Gemella Morbillorum as a Cause of Septic Shock.

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NOTES

Gemella morbillorum as a Cause of Septic Shock

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The gram-positive bacterium *Gemella morbillorum* has been recovered from patients with endocarditis but has rarely been associated with acute fulminant infections. We describe two children with a rapid onset of septic shock, which was fatal in one, following infection with this organism. *G. morbillorum* is a commensal organism of the upper respiratory tract; it gained access to the bloodstreams in these patients, and bacteremia occurred. A clinical drawback is that the initial colonial morphology of this organism leads to presumptive identification as a viridans streptococcus, an organism not commonly associated with septic shock syndrome. Resistance of *G. morbillorum* to penicillin appears to be common; therefore, initial empirical combination therapy (a β-lactam agent and an aminoglycoside) or vancomycin treatment should be considered.

The anaerobic or microaerophilic gram-positive coccus *Gemella morbillorum* is a normal inhabitant of the oral cavity. Previously known as *Streptococcus morbillorum,* it was reclassified into the genus *Gemella* in 1988 on the basis of DNA hybridization [1]. This organism has been implicated in endovascular infections, chiefly endocarditis, but acute invasive infections due to this bacterium, such as septic arthritis, meningitis, and septicemia, have only recently been recognized. We describe two children with septic shock caused by *G. morbillorum,* one of whom died. In one case, the isolate was resistant to penicillin.

Case Reports

Case 1. A 2-year-old girl with Down syndrome, a single ventricle, transposition of the great arteries, and pulmonic stenosis underwent a Fontan procedure (shunt between the right atrium and pulmonary artery). Her convalescence was uneventful, although she continued to require ventilatory support. Three days after the procedure, she had fever (temperature to 103°F), and there was a sudden onset of hypotension and diminished peripheral pulses. The diagnosis of septic shock was made, and appropriate supportive treatment was begun. Therapy with vancomycin, ceftazidime, and amikacin was initiated. Cultures of blood obtained by peripheral venipuncture and through two separate central venous catheters yielded *G. morbillorum.* The organism was susceptible to all β-lactam antibiotics tested (MIC of penicillin, ≤ 0.03 μg/mL) as well as to aminoglycosides and vancomycin. An echocardiographic study was negative for endocardial vegetations, and no other focus of infection could be identified. The patient's clinical status continued to deteriorate, and ascites, bilateral pleural effusion, and adult respiratory distress syndrome developed. On the 12th postoperative day, she died of the effects of multiorgan failure.

Case 2. An 11-year-old girl who was receiving chemotherapy for nasopharyngeal Burkitt's lymphoma was admitted to the hospital because of complaints of fever (temperature, 104.8°F), nausea, and vomiting. She was toxic-appearing, but apart from a temperature of 103°F, the rest of the physical examination was unremarkable. A subcutaneously implanted central venous access device was in place, and there was no evidence of local infection. Laboratory studies disclosed the following significant findings: leukocyte count, 200/mm^3 (no neutrophils); hematocrit, 23.2%; and platelet count, 11,000/mm^3. Therapy with intravenous ticarcillin/clavulanic acid and tobramycin was initiated empirically. The following day, intravenous vancomycin was added to the therapeutic regimen as cultures of blood obtained from the central venous catheter and from a peripheral vein during admission were reported preliminarily as positive for a gram-positive coccus.

Her medical history included an admission to the hospital 6 weeks before for an episode of fever and neutropenia. She was found to have maxillary sinusitis; she received broad-spectrum antibiotic therapy and antifungal treatment and underwent surgical drainage of the sinus. Culture of the drainage yielded a viridans streptococcus; this organism was not identified further.

One day after admission, she complained of a generalized, intractable headache. Because of her history of sinusitis and because she had profound thrombocytopenia, CT of the head was performed to rule out intracranial complications. The only

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abnormality found was a recurrence of right maxillary sinusitis. The following day, she became delirious. Physical examination revealed that she was disoriented and had nuchal rigidity and nystagmoid eye movements; no focal neurological deficits were noted. Analysis of CSF obtained by lumbar puncture demonstrated pleocytosis and an elevated protein level of 101 mg/dL, which was attributed to recent intrathecal chemotherapy. A few hours later, she had an acute onset of hypotension followed by cardiac arrest, and cardiopulmonary resuscitation was performed. The isolates from the blood obtained on the day of admission were identified as *G. morbillorum.* The organism was resistant to penicillin (MIC, ≥ 4 μg/mL) but was apparently susceptible to ticarcillin/clavulanic acid (by the Kirby-Bauer disk diffusion test; an MIC was not determined). The patient's clinical status improved gradually; she became afebrile, and several follow-up blood cultures were negative. Treatment with vancomycin was discontinued after 14 days.

Discussion

G. morbillorum was originally isolated in 1917 by Tunnicliff [2]; the organism was recovered from blood from 42 patients during the early stages of measles and was identified as a micrococcus. The name was changed later to *Diplococcus rubeolae,* and still later the name *Diplococcus morbillorum* was adopted [3]. Because of its anaerobic nature, especially during isolation, the organism was transferred to the genus *Peptostreptococcus* and later to the genus *Streptococcus* on the basis of the fact that lactic acid is its major metabolic product [4]. Recently, DNA-DNA filter hybridization, guanine and cytosine content analysis, and 16S rRNA oligonucleotide cataloging revealed its close resemblance to *Gemella haemolysans,* thereby resulting in another change of nomenclature [1, 4].

