Numerous Eruptive Lesions of Panniculitis Associated with Group A Streptococcus Bacteremia in an Immunocompetent Child

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A previously healthy 13-month-old boy developed group A \( \beta \)-hemolytic streptococcus bacteremia coinciding with numerous eruptive subcutaneous lesions primarily on his extremities. Skin biopsy revealed infectious panniculitis; gram-positive cocci were present within both fat lobules and septa. Molecular genetic analysis of an isolate from the patient’s blood revealed an \( emm \) type 4 organism displaying the \( emm \) chromosomal pattern E that is characteristic of opacity factor–producing strains; the organism also harbored the gene encoding for streptococcal pyrogenic exotoxin C (\( speC \)). To our knowledge, this clinical presentation has not yet been described in the spectrum of infections directly caused by group A \( \beta \)-hemolytic streptococci.

Group A \( \beta \)-hemolytic streptococcus (GABHS) can cause a wide variety of cutaneous and soft-tissue infections [1–3]. The clinical spectrum of lesions ranges from impetigo, which affects superficial layers of the skin (i.e., epidermis); to erysipelas and cellulitis, affecting intermediate layers (dermis); to necrotizing fasciitis, which involves deeper tissue (fascia) (figure 1). Panniculitis arises through inflammation of the subcutaneous fat and can be associated with GABHS upper respiratory tract infection, as observed with erythema nodosum (EN) [5, 6]. However, EN develops as a result of nonspecific immunologic processes [7]. To our knowledge, we present the first confirmed case of widespread eruptive panniculitis in an immunocompetent infant that was associated with GABHS bacteremia, clinical signs of sepsis, and the presence of gram-positive cocci within the affected tissue.

Case Report

A 13-month-old Hispanic boy was in good health until 2 days before admission when he became irritable and developed a rectal temperature of 38.9°C. He was brought to the Emergency Department at Yale–New Haven Hospital (New Haven, CT); a viral illness was diagnosed, and he was treated with acetaminophen as an outpatient. The day before admission, according to the patient’s mother, a rash appeared on his arms that spread to his face, chest, abdomen, legs, and buttocks. Additional symptoms included rhinorrhea, recurrent high rectal temperatures (to 40.0°C), vomiting of nonbilious material, and decreased urinary output despite good liquid intake. His mother also reported that the child seemed to have diffuse abdominal tenderness. She denied any diarrhea, bloody stools, joint swellings, joint tenderness, or decreased range of motion in his extremities.

His medical history was significant for prematurity (25 weeks’ gestation) and for intubation for the first month of life that was secondary to respiratory distress. In addition, he had a history of mild asthma and iron deficiency anemia at age 12 months, for which he was being treated with nebulizers and iron supplements, respectively, at home. He had no known drug allergies. The child’s immunizations were up-to-date. The mother denied any family history of immunodeficiency. No close contacts were noted to have similar symptoms.

Physical examination at the time of admission revealed an easily aroused, lethargic, and irritable child in no acute distress whose tympanic temperature was 38.2°C, heart rate was 168, and blood pressure was 111/66 mm Hg. Numerous blotchy erythematous nodules, primarily on the upper and lower extremities (figure 2), were found on his skin. A few lesions were located on the chest and face. The nodules measured 1–2 cm in diameter. Several lesions on his arms and legs had central petechiae, with surrounding petechiae in several areas. The remainder of the physical examination findings were unremarkable. There was no evidence of cardiac murmurs, lower extremity edema, or joint swelling.

Laboratory evaluation revealed a slightly elevated WBC count (12,400/mm\(^3\)) and a normal differential blood cell count. The patient’s erythrocyte sedimentation rate (Westergren method) was 32 mm/hour (normal, <20 mm/hour). His total hemolytic complement level and “pitted” RBC count [8] were both within normal limits. Urinalysis showed 1+ protein, small amounts of occult blood and leukocyte esterase, 6–10 WBCs per high-power field, and 0–1 RBCs per high-power field. Blood, urine, and throat specimens were obtained for culture. A chest roentgenogram showed mild peribronchiolar thickening but no focal infiltrates. On the basis of the rash, the vague symptoms of abdominal pain, and the occult blood in the urine, the presumptive diagnosis was Henoch-Schönlein purpura.
Necrotizing fasciitis develops in deeper fascial tissues. Reprinted with permission [4].

