Cases of Clindamycin-Resistant MRSA Seen in U.S.

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

WASHINGTON — Methicillin-resistant strains of *Staphylococcus aureus* in both healthy and hospitalized children are increasing throughout the country, accompanied by small, but significant, increases in strains that are resistant to both methicillin and clindamycin, according to researchers at the annual meeting of the Pediatric Academic Societies.

Houston has seen ever-increasing rates of methicillin-resistant *S. aureus* (MRSA) since February 2000, when one-third of community-acquired *S. aureus* infections were already positive for MRSA, Sheldon Kaplan, M.D., of Texas Children's Hospital, Houston, told this newspaper.

During his poster presentation, Dr. Kaplan said that by November 2000, that rate had increased to 50% and has continued to increase every year. Recently, MRSA isolates that also are resistant to clindamycin have been identified.

His study tracked community-acquired *S. aureus* infections among pediatric inpatients and outpatients from August 2001 to July 2004. During the study period, 3,578 isolates were associated with community-acquired infections; 74% were MRSA.

The data do not support the hypothesis that use of the 7-valent PCV is associated with the increasing numbers of *S. aureus* infections.

In year 1, 72% of the community-acquired *S. aureus* isolates were MRSA (551 of 771); in year 2, 74% were MRSA (915 of 1,245); and in year 3, 77% were MRSA (1,193 of 1,562). Community-acquired MRSA (CA-MRSA) isolates increased by 2.2-fold, while the increase in community-acquired methicillin-susceptible *S. aureus* (CA-MSSA) isolates was 1.7-fold.

Of the CA-MRSA isolates, 2,542 (96%) were recovered from children with skin and soft-tissue infection; 62% of these children were admitted to the hospital. Most of the CA-MSSA isolates (92%) were also recovered from skin and soft-tissue infections, with 53% of these children admitted to the hospital.

Most of the CA-MRSA isolates (95%) and about half of CA-MSSA isolates were also resistant to erythromycin; the levels were steady throughout the study. Clindamycin resistance increased among both CA-MRSA and CA-MSSA, although the rates remained low: 2%-6% for MRSA; 3%-11% for MSSA.

This association appears to contradict the theory that the 7-valent pneumococcal conjugate vaccine is related to the increase in community-acquired *S. aureus* infections, Dr. Kaplan noted.

Although the Texas increase in CA-MRSA occurred in the same year as the PCV7 was licensed for use in children younger than 24 months, there was no significant increase in CA-MRSA infections in that age group during the 3 years of the study. "Our data would not support the idea that the use of PCV7 is associated with the increasing numbers of *S. aureus* infections we encountered," Dr. Kaplan said at the meeting, which was sponsored by the American Pediatric Society, the Society for Pediatric Research, the Ambulatory Pediatric Association, and the American Academy of Pediatrics.

CA-MRSA was largely responsible for a dramatic increase in deep venous thrombosis among children hospitalized at the center, according to a poster presented by Blanca Gonzalez, M.D., also of Texas Children's Hospital.

" From 1999 to 2004, we identified 10 children who presented with or developed a venous thrombophlebitis during their hospitalization with an invasive *S. aureus* infection; nine of those occurred after 2001."

Of the 10 cases, she said, 8 were associated with CA-MRSA infections and 2 with CA-MSSA infections. Eight of the isolates were positive for Panton-Valentine leukocidin (PVL), a cytotoxin that causes leukocyte destruction and tissue necrosis, and which is produced by most CA-MRSA strains.

"The current PVL-positive clone circulating in Houston appears to have an enhanced propensity to cause DVT in association with osteomyelitis," Dr. Gonzalez said.

The children ranged in age from 9 months to 14 years. Although six had central catheterization lines, the youngest child was the only one whose DVT was clearly associated with a catheter. The most common site of thrombosis was the femoral vein (60%), and clots frequently extended into the popliteal veins. All of the patients had osteomyelitis and pyomyositis; in nine children, these infections were located adjacent to the site of the thrombosis.

Four patients had septic pulmonary embolisms and required inferior vena cava (IVC) filters. All the children were treated with anticoagulation therapy with either low-molecular-weight heparin or warfarin. Therapy was maintained for a mean of 3.7 months (2.5-7 months).

The thromboses completely resolved in eight patients by a mean of 10 weeks. One child was lost to follow-up and the last child remains on anticoagulation therapy, she said.

In Nashville, Tenn., nasal carriage rates of MRSA are increasing dramatically, said Clarence Buddy Creech, M.D. His study also identified clindamycin-resistant MRSA.

In 2004, Dr. Creech of Vanderbilt University in Nashville studied nasal carriage rates of *S. aureus* in 500 healthy children, and then compared the rates with a similar study of 500 other healthy children performed at the center in 2001.

In 2001, the nasal carriage rate of MSSA was 28% and the nasal carriage rate of MRSA was just 0.8%. " We had a small—but important—reservoir of MRSA in our community, " Dr. Creech said.