Gemellae are anaerobic-to-aerotolerant gram-positive cocci that exist as part of the normal oropharyngeal microflora in humans. They may exhibit α-hemolysis on blood agar, thus leading to initial presumptive identification as a viridans streptococcus. A positive L-pyrrolidonyl-β-naphthylamide hydrolysis test can rapidly distinguish the isolate from a viridans streptococcus [5]. In addition, gemellae tend to grow slowly and therefore may be confused with nutritionally variant streptococci. Other microbiological characteristics include susceptibility to vancomycin and negative reactions to oxidase and catalase.

Cases of endocarditis, other endovascular infections, meningitis, and septic arthritis due to *G. morbillorum* have been reported, but these cases have rarely been fatal [6]. In addition, a report on septicemia due to viridans streptococci in patients with cancer [7] included six patients with infection due to this organism, identified therein as *S. morbillorum.* Only two pediatric cases have been reported [8, 9]. The first case is prototypical of *G. morbillorum* infection because the patient had endocarditis [8]. A 19-year-old heroin addict had tricuspid valvulitis due to intravenous contamination. The patient's illness resolved after 4 weeks of therapy with intravenous penicillin and gentamicin, and the size of the tricuspid valve vegetations diminished. The other case occurred in a 15-year-old boy with purulent meningitis and bacteremia as a complication of acute frontal sinusitis; he died of neurological complications [9].

Our two cases demonstrate an association of *G. morbillorum* infection with septic shock syndrome, which was fatal in one case. In case 1, the patient had no obvious predisposing factors for overwhelming septicemia other than Down syndrome and recent surgery, yet systemic infection developed while the patient was intubated in the postoperative period. The organism was presumably seeded into the bloodstream from the oral flora, which was perhaps related to intubation.

In case 2, the patient, who had neutropenia and cancer, probably acquired the systemic infection as a consequence of recent sinusitis. An organism reported as a viridans streptococcus had been recently isolated from a sinus aspirate, but this organism was considered to represent normal upper respiratory tract bacteria, which are not routinely identified further. However, the bacterium grew well on routine media, not slowly as gemellae usually do. Nevertheless, the systemic infection did occur in conjunction with a recurrence of maxillary sinusitis, which we presume was the source. However, the possibility of infected central venous catheters cannot be excluded, as both patients had catheters in place at the time blood was obtained for cultures. There was no evidence of bacterial invasion of the subarachnoid space, and the neurological manifestations were consistent with toxic encephalopathy. The fact that infection occurred in two high-risk patients, at least one of whom was overtly immunocompromised, suggests the possibility that *G. morbillorum* may be encountered as an opportunistic pathogen in immunocompromised patients.

In the report by Elting et al. [7], at least one patient with endocarditis due to this organism had "alpha strep shock syndrome." Although the presentation was stated to be comparable with streptococcal toxic shock syndrome [10], it is not clear whether characteristic diagnostic features (e.g., desquamation of the palms or soles) were present. Neither of our patients had skin desquamation or a rash. To our knowledge, toxin production by *Gemella* species has not been reported, and, in fact, little is known about the virulence factors of *G. morbillorum,* although exopolysaccharide production has been implicated in endocarditis and genital infections in adults [11, 12].

The isolate from one of our patients was resistant to penicillin (MIC, ≥ 4 μg/mL). Resistance of *Streptococcus pneumoniae* to penicillin is seen increasingly, but, to our knowledge, this is the first report of high-level or "absolute" resistance of *G. morbillorum* to penicillin. The mechanism of resistance is unknown. β-Lactamase production has not been described; therefore, resistance could be related to an alteration of penicillin-binding proteins. Tolerance to β-lactam antibiotics, a known characteristic of uncertain significance in other gram-positive cocci, has also been reported. The MIC and MBC of

both penicillin and ampicillin for an isolate from the blood of an adult with endocarditis were both 0.015 μg/mL and >16 μg/mL, respectively [13]. Three isolates have been reported to be resistant to penicillin; resistance was determined by a Kirby-Bauer method that measured a zone diameter of <19 mm, which does not distinguish between intermediate and high-level resistance [7].

Unless high-level resistance is found to occur more commonly, initial therapy for *G. morbillorum* infection should probably consist of a combination of a β-lactam agent and an aminoglycoside (e.g., penicillin and gentamicin). It is probably necessary to treat infection caused by a strain with high-level resistance to penicillin (MIC, >1 μg/mL) with vancomycin, analogous to current therapeutic practice for infections due to penicillin-resistant *S. pneumoniae.* In our patient with infection due to the penicillin-resistant isolate, deterioration occurred while treatment with ticarcillin/clavulanic acid was being administered. It is possible that the isolate was truly resistant to this combination therapy, as the MIC was not available on the panel tested. The role of cephalosporins in the management of *G. morbillorum* infection and the in vitro susceptibility breakpoints for cephalosporins are unknown.

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