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A 30-Day-Old Infant with Necrotizing Fasciitis of the Perineal Region Involving the Scrotum Due to Methicillin-Resistant *Staphylococcus aureus* (MRSA) and Extended-Spectrum β -Lactamase (ESBL)-Producing *Klebsiella pneumoniae*: A Case Report

Authors' Contribution:

Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Patient: Male, 30-day-old
Final Diagnosis: Fournier's gangrene • methicillin-resistant *Staphylococcus aureus* bacteremia
Symptoms: Necrosis • scrotal swelling • ulcer
Medication: —
Clinical Procedure: —
Specialty: Infectious Diseases • Pediatrics and Neonatology
Objective: Rare disease
Background: Fournier's gangrene is an idiopathic form of necrotizing fasciitis involving the genital and perineal regions; it is associated with high complication and mortality rates. Rarely, perineal infection may be caused by hospital-acquired antimicrobial-resistant bacteria. This report is of a 30-day-old infant with methicillin-resistant *Staphylococcus aureus* (MRSA) and extended-spectrum β -lactamase (ESBL)-producing *Klebsiella pneumoniae* necrotizing fasciitis involving the perineal region.
Case Report: A 30-day-old male infant presented to the Emergency Department with rapidly progressive white discoloration of scrotal skin since 3 days prior to admission, progressing from 2-3 white spots to covering two-thirds of the scrotal skin. Pain upon urination was noted, with normal appetite and bowel movements. He had a history of diaper rash 6 days earlier accompanied by fever, and the rash was treated with topical antifungal and corticosteroid ointment. He was born at term by caesarean delivery, with birth weight 2900 g. Laboratory examinations revealed leukocyte count 23 000/ μ L and CRP 26.8 mg/dL. Hemoglobin was 10.6 g/dL, serum sodium was 134 mEq/L, blood glucose was 80 mg/dL, serum urea was 15 mg/dL, and creatinine was 0.27 mg/dL. Chest and abdominal X-rays were normal. He received broad-spectrum antibiotics and underwent surgical debridement, and necrotic tissue was obtained for biopsy and culture. Histology examination showed non-specific granulation tissue consistent with Fournier gangrene. Soft-tissue culture isolated MRSA and ESBL-K. Antibiotics were changed according to the sensitivity report. Blood and urine cultures were negative.
Conclusions: Immediate surgery and antibiotics are essential in treating Fournier gangrene to avoid life-threatening complications. Initial symptoms are non-specific. Diagnosis remains primarily clinical, confirmed by intraoperative macroscopic findings.
Keywords: Fasciitis, Necrotizing • Fournier Gangrene • *Klebsiella pneumoniae* subsp. *Pneumonia* • Methicillin-Resistant *Staphylococcus aureus*

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Background

Necrotizing fasciitis (NF) is a rare disease in the pediatric population and has high complication and mortality rates [1]. Rapid progression of inflammation is characteristic of NF, and can be seen as erythema or necrotic tissue, which involve the superficial fascia, subcutaneous tissue, and skin [2,3]. Fournier gangrene is a specific form of necrotizing fasciitis involving the perineal and genital regions due to polymicrobial infection [4,5]. Delay in diagnosis and treatment can lead to systemic complications, with poor prognosis [1,6].

Methicillin-resistant *Staphylococcus aureus* (MRSA) infection causes significant morbidity and mortality in neonates [7]. Prevalence is estimated as 1.5% in the neonatal population, with initial colonization sites predominantly at the anterior nares and umbilicus [8,9]. Transmission of MRSA is through breastmilk, during delivery, and by contact with healthcare workers and others [8-11]. Multiple gestation was shown to be associated with an increased risk of MRSA colonization in neonates [8].

Extended-spectrum beta-lactamases (ESBL) form a group of enzymes that can hydrolyze most β -lactam antibiotics, such as first-, second-, and third-generation cephalosporin and aztreonam [12,13]. Therefore, treatment options for ESBL-producing organisms are limited [13]. Risk factors for infection or colonization by ESBL-producing organisms include long hospital stay and prolonged use of invasive medical devices. Thus, effective infection control among healthcare providers is essential to minimize spread of these organisms and to prevent outbreaks [12].

In a previous case report, *S. aureus* was identified as the cause of necrotizing fasciitis in an adult patient with history of receiving high doses of glucocorticoid and type II diabetes mellitus [14]. Here, we report a case of MRSA and ESBL-K-related Fournier gangrene in a previously healthy newborn.

