Pseudomonas aeruginosa skin infections in two immunocompetent children under one year of age

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Abstract

We describe two cases of Pseudomonas aeruginosa skin infections in immunocompetent children, both following viral infections. The first one presented with fever and erythematous cutaneous nodules that enlarged and developed into abscesses. Biopsy of a nodule revealed panniculitis with P. aeruginosa. The second case presented with deep necrotic inguinal ulcers consistent with ecthyma gangrenosum. These two presentations are rare conditions in healthy infants without bacteremia. This report aims to answer questions such as the source of the contamination, the usefulness of the antibiotics or surgical drainage in the treatment, and the association of leukopenia with infection or immunodeficiency.

Introduction

Pseudomonas aeruginosa is a ubiquitous, aerobic, gram-negative bacillus that preferentially thrives in moist environments (1). The primary condition for a *P. aeruginosa* infection is to be colonized. After that, several conditions must be present such as a huge bacterial load, virulence factors (adhesion, antibiotic resistance, biofilm formation, secretion of toxins and enzymes), or an immune deficiency (transient or permanent). *P. aeruginosa* is frequently reported in cutaneous infections, more often in primary infections, by contact with a damaged skin or skin maceration, as seen in conditions such as pyoderma, folliculitis, bathtub contact, intertrigo, but also in secondary infections by blood dissemination in immunocompromised patients, such as in ecthyma gangrenosum (EG), a necrotic ulcerating skin lesion (1). Recently, however more cases have been reported in immunocompetent children (2). Although ecthyma gangrenosum is a well-described entity, a case of nodular *P. aeruginosa* panniculitis in an immunocompetent child without bacteremia has never been described in the literature so far.

Cases Reports

We report a 6-month-old girl with a 3-day history of fever and bronchitis. She presented with three erythematous cutaneous nodules on the right arm and left leg (Figure 1A). A blood analysis revealed a C-reactive protein (CRP) level of 177.1 mg/L [N < 5.0 mg/L] with hyperleukocytosis. The next day, the number of nodules increased to eight. Systemic antibiotherapy was started for suspected cutaneous bacterial infection, first with intramuscular ceftriaxone for two days due to lack of easy venous access, then with intravenous amoxicillin plus clavulanic acid for nine days. The neutrophil count dropped to 1590/mm3 [N 6000-17500/mm3], while the CRP level decreased. In the following days, the nodules evolved into clinical, ultrasound-documented abscesses with a dark erythematous central aspect and painful fluctuation. On the seventh day, the skin began to peel (Figure 1B). Biopsy of a nodule showed panniculitis with pus, leukocyte infiltrate, and culture showed massive growth of *P. aeruginosa*. Surgical punctures of the other abscesses also drained pus with positive *P. aeruginosa* cultures. The child recovered rapidly. On day 10, systemic antibiotics were discontinued and oral ciprofloxacin was started for two weeks. Repeated blood cultures were negative. An extensive workup did not reveal any deep infectious damage (cardiac and abdominal ultrasound, bone scintigraphy). Humoral immunity (dosage of all types and subtypes of immunoglobulins) and cellular immunity (dosage and types, subtypes of lymphocytes) were normal. The child experienced a progressive decrease of abscesses with and after antibiotics. An uneventful second decrease in the neutrophil count was noted after one month (minimal at 260/mm^3), but later it remained steadily normal, and complete cutaneous healing was noted after three months.

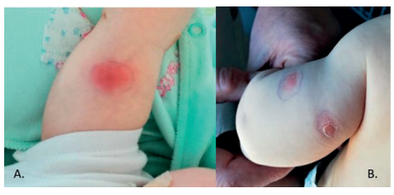

Figure 1: A. The nodule on the right arm at admission. / B. New nodules appeared the next day on the left arm and began to peel 7 days after admission.

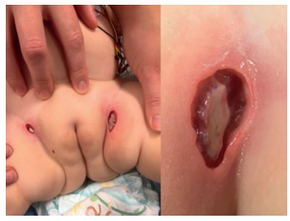

Figure 2: inguinal ulcerative necrotic lesions. Left ulcer close-up view.

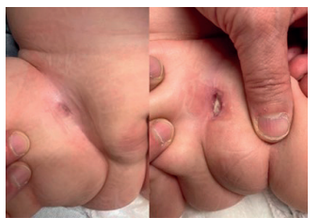

Figure 3: healing status at the time of discharge.

The second case is a 10-month-old girl who presented to the pediatric emergency department with a 4-day history of fever and two inflammatory necrotic lesions on both inguinal folds. She had a recent history of bronchiolitis and right otitis media. The cutaneous lesions rapidly progressed to deep ulcers with inflammatory margins and fibrin deposition (Figure 2). Blood samples initially showed an elevated CRP level (167 mg/L) and a decreased neutrophil count (940/mm3). Cellular immunity (dosage and types, subtypes of lymphocytes) and humoral immunity (dosage of all types and subtypes of immunoglobulins) were normal. Nitroblue tetrazolium blood test was unremarkable. Blood cultures remained negative. Ulcer swab cultures grew *P. aeruginosa* and confirmed the diagnosis of ecthyma gangrenosum. Piperacillin and tazobactam were administered intravenously for 10 days, and ciprofloxacin was continued per os until ulcer swab cultures were negative. Wound management consisted of physiologic solution cleansing, alginate foam, and silver dressing. Both ulcers healed completely within one month (Figure 3). Neutrophil counts remained consistently normal after discharge.

Discussion

Our two cases are similar in that they were immunocompetent children who had a viral infection prior to the *P. aeruginosa* skin infection and both developed mild neutropenia. They hadn't received antibiotics before and they didn't have sepsis or bacteremia proven by a positive blood culture.

