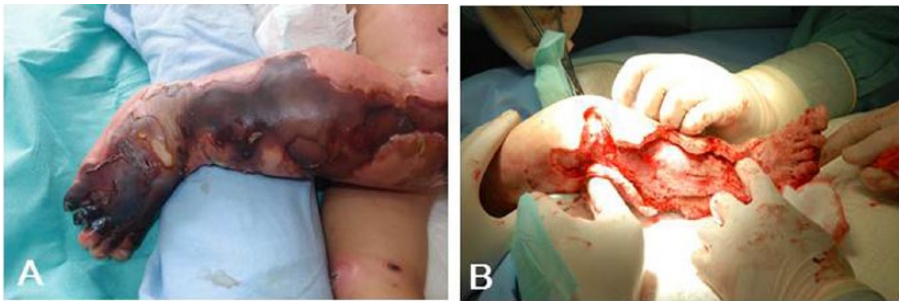

Figure 1. (A) Extensive tissue necrosis on right leg. (B) Surgical debridement of the necrotic lesion.

platelet count, and anemia. C-reactive protein was consistently >100 mg/L. On hospital day 10, he was transferred to the orthopedic wards. He was continued on antibiotics and underwent surgical debridement of the necrotic lesions and skin grafts (Figure 1B). His temperature gradually returned to normal after the surgical treatment. On hospital day 52, he was discharged from the hospital in a stable condition.

Discussion

PAS in immunocompetent infants or children is not often seen, but it can occur in healthy children, particularly in those <1 year old. In fact, an age of <1 year is the only identified host factor that predisposes previously healthy children to PAS. Huang et al reported 43 cases of community-acquired PAS in previously healthy infants and children and most were <1 year old.[1] This finding is in accord with observations from other studies. *P aeruginosa* is found in the intestinal tract of 5% to 30% of healthy hosts.[2] *P aeruginosa* intestinal infection may either directly weaken the mucosal barrier of the gastrointestinal tract or temporarily disrupt the host defenses.[3] Both of these conditions may facilitate *P aeruginosa* entry into the bloodstream. Furthermore, antibiotic therapy may increase the relativity density of *P aeruginosa* in gastrointestinal tracts of patients.[4]

PAS has a wide range of clinical features that involve multiple organs and tissues including the blood, skin, respiratory system, urinary tract, and gastrointestinal tract. Fever and diarrhea are common clinical presentations of PAS. Community-acquired enteric illness associated with *P aeruginosa* was first described as "Shanghai fever."[5] Patients with "Shanghai fever" may develop necrotizing enteritis or bowel perforation. Although airway involvement caused by *P aeruginosa* is rare, pseudomembranous pharyngolaryngitis, epiglottitis, and progressive respiratory distress could manifest.[6] The seizures that often occur with PAS may be caused by either hyponatremia or meningitis. A study shows that a complication of meningitis resulted in severe neurological sequelae.[5]

Skin lesions include EG, subcutaneous nodules, gangrenous cellulitis, hemorrhagic vesicles, and bullae, papules, macules, petechial, and purpura.[1] EG is a rare but characteristic cutaneous sign of PAS that occurs early in the disease process. EG is an uncommon vasculitis that affects the tunica media and tunica adventitia of blood vessels.[7] Initially, the EG rash presents as a painless round erythematous macula, which rapidly becomes an indurated erythematous nodular. Subsequently, a hemorrhagic purple-black bullae forms and ruptures. Finally, an eschar-covered ulcer forms. This EG lesion can be found anywhere on the body, but the gluteal and perineal regions are the more common sites.

Neutropenia often occurs in PAS patients and is an important risk factor that predicts mortality. *P aeruginosa* infection may cause the neutropenic state by producing a toxin that both inhibits migration of neutrophils into infected areas and also decreases the number of neutrophils in the circulation.[8] Whether this phenomenon represents a secondary immunosuppressed state or a predisposition for severe *P aeruginosa* infection in previously healthy children need to be further validated.[4] Thrombocytopenia is another common hematologic finding. In our patient, the platelet count was decreased, but neutropenia was not observed as in most reported previously cases.

Community-acquired PAS can be the initial manifestation of an underlying immune deficiency,[5] most commonly hypogammaglobulinaemia.[4] However, some studies suggest that the immunoglobulin levels in most PAS patients are normal and that the hypogammaglobulinaemia that occurs during their illness is transient. One study showed that a patient with PAS had a prolonged hypogammaglobulinaemia, but no recurrent infection.[5] Our patient had no known immunodeficiency disease, but the serum immunoglobulin level and B cell percentage were decreased in the disease process. Whether the low immunoglobulin level in our patient is transient or the

result of an underlying immune deficiency needs further observation.

The overall reported mortality rate associated with PAS in children is variable, ranging from 20% to more than 50%.[9] In addition, the fatality rate is higher for infants (<1 year old) than older children (>1 year old). One of the independent factors that influences the outcome is inappropriate antibiotic therapy.[10] Given the high death rate of PAS, treatment with broad-spectrum antibiotics sensitive to *P aeruginosa* should be started immediately. A delay of even 1 to 2 days in appropriate antibiotic treatment will negatively affect the cure rate. Therefore, early recognition of PAS is of great importance. The characteristic EG skin lesion should dictate early appropriate antibiotic therapy. In addition, surgical debridement may be necessary in patients with extensive tissue necrosis.

Authors' Note

Authors Jing Yin and Chong-Wei Li contributed equally to this work.

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Author Contributions

JY and CWL participated to the patient care treatment, drafted the initial manuscript, and approved the final manuscript as submitted. NL participated to the draft of the manuscript, and corrected/approved the final manuscript as submitted. JJM, LL, XJL and XJD participated to the patient care treatment and approved the final manuscript as submitted. JH participated to the patient care treatment and to the draft of the manuscript, and corrected/approved the final manuscript as submitted.

Declaration of Conflicting Interests

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