Figure 1. Schematic drawing of the skin and soft tissue that shows the location of inflammation in lobular and septal panniculitis. Group A β-hemolytic streptococcus–associated affects the epidermal layer, whereas erysipelas and cellulitis affect the dermal layer. Necrotizing fasciitis develops in deeper facial tissues. Reprinted with permission [4].

Twelve hours after admission, his tympanic temperature increased to 40.6°C, and tachycardia (heart rate, 180), tachypnea (respiratory rate, 48), and a blood pressure of 114/68 mm Hg were noted. These findings were consistent with a septic condition. Out of concern for the development of bacterial sepsis and meningitis, parenteral therapy with ceftriaxone (500 mg) was initiated and a lumbar puncture was performed. Analysis of CSF revealed no nucleated cells, and gram staining of CSF was negative; CSF cultures were performed. To rule out the possibility of acute hemorrhagic edema of childhood (Finkelstein’s disease) or EN, a 4-mm punch biopsy specimen that included subcutaneous fat was obtained.

After 26 hours of hospitalized, gram-positive cocci were noted to be growing in the cultures of blood (both aerobic and anaerobic bottles) obtained during admission. Empirical therapy with intravenous vancomycin (15 mg/kg) was initiated. Subsequently, the organism was identified as GABHS; vancomycin therapy was discontinued, and treatment with parenteral ampicillin (50 mg/kg) was begun. Over the ensuing 48 to 72 hours, the cutaneous lesions faded, and the child became afebrile. Repeated cultures of blood obtained just before ceftriaxone administration were negative for bacterial growth. Urine, CSF, and throat cultures also showed no growth of GABHS. After 7 days of intravenous antibiotic therapy, the patient’s skin lesions had faded without any residual skin markings, and he was discharged to home receiving oral amoxicillin therapy. The patient never developed an audible cardiac murmur or hematuria.

Examination of the skin biopsy specimen demonstrated an unremarkable epidermis and dermis, and examination of the subcutaneous fat showed neutrophilic infiltrates in both septal and lobular areas (figure 3A), which is characteristic of mixed septal-lobular panniculitis (figure 1). There was no evidence of vasculitis or fat necrosis. Inspection of the fat revealed one basophilic oval collection of cocci (figures 3B and 3C). Brown-Brenn staining of a serial histological tissue section for bacteria [9] revealed gram-positive cocci and showed cocci scattered throughout the fat lobules and septae that were admixed with neutrophils (figure 3D). Staining for fungi and acid-fast bacilli was negative. Cultures of the skin biopsy specimen were not performed.

The GABHS recovered from the patient’s blood (designated as strain YL05) was subjected to molecular genetic analysis. Nucleotide sequence determination of the 5′ end of the emm gene revealed an emm sequence type 4. A PCR-based chromosomal mapping method demonstrated an emm chromosomal pattern E [10], characteristic of opacity factor–producing organisms. The presence or absence of genes encoding for streptococcal pyrogenic exotoxins (spe) was ascertained by hybridization of whole gene probes to chromosomal DNA. Strain YL05 harbored the speC gene but lacked the speA gene (data not shown).

Discussion

Infectious panniculitis is infrequently observed during childhood [11]. Classically, this clinical entity occurs in adults, particularly in the setting of underlying immunodeficiency, and it is not known to be caused by GABHS [12]. Moreover, the lesions of infectious panniculitis are commonly confined to one area, such as a portion of one extremity. The only reported case of infectious panniculitis in a child (due to Fusarium solani) followed the adult paradigm and occurred in an immunocompromised 5-year-old boy whose lesions were restricted to a single upper extremity [12]. The case reported here has several unusual aspects: it developed in a previously healthy child, and the lesions erupted in an explosive manner with wide dissemination of subcutaneous nodules on both upper and lower extremities as well as on the face and chest.

Clinically, infectious panniculitis should be included in the differential diagnosis when an immunocompetent child presents with skin lesions suggestive of panniculitis, especially in the setting of fever. Other conditions to be considered include EN, Henoch-Schönlein purpura, and acute hemorrhagic edema or Finkelstein’s disease. Several findings argue against the case presented herein as being EN, the most frequent type of panniculitis in children [6, 11].