Case Report

A 30-day-old male infant presented to the Emergency Department with rapidly progressive white discoloration of scrotal skin since 3 days prior to admission, which had spread from 2-3 white spots to covering two-thirds of the scrotal skin. Pain upon urination was noted, with normal appetite and bowel movement. Six days earlier, he had fever and skin redness around the groin area, was diagnosed as having diaper rash, and was treated with topical antifungal and corticosteroid ointment. The rash spread to the lower abdomen and both legs and feet, followed by swelling. His mother never bathed him since the onset of fever, and only cleaned the



Figure 1. Clinical features of Fournier gangrene and follow-up after surgical management. (A) Appearance on the day of admission. Two-thirds of scrotal skin was covered by white-grayish tissue (slough) and the rest of the scrotum up to the preputium appeared erythematous. (B) Day 5 postoperative debridement; minimal sloughing and no erythema at the testes, scrotal skin, and penis.

groin and perianal region with wet tissue after urination or defecation. He had no history of trauma, injury, or insect bite, and had no history of systemic illness or infection, malignancy, or surgery. He was born at term by caesarean delivery with indication of multiple pregnancy (twins) and transversal position from a 39-year-old mother with history of hypertension. Birth weight was 2900 g.

At the time of admission, he was afebrile, alert, and active, but was irritable. Vital signs were stable, no sign of dehydration or respiratory distress. On local examination, two-thirds of the scrotal skin was covered by thick, dry, white-grayish tissue (slough), and the surrounding scrotal skin and preputium appeared erythematous and edematous (Figure 1). Mild edema was noticed

in the right leg. Other physical examinations were within normal limits. Laboratory examinations revealed leukocyte count 23 000/ μ L and CRP 26.8 mg/dL. Hemoglobin was 10.6 g/dL, serum sodium was 134 mEq/L, blood glucose was 80 mg/dL, serum urea was 15 mg/dL, and creatinine was 0.27 mg/dL. Liver and coagulation functions were normal. Chest and abdominal X-rays were normal. Blood and urine cultures were negative (no growth).

The patient was given maintenance intravenous (i.v.) fluid and broad-spectrum antibiotics that covered both aerobic and anaerobic organisms. Cefotaxime 50 mg/kg/dose i.v. every 8 h and Amikacin 20 mg/kg/day i.v. on the first day, continued with 15 mg/kg/day i.v. Surgical debridement under general anesthesia was done. Sloughing necrotic tissue was identified on the lower two-thirds of the scrotal region. All necrotic tissue was excised, thus exposing the unaffected testes. Wound swabbing, soft-tissue biopsy, and culture-sensitivity were performed during surgical debridement. Histology examination of this necrotic tissue showed non-specific granulation tissue, consistent with Fournier gangrene. The wound swab showed no growth, but the soft-tissue culture isolated MRSA and ESBL-K. Based on the sensitivity report, antibiotics were switched to Tigecycline 2 mg/kg/day i.v. for 10 days and metronidazole loading dose 15 mg/kg/day i.v., continued with 7.5 mg/kg/dose i.v. every 8 h for 7 days. The parents was advised to perform a decolonization protocol including nasal decolonization with mupirocin twice per day for 10 days plus topical body decolonization with chlorhexidine for 14 days. Personal hygiene and wound care were also provided, including regular bathing and hand washing with soap and water or an alcohol-based hand gel, especially after touching infected skin.

Discussion

Necrotizing fasciitis is a severe bacterial infection of soft tissue, which includes the superficial fascial layers [1]. It is uncommon in children, especially in those without know risk factors, with potentially life-threatening complications and increased mortality [2]. Thus, early diagnosis and prompt therapy are important to avoid unwanted complications.

Generally, according to microbiological findings, necrotizing fasciitis can be divided into 2 types. Type I, the most common type (70-90% of cases), is polymicrobial infection, and type II, mainly caused by Group A Streptococcus (GAS) and *S. aureus*, is known as monomicrobial infection [15]. Recent studies concluded that classification of necrotizing fasciitis consists of 4 types (Table 1), with type III including infection by Clostridium sp. or Gram-negative bacteria (monomicrobial infections) and type IV is caused by fungal infections [16]. The annual incidence is estimated to be 0.8 per million [3]. The overall mortality rate in children, based on studies and several

Table 1. Classification of necrotizing fasciitis [15,16].

