Gene Predicts MRSA-Related Pulmonary Complications

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

Children with methicillin-resistant *Staphylococcus aureus* infections are more likely to show abnormal pulmonary imaging than those with methicillin-susceptible *S. aureus* infections.

The presence of genes encoding for Panton-Valentine leukocidin (PVL), which is much more common in methicillin-resistant *S. aureus* (MRSA), may be a factor in MRSA-associated pulmonary complications, said Blanca Gonzalez, M.D., and her colleagues.

The gene has been associated with severe necrotizing pneumonia and osteomyelitis, said Dr. Gonzalez of the Texas Children's Hospital, Houston, and her associates (Clin. Infect. Dis. 2005;41:583-90).

The investigators examined pulmonary complications in 70 pediatric patients with MRSA and 43 with methicillin-susceptible *S. aureus* (MSSA). Pulmonary complications were much more common in the MRSA group than the MSSA group (67% vs. 28%). Two patients with MRSA died, as did one with MSSA.

Of the 47 MRSA patients with abnormal pulmonary imaging, 21 (45%) received a primary diagnosis of pneumonia. Four of these had bacteremia; 14 had empyema; 3 had uncomplicated pneumonia with bacteremia; and 4 had lung abscess. A total of 20 patients (43%) received a primary diagnosis of osteomyelitis; most (85%) had bacteremia. Imaging showed atelectasis in four; eight had pneumonia (three with effusions); and four had pneumatoceles. Six patients had septic emboli, and the rest had multifocal air space disease or interstitial disease.

Patients with a primary diagnosis of pneumonia were significantly younger than those with other invasive MRSA disease (3.5 years vs. 10 years). Again, patients with MSSA who had a primary diagnosis of pneumonia also were significantly younger than those with other invasive disease (7 months vs. 12 years). Only 10 patients with MSSA had pulmonary complications: 2 had a primary diagnosis of pneumonia and also had loculated empyema, 6 had bone or joint infections, and 2 had endocarditis.

Isolates from 103 children were tested for genes encoding for PVL. All but one of the MRSA isolates was positive for PVL, compared with only 2 (26%) of the MSSA isolates. Among the 80 PVL-positive isolates, 51 came from children with abnormal chest radiographs, compared with 2 of 23 PVL-negative isolates.

In an accompanying editorial, Jerome Etienne, M.D., argued for routine testing for PVL.

"Regardless of the localization of the infection, the presence of PVL appears to be associated with increased severity, ranging from cutaneous infection requiring surgical drainage to severe chronic osteomyelitis and deadly necrotizing pneumonia," said Dr. Etienne of the National Reference Center of Staphylococcus, Lyon, France. "With the increased prevalence of community-acquired MRSA, which usually contain the genes encoding PVL, it is important that clinical laboratories test for detection of this toxin in routine *S. aureus* isolates" (Clin. Infect. Dis. 2005;41:591-93). ■

S. Aureus *Is Agent Of Fatal Syndrome*

Three children diagnosed with Waterhouse-Friderichsen syndrome died after rapidly progressive illness was traced to severe *Staphylococcus aureus* infection, said Patricia V. Adem, M.D., of the University of Chicago, and her associates.

The three patients—a 15-month-old girl, a 9-month-old girl, and a 17-month-old boy—had been in good health prior to the onset of infection. Premortem cultures yielded methicillin-susceptible *S. aureus* in the first patient and methicillin-resistant *S. aureus* (MRSA) in the next two patients. All the isolates were genetically related, which underscores the rise in community-associated MRSA, the investigators said (N. Engl. J. Med. 2005;353:1245-51).

Characteristics of Waterhouse-Friderichsen syndrome include petechial rash, coagulopathy, cardiovascular collapse, and bilateral adrenal hemorrhage. Although extracorporeal membrane oxygenation has been associated with adrenal hemorrhage in other studies, it was not associated with fatal illness in the two patients in this review who received it.

Noteworthy clinical features in all three children included leukopenia, neutropenia, profound tachycardia, and profound metabolic acidosis, and the course of the disease resembled fulminant meningococcemia.

Pathologic findings revealed severe sepsis and disseminated intravascular coagulation, but there was no evidence of myocarditis or endocarditis. The lungs of all three patients showed gram-positive cocci in clusters, some of which were found in the vascular walls.

—Heidi Splete

Hyperglycemia Associated With Complications in Septic Neonates

BY JANE SALODOF MACNEIL
Southwest Bureau

PHOENIX — Critically ill infants on total parenteral nutrition may face more complications and worse outcomes as a result of hyperglycemia induced by overfeeding, reported Diya I. Alaedeen, M.D., at the annual meeting of the American Pediatric Surgical Association.

