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LETTERS

Granulicatella adiacens and Early-Onset Sepsis in Neonate

To the Editor: Granulicatella and Abiotrophia, formerly known as nutritionally variant streptococci, are normal flora of the human upper respiratory, gastrointestinal, and urogenital tracts (1). G. adiacens has been associated with bacteremia and endovascular, central nervous system, oculocutaneous, and genitourinary infections (1–4).

Although streptococci are a frequent cause of early-onset sepsis in newborns, non–group B or D streptococci comprise only ≈1% of cases of early-onset neonatal sepsis; the condition is primarily associated with viridans streptococci (5). This report describes a male infant with early-onset sepsis caused by G. adiacens. Molecular genetic studies identified the same organism in flora isolated from the maternal cervix, which suggests vertical transmission.

After 36 weeks’ gestation, a male infant, weighing 2,850 g, was born by repeat cesarean section to a 37-year-old woman who was negative for group B streptococcus; she began labor without rupture of membranes. Apgar scores were 9 and 9 at 1 and 5 minutes, respectively. Respiratory distress developed in the infant within an hour of birth. Peripheral blood and cerebrospinal fluid (CSF) samples were obtained, and intravenous ampicillin (150 mg/kg every 12 h) and gentamicin (4 mg/kg every 24 h) were administered. Leukocyte count was 27,000/mm³ with 79% polymorphonuclear leukocytes and 2% band forms; platelet count was 223,000/mm³. CSF cell counts were 3 leukocytes/mm³ and 18 erythrocytes/mm³.

Respiratory distress progressed rapidly, and at 20 hours of life, mechanical ventilation was instituted. Chest radiograph demonstrated diffuse, bilateral interstitial infiltrates consistent with pneumonia. Persistent pulmonary hypertension was diagnosed by echocardiography. Peripheral blood culture yielded G. adiacens (API 20 STREP, bioMérieux Clinical Diagnostics, Durham, NC, USA) that was sensitive to vancomycin. Repeat blood samples were obtained before and after antimicrobial drug treatment was changed to vancomycin, 10 mg/kg every 12 h, and gentamicin, 4 mg/kg every 24 h. CSF culture and repeat blood cultures had no growth. Vancomycin and gentamicin were administered for 14 days. The patient eventually recovered and was discharged after 25 days of hospitalization. The biochemical identification of G. adiacens in the blood culture was confirmed by 16S rRNA gene sequencing.


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Cervical samples for culturing were obtained from the mother 4 days after delivery. After samples were plated on blood and chocolate agar, colonies were harvested from the primary plates, and pooled bacterial DNA was isolated for further analyses. A primer pair was designed to amplify a 422-bp fragment unique to *Granulicatella adiacens*. These primers (sense, 5′-GGTTTATCTTAGAAAGGAGGT-3′; and antisense, 5′-GAGCATTCGGTTGGGCACTCTTAG-3′) were used to amplify *Granulicatella adiacens* from DNA prepared from the bacterial pools isolated from maternal cervix and, as control, from DNA prepared from the infant’s blood culture isolate. DNA amplicons underwent agarose gel electrophoresis with ethidium bromide staining and were visualized under ultraviolet light. PCR amplification showed DNA amplicons for the patient’s blood culture, his mother’s cervical swab sample, and a positive control but not for negative controls (Figure). Capillary nucleotide DNA sequence analysis confirmed all 3 amplicons as *Granulicatella adiacens* (not shown).

Nutritionally-variant streptococci have been difficult to identify because they have unique culture requirements, they exhibit pleomorphic phenotypic features (1), and they demonstrate satellitism around colonies of other bacteria. This has led to misidentification or nonidentification by using commercially available phenotypic testing, prompting the recommendation that 16S rRNA gene sequencing be used for *Granulicatella adiacens* identification (6).

The Clinical and Laboratory Standards Institute does not recommend disk-diffusion testing to determine the susceptibility of *Granulicatella adiacens* to antimicrobial drugs and suggests broth microdilution MIC testing in cation-adjusted Mueller-Hinton broth with 2.5%–5% lysed horse blood and 0.001% pyridoxine hydrochloride (7,8). Under these conditions, 55% of *Granulicatella adiacens* isolates were susceptible to penicillin, 63% were susceptible to ceftriaxone, 96% were susceptible to meropenem, and 100% were susceptible to vancomycin (4). A more recent report indicates that the resistance of *Granulicatella adiacens* to β-lactam and macrolide antimicrobial drugs may be increasing (3).