The 2004 follow-up study revealed a 10-fold increase in MRSA nasal carriage. Of the 500 children swabbed, 46 (9.2%) were colonized with MRSA.

Of the 46 MRSA isolates, 45 were susceptible to rifampin, gentamicin, and trimethoprim-sulfamethoxazole. However, 25 (54%) were resistant to erythromycin and 12 (26%) were resistant to clindamycin.

Of the erythromycin-resistant isolates, eight (32%) showed characteristics of inducible resistance by the disk diffusion test. Only 4 of the 46 isolates (8%) expressed constitutive resistance to clindamycin.

Ten of the 46 isolates (21%) were positive for the cytotoxin PVL. ■

Opportunistic Disease and AIDS: Use Neuroimaging

BY KERRI WACHTER
Senior Writer

ORLANDO, FLA. — Neuroimaging can make a big difference in the care of AIDS patients, who are vulnerable to several opportunistic diseases, one expert said at the annual meeting of the American Society of Neuroimaging.

James G. Smirniotopoulos, M.D., chairman of radiology at the Uniformed Services University of the Health Sciences in Bethesda, Md., noted that AIDS patients are vulnerable to both infectious and neoplastic opportunistic diseases. Neuroimaging is indicated in any AIDS patients who manifest:

- ▶ Mental status changes.
- ▶ Neurologic deficits.
- ▶ Seizures (focal or generalized).
- ▶ Headaches.
- ▶ Meningeal signs.

There are some cautions to keep in mind though. AIDS patients typically have depression and other psychological conditions as a result of their situation, and these should be separated out from genuinely neurologic causes. In addition, in a substance abuse population, seizures can be the result of substance withdrawal. Lastly, when AIDS patients complain of headaches, their immune status can determine the type of imaging used. For patients with very suppressed CD4 counts (less than 200 cells/μL), get a CT scan. However, if the CD4 count is mildly suppressed (greater than 200 cells/μL), get an MRI.

Once AIDS patients have been imaged, Dr. Smirniotopoulos and his colleagues triage them based on whether they have normal imaging results, atrophy, lesions without mass effect, or mass lesions.

"When you see a scan that looks like atrophy, you want to remember that you can have the spurious appearance of atrophy in patients with malnutrition, patients with dehydration, patients who are on steroids, patients who are on [long-term] renal dialysis—they all appear like atrophy," he said.

AIDS encephalopathy—formerly known as AIDS dementia complex—can also appear as atrophy. On images, typically this condition appears as bilateral white matter volume loss that can be symmetrical or not.

"This is a disease process that is destructive of the parenchyma, but there's a lot of debate about what's really going on," Dr. Smirniotopoulos said. Some have suggested that this condition is the result of the direct effect of the AIDS virus on the neurons and/or oligodendrocytes. Others have suggested that it may be a toxic reaction stimulated or produced by the macrophages or some type of autoimmune effect. Regardless of the exact cause, AIDS encephalopathy "is somehow related to the fact that the macrophages themselves are infected by the HIV virus," he said.

Progressive multifocal leukoencephalopathy (PML) is a lesion that has geographic signal and density abnormalities but without a mass effect. This lesion usually does not show any effect when enhanced using gadolinium. PML is a demyelinating white matter disease. On images, look for big geographic lesions that come right up to the gray matter and stop, Dr. Smirniotopoulos said.

The lesions are the result of infection with the ubiquitous JC papovavirus. As many as 70% of adults have antibodies to this virus, and almost 20% of patients with AIDS express antigens. PML is responsible for about 4% of AIDS deaths. Mortality is high in these patients. In the past, most patients with PML died within 4-6 months of diagnosis. Zidovudine and other antiretroviral drugs have improved survival only somewhat.

The two most common mass lesions seen on images in patients with AIDS are from primary infections and CNS lymphomas—with toxoplasmosis being the most common of the infections. "Toxoplasmosis is still probably what we think about first and foremost when an AIDS patient has a mass lesion," Dr. Smirniotopoulos said.

If toxoplasmosis is suspected, try empiric therapy for 3 weeks. If any of the lesions fail to respond, it's time to get a biopsy, he said. The infection results primarily in paracentral brain abscesses. "Abscesses in toxoplasmosis tend to be relatively deep rather than being peripheral," he said. The abscesses can be in gray or white matter. Abscesses are round, uniformly convex with smooth, thin walls and are often multifocal.

It can be difficult to distinguish between a toxoplasmosis infection and lymphoma. "Lesions that involve the deep white matter and the deep gray matter at the same time might be CNS lymphoma or toxoplasmosis, and the problem is that both of these diseases occur in immunosuppressed patients," Dr. Smirniotopoulos said.

The good news is that in most cases—roughly five out of six—primary CNS lymphoma has distinguishing features on imaging that allow diagnosis. Lymphoma is a small round tumor with densely packed cells that result in hyperattenuation on a noncontrast scan. ■