A retrospective review of 37 premature infants treated for sepsis during a 1-year period found associations between hyperglycemia, morbidity, and mortality. The higher their maximum serum glucose concentration, the longer the babies were on mechanical ventilation and the longer they stayed in the hospital, Dr. Alaedeen said.

The average maximum glucose level was 100 mg/dL higher in 6 babies (16%) who died than in 31 babies who lived. It reached 241 mg/dL in nonsurvivors vs. 141 mg/dL in survivors.

Avoiding caloric overfeeding, possibly with tight glycemic control, may help reduce hyperglycemia-associated morbidity and mortality.

"Avoiding caloric overfeeding, perhaps with tight glycemic control, in critically ill infants might be effective for reducing hyperglycemia-associated morbidity and mortality," said Dr. Alaedeen of Rainbow Babies and Children's Hospital in Cleveland.

Dr. Alaedeen and his colleagues reviewed all ventilator-dependent premature infants who weighed less than 1,500 g, had culture-proven sepsis, and required total parenteral nutrition while treated in the hospital's neonatal intensive care unit during 2002. Coagulase-negative staphylococci were the most common cause of sepsis, identified in 76% of cases.

Among survivors, 20 infants had maximum glucose levels above 120 mg/dL; their average length of stay exceeded 100 days. The other 11 survivors had levels at or below 120 mg/dL and stayed a little more than 60 days on average.

The study found that the average caloric intake for all infants was 83 ±19 kcal/kg per day during the first week after sepsis was proved by culture. This intake exceeds the average measured energy expenditure of 40-60 kcal/kg per day observed in infants during states of acute metabolic stress, according to Dr. Alaedeen.

"It is likely that our babies were overfed. When [infants] are ill, they are not using these calories to grow," he added in an interview.

Dr. Alaedeen noted that the project could not discern to what degree hyperglycemia was a result of overfeeding by total parenteral nutrition as distinguished from a response to injury. To resolve that issue, he called for a prospective study "correlating C-reactive protein, as a measure of acute metabolic stress, and/or MEE [measured energy expenditure] with caloric delivery."

Moderator Daniel H. Teitelbaum, M.D., of the University of Michigan in Ann Arbor, praised the presentation as "a wonderful study." He noted that it echoes correlations in an influential paper associating hyperglycemia with worse outcomes in critically ill adults (N. Engl. J. Med. 2001; 345:1359-67). ■

Incidence of Sepsis Continues To Rise in the United States

SAN DIEGO — The rising incidence of severe sepsis in the past 2 decades has been accompanied by a decline in the case fatality rate, Charmaine Lewis, M.D., reported in a poster session at the 100th International Conference of the American Thoracic Society.

The incidence of severe sepsis in the United States rose from about 10 cases per 100,000 people in 1979 to 106 cases per 100,000 people in 2002.

"Severe sepsis is a common diagnosis for ICU admission—it's the 10th most common cause of death in the United States, and it's increasing in incidence," Dr. Lewis told FAMILY PRACTICE NEWS.

Key reasons for the increase since 1979, she said, include the emergence of HIV and the aging population. In addition, "we use a lot more immunosuppressive agents to treat what we used to consider mundane problems, such as rheumatoid arthritis," said Dr. Lewis, of the division of pulmonary, allergy, and critical care at Emory University, Atlanta.

Meanwhile, the case fatality rate among patients with severe sepsis dropped from 56% in 1979 to 36% in 2002. Fatality rates were highest among patients with respiratory, metabolic, or cardiovascular organ failure, Dr. Lewis said.

Reasons for the decline in deaths remain unclear, she said, but may have to do with improved recognition and treatment of sepsis in acute care settings.

Dr. Lewis and her associates identified patients with severe sepsis by ICD-9 codes for sepsis and acute organ dysfunction contained in National Hospital Discharge Surveys between 1979 and 2002. They normalized incidence rates to the 2002 Census.

From 1979 to 2002 there were 3,302,635 cases of severe sepsis in the United States. Over that period the incidence increased from about 10 cases per 100,000 people in 1979 to a peak of 106 cases per 100,000 people in 2002. The incidence increased about 8.1% per year between 1982 and 2002.

The average age for all patients (65 years) did not change during the study period, but it was slightly lower for men than for women (63 vs. 67 years) and was lowest for African American males (56 years).

Each year about $17 billion is spent on the care of patients with sepsis.

The National Institutes of Health funded the study.

—Doug Brunk