Treatment of *Granulicatella adiacens* infection may be difficult. In vitro antimicrobial drug susceptibility patterns do not correlate well with clinical response to treatment, and *Granulicatella adiacens* infections often respond poorly to antimicrobial drug treatment. Higher rates of bacteriologic failure and relapse rates after treatment have been observed for *Granulicatella adiacens* infection than for infections with streptococci and other related genera (9). *Granulicatella adiacens* endocarditis has been associated with a more severe clinical course than endocarditis caused by enterococci or viridans group streptococci, with higher rates of illness and death. On the basis of studies demonstrating synergy in vitro and in vivo, empiric combination therapy with vancomycin and an aminoglycoside has been suggested until susceptibility data are available (10), particularly when treating serious conditions such as endocarditis (3).

Reports have increased of serious infections caused by *Granulicatella* and *Abiotrophia*, including this report of early onset neonatal sepsis due to *Granulicatella adiacens*. One recent study described 8 isolates associated with invasive infection in a 4-year period (3). Increased awareness and identification of *Granulicatella adiacens* are likely contributing to this increased recognition, with earlier cases not detected or diagnosed. 16S rRNA gene sequencing may facilitate or confirm *Granulicatella adiacens* and *Abiotrophia* spp. as the etiologic agents of infection.
Lymphocytic Choriomeningitis with Severe Manifestations, Missouri, USA

To the Editor: Lymphocytic choriomeningitis virus (LCMV) is an arenavirus maintained zoonotically in house mice (Mus musculus) and may also be carried by pet rodents, especially hamsters (1–3). Infection of healthy humans usually results in nonspecific febrile illness. However, LCMV infection can cause severe symptoms, including aseptic meningitis (4).

Early data suggested ≤8% of central nervous system manifestations of viral etiology were caused by LCMV (5). In contrast, in a more recent study of 91 cases of encephalitis among persons with potential rodent contact, LCMV was not detected (6). We describe 2 recent unrelated LCMV infections with central nervous system manifestations, which were associated with rodent exposures, as a reminder that LCMV should be considered in cases of aseptic meningitis of unknown etiology.

In July 2008, an 89-year-old man in Missouri, USA, with a history of hypertension received a prescription for metolazone and was given methotrexate (2.5 mg orally, 3×/wk) because of a pharmacy error. Two weeks later, he showed confusion, speech difficulty, and had a fever. When hospitalized 3 weeks after symptom onset, the patient was drowsy but able to answer questions and had a supple neck, plantar responses in extension, and a temperature of 38.8°C. Methotrexate treatment was then stopped.

Routine laboratory test results were within reference ranges, with the exception of a serum aspartate aminotransferase level of 92 U/L (reference range 0–37 U/L) and an alanine aminotransferase level of 78 U/L (reference range 0–65 U/L). Two blood cultures were sterile, a chest radiograph showed cardiomegaly, and cranial computed tomography without contrast showed moderate cerebral atrophy.

The patient was empirically given intravenous ceftriaxone (1 g) and intravenous azithromycin (500 mg, 1×/d for 7 days). Two days after he was hospitalized, cranial magnetic resonance imaging showed mild-to-moderate, chronic, small vessel ischemia and involutional changes. Serologic test results for HIV and West Nile virus were negative. On the fourth hospital day, lumbar puncture yielded clear, colorless cerebrospinal fluid (CSF) containing 1 erythrocyte and 98 leukocytes/high-powered field (1% neutrophils, 95% lymphocytes, 4% monocytes); protein level was 127 mg/dL (reference range 15–45 mg/dL), and glucose level was 40 mg/dL (reference range 43–70 mg/dL). CSF test results for bacteria, cryptococcal antigen, and herpes simplex virus (HSV) and PCR result for Borrelia burgdorferi were negative. CSF and serum submitted to the Centers for Disease Control and Prevention showed LCMV-specific

References

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