In the first case, the eruption could be mistaken for erythema nodosum, but this hypersensitivity reaction is usually located on the lower limbs. It belongs to a broader group of cutaneous manifestations called panniculitis. Panniculitis is characterized by inflammation of the subcutaneous adipose tissue. It can be associated with infections, enzymatic disorders, post-steroid, malignant, lipoatrophic, physiological agents (cold panniculitis, injections, blunt trauma), subcutaneous fat necrosis of the newborn, sclerema neonatorum, selected syndromes (H syndrome, CANDLE syndrome) (3). When panniculitis is due to bacterial infection, a neutrophilic infiltrate is found throughout the fat lobules, sometimes extending into the dermis, and very often developing into an abscess. In erythema nodosum, the inflammation is localized in the septa of the hypodermis. Differential diagnosis with erythema nodosum or other causes of panniculitis can be challenging before evolution to abscess (4). Bacterial panniculitis may be caused directly by contamination in close proximity (an infected skin wound or a device containing a contaminated fluid) or by hematogenous spread (bacteremia) (4). Most cases of nodular panniculitis due to *P. aeruginosa* presented with bacteremia and in immunocompromised patients (5,6,7). Three cases of nodular panniculitis in the adult population have been reported in the absence of bacteremia but with the presence of an infected skin defect in close proximity (6). In our case, the child did not have a skin-breaking lesion before the appearance of the nodules. Given the presence of disseminated lesions, we postulate a blood, intestinal, or respiratory route rather than a cutaneous source. We therefore searched for an external source of *P. aeruginosa* contamination, but found none at home in the plastic bathtub, the tap used for filling, the aerosol mask and connector used for bronchitis treatment, and the "Babycook" device. However, the aerosol mask and connector were tested after being properly washed by the mother. Her twin brother and the family did not have any skin lesions. Azapagası et al. described a case of sepsis associated with subcutaneous nodules rapidly progressing to ecthyma gangrenosum in a 6-month-old infant with bilateral otitis media (5). In our case, the immune defense of the child, a transient, undetectable bacterial entry with less virulent associated factors could explain the less aggressive local evolution and the absence of ecthyma gangrenosum.

In the second case, ecthyma gangrenosum (EG) is a rare skin lesion caused by *P. aeruginosa* in 73.65% of cases, but other bacteria have been described such as *Escherichia coli, Citrobacter freundii, Klebsiella pneumoniae*, as well as some fungi (*Candida albicans, Fusarium*, and others) (8). The clinical presentation is hemorrhagic bullae or red nodules that develop into necrotic ulcers surrounded by an inflammatory halo within 12-24 hours, with a central black crust masking the deep ulcer. The mechanism is an uncommon vasculitis involving the media and adventitia of blood vessels in the dermis. It can be due to a hematogenous infection or primary cutaneous infection. This skin manifestation often heralds a *P. aeruginosa* sepsis, but may also reveal a predisposing condition such as malignancy or immunodeficiency (9). It has also been described in preterm infants, skin burns, and malnutrition. In our case, we cannot confirm the route of inoculation, but given preserved clinical condition of the child, we assume a cutaneous contamination due to local maceration of the napkin area. This maceration site may explain the absence of black crust.

The neutropenia present in both cases may be due either to the viral bronchitis, causing a transient neutropenia, or to a direct neutropenic effect of *P. aeruginosa*. *P. aeruginosa* is known to secrete toxins that reduce the number of neutrophils in the blood vessels and inhibit their migration to infected areas (10). We know that neutrophils are the predominant host defense against *P. aeruginosa*. Immune deficiency should be evaluated in all patients, especially chronic or cyclic neutropenia, hypogammaglobulinemia or immunodeficiency (acquired and primary), and malignancy (2). Cohen et al. discussed five cases of previously healthy children who presented with ecthyma gangrenosum (2). Two of them had a viral infection and neutropenia. The presence of a viral infection or recent antibiotic therapy are risk factors in immunocompetent children (2,9). Chusid and Hillmann postulated that viral infection affects the gastrointestinal mucosal barrier and subsequently reduces host defense (11).

The need for antibiotic therapy targeting *P. aeruginosa* and careful wound care is well known in EG. However, in the healing of abscess lesions, it is discussed in addition to surgical drainage (12). In the first case, the identification of *P. aeruginosa* was delayed due to the initial absence of abscesses and negative blood cultures. We were not able to assess the efficacy of the intravenous non-targeted antibiotics, but we noted an actual improvement with the surgical punctures and decided not to change the antibiotics until the results of the skin biopsy were available. Ciprofloxacin, although theoretically more appropriate, did not seem to improve the presumed spontaneous healing process after surgery and was not timely correlated with the previous decrease in blood inflammatory tests. In comparison, we know that the surgical treatment is more effective than antibiotic therapy alone in cutaneous abscesses caused by *Staphylococcus aureus* (12). It is important to perform this initial step of surgical drainage and bacteriologic sampling when faced with multiple abscesses.

Conclusion

Skin infections due to *P. aeruginosa* in healthy children have been described in recent years. Transient neutropenia induced by viral infection is a risk factor that allows *P. aeruginosa* to infect the child, but may also be a consequence of the direct action of *P. aeruginosa*. Immunodeficiency must always be excluded. Ecthyma gangrenosum requires prompt diagnosis and treatment with the appropriate antibiotic because of the serious skin injury and the potential association with sepsis. The diagnosis and the treatment of a panniculitis due to *P. aeruginosa* is more challenging as this entity is not well described. In our case, the surgical approach seemed more valuable than the antibiotics.

Conflict of interest

The authors have no conflicts of interest to declare with regard to the topic discussed in this manuscript.

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