Type	Pathogen
I (polymicrobial)	Gram-positive cocci Enterobacteriaceae Obligate and facultative anaerobes
II (monomicrobial)	Beta-hemolytic streptococcus A
III	Clostridium sp. Gram-negative bacteria Vibrios spp. <i>Aeromonas hydrophila</i>
IV	Candida spp. Zygomycetes

recent meta-analyses, is reported at 5-25% and 15.4% [3-6] and may be as high as 59% in neonates [6,17].

Fournier gangrene is a polymicrobial necrotizing fasciitis of the genital, perineal, and perianal regions [16,18,19]. It can be either idiopathic (primary) or with predisposing factors (secondary) [17]. It usually develops in children with risk factors, such as trauma, minor lacerations, diaper rash, insect bites, surgical or invasive procedure, burns, urethral instrumentation, varicella, systemic illness, malnutrition, and immunocompromise (eg, cancer, chemotherapy) [1,2,4,20]. However, many cases occur in otherwise healthy children [4]. In our case, there was a history of diaper rash that seemed to be precipitated by the use of topical antifungal and steroid cream, and later on was aggravated by poor body hygiene. Previously, poor general hygiene has been suggested to be a predisposing condition in 2 cases – a 10-month-old boy and a 2-year-old boy – diagnosed with Fournier gangrene [19,21].

Diagnosis primarily depends on clinical findings and remains a significant challenge because of lack of “toxic” features [20]. Classic local symptoms include severe pain (97%) or tenderness, skin rash (73%) or erythema, warm skin, and edema. Assessing pain in children is often difficult and not as relevant as in adult patients [1,4]. These symptoms can rapidly spread and progress, with the presence of bullae, skin ecchymosis, and tissue necrosis or sloughing, resulting in localized anesthesia because of superficial nerve damage [2,17]. Soft-tissue crepitation can be found and represents gas in the tissue, which is mainly caused by anaerobic bacteria [1,17]. Systemic signs of fever and tachycardia are usually present [1,4]. In several cases, the children mostly presented on admission with dehydration, fever, and lethargy [19,21,22]. Complications such as sepsis, shock, coagulopathy, electrolyte imbalance, respiratory failure, renal failure, and multi-organ failure are frequent and significantly increase mortality [3,19,23].

Definitive diagnosis is obtained by macroscopic surgical findings confirming soft-tissue necrosis [1]. Laboratory findings

are unspecific. The presence of leukocytosis, coagulopathy, decreased sodium level, elevated C-reactive protein, creatinine, creatinine kinase, and anemia can raise suspicion of NF [1,4,20]. In adults, a validated scoring system called the Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) was used to diagnose NF, but its diagnostic value in children is unknown [20,24].

Currently, there is no recommendation of standard imaging studies to diagnose NF in children [4]. Radiologic studies should not delay the final treatment [1]. X-ray images may show subcutaneous emphysema. Ultrasound may be useful to identify gas or fluid collection (differentiating cellulitis and abscess) [19]. CT and MRI have been used for NF evaluation in children [4]. Microbiologic studies such as blood, urine, tissue, and wound swab cultures should be done to identify the causative organisms [1,15].

Management of Fournier gangrene consist of early and aggressive fluid resuscitation, broad-spectrum antibiotics, and immediate surgical debridement [19,20]. As soon as possible, empiric antibiotic treatment should be started, covering anaerobic, Gram-positive, and Gram-negative organisms for 7-14 days [1]. At first, our patient received a combination of third-generation cephalosporin and aminoglycoside. Antibiotics were switched to linezolid and metronidazole after the culture and sensitivity results were known, which revealed MRSA and ESBL-K infection. Tissue recovery was likely improved by use of organism-specific therapy. Serial debridement was performed to obtain viable and clean margins. For MRSA infection, a decolonization

protocol was followed, including nasal decolonization with mupirocin twice/day for 5-10 days and topical body decolonization with a skin antiseptic solution (chlorhexidine) for 5-14 days [25]. A previously published case of Fournier gangrene reported MRSA as one of the organisms isolated from scrotal aspirate; the patient was treated with a combination of meropenem, teicoplanin, and clindamycin for 14 days and the condition significantly improved [26].

Conclusions

A 1-month-old male who developed Fournier gangrene caused by MRSA and ESBL-K was successfully treated. Early diagnosis and prompt treatment including broad-spectrum antibiotic and surgical debridement are mandatory to avoid life-threatening complications.

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Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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