EN is often described as a delayed-type hypersensitivity response that can be preceded by GABHS upper respiratory tract infection. EN can also have other infectious or noninfectious etiologies, and it is far more common in adults than in children. Classically, EN is a septal type of panniculitis (figure 1). By contrast, examination of the skin biopsy specimen from the patient we described revealed inflammation in both septal and lobular areas of fat (figure 3); mixed septal-lobular patterns of inflammation are also observed in cases of panniculitis caused by tissue infection with other microbial organisms [12]. Furthermore, EN lesions typically contain lymphocytic and histiocytic infiltrates without microorganisms, whereas extensive neutrophilic infiltration as well as gram-positive cocci were found in this child’s lesions. A striking feature of this case
**Figure 2.** Multiple blanching erythematous nodules, 1–2 cm in diameter, on the upper extremity of a patient with panniculitis associated with group A β-hemolytic streptococcus bacteremia. Petechiae are scattered throughout the arm. The photo was taken ~12 hours after admission; at that time ~75 erythematous nodules were noted, primarily on the upper and lower extremities.

**Figure 3.** Stains of a biopsy specimen from a patient with panniculitis associated with group A β-hemolytic streptococcus bacteremia. *A.* Extensive neutrophilic infiltration involving septal and lobular areas within subcutaneous fat; epidermis and dermis are normal (hematoxylin-eosin stain; original magnification, ×40). *B.* Oval collection (arrow) of cocci detected within the tissue section in an area of inflammation (hematoxylin-eosin stain; original magnification, ×400). *C.* Higher magnification of oval collection of cocci (hematoxylin-eosin stain; original magnification, ×1,000). *D.* Gram-positive cocci scattered throughout area of inflammation (Brown-Brenn stain; original magnification ×1,000).
was the rapid resolution of cutaneous lesions following the administration of antibiotics; EN lesions usually last from 3 to 6 weeks and evolve like bruises [7]. Likewise, Henoch-Schönlein purpura and acute hemorrhagic edema can be excluded from the differential diagnosis in this case because both of these clinical entities are associated with leukocytoclastic vasculitis that may extend into the subcutaneous fat [13]; skin biopsy specimens in the case we described showed no evidence of vasculitis.

The GABHS isolate from this patient (strain YL05) was identified as emm type 4 and as having the emm chromosomal pattern E [10]. During 1995, a 6-month survey of GABHS isolated from normally sterile tissue sites in 64 residents of Connecticut yielded only one emm type 4 isolate [14]. Strainspecific fingerprints generated by arbitrary-primed PCR reveal that strain YL05 is genetically similar to the invasive emm type 4 organism isolated in Connecticut in 1995 as well as to the two isolates recovered in New York and the United Kingdom during the 1950s (data not shown). The data suggest that strain YL05 does not represent a newly emerged clone; therefore, the unique clinical features observed in this patient are not likely to be due solely to a newly acquired virulence property of GABHS. An emm type 4 isolate having a random amplified polymorphic DNA pattern identical to that of strain YL05 was isolated from the blood of an adult patient at this hospital 1 week before the isolation of strain YL05. Thus, this particular clone appears to be present in the local community. The presence of the speC gene, and the lack of the speA gene, differentiates the YL05 isolate from many GABHS isolates found in association with necrotizing fasciitis and toxic shock syndrome, which typically harbor the speA gene [3].

The precise mechanisms by which GABHS infections give rise to multiple lesions of widely distributed foci containing bacteria, as appears to be the case for this patient with septic panniculitis, are unclear. Although only a single skin biopsy specimen was obtained, the direct observation of gram-positive cocci within the subcutaneous fat that were accompanied by neutrophilic infiltration, the GABHS-positive blood culture, the clinical signs of sepsis, and the resolution of the lesions and sepsis shortly after the initiation of antibiotic therapy all provide strong evidence in support of the idea that multiple lesions were infected with GABHS. Disseminated lesions with bacteria have also been readily found in petechial areas in patients with meningococcemia [15]. GABHS organisms have a predilection for establishing primary infection in certain tissue: the nasopharyngeal mucosa and the epidermis [16]. Conceivably, the organism that seeded the bloodstream of the child we described may have an unusual affinity for fat tissue. Such an infection might be mediated by a bacterial adhesin [17] that specifically binds to components of the extracellular matrix found in fat, such as collagen type III. Consistent with this idea is the identification of a 57-kD collagen-binding protein derived from GABHS [18].

GABHS infection can give rise to several different types of cutaneous and subcutaneous lesions [1–3, 19]. This case is notable for the identification of gram-positive cocci within the adipose tissue of a subcutaneous nodule specimen from a child with widespread eruptive skin lesions and GABHS bacteremia who exhibited clinical signs of sepsis.

Acknowledgments

The authors thank Dr. Michael Gerber for helpful discussions and critical review of the article, Dr. Bernard Beall for emm sequence typing, and Dr. Doug Grossman for the photograph in figure 2.

References