

Necrotizing Pneumonia: Nothing Subtle About It

BY TIMOTHY F. KIRN
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SAN FRANCISCO — There are two important things to know about the recently identified threat of staphylococcal necrotizing pneumonia: It generally follows an influenza illness, and a physician seeing a patient in the clinic or office is not going to miss it.

That was the message of John G. Bartlett, M.D., who has been involved with four cases of necrotizing pneumonia seen in Baltimore recently. All of the cases occurred during a period of 2 months in the winter of 2003-2004, and all were community acquired, he said at the annual meeting of the American College of Physicians.

"These patients are not subtle. They are severely ill," said Dr. Bartlett, chief of the division of infectious diseases at Johns Hop-

kins University, Baltimore.

Each of the four cases occurred in previously healthy individuals without risk factors for staphylococcal infection. This is what makes the cases worrisome and something physicians everywhere should be familiar with, even though the chances of seeing a case at present are extremely low and a physician encountering such a patient would likely recognize right away that he or she was not dealing with bronchitis or viral pneumonia, Dr. Bartlett said.

The course of these infections appears to progress very rapidly. Two of the patients had been vomiting, and each had severe dyspnea and/or hemoptysis and shock.

All of the patients appeared to have had influenza prior to their bacterial pneumonia, and it is well known that staphylococcal pneumonia is generally a super-

infection following influenza, Dr. Bartlett said.

Two of the patients had serologic evidence of influenza A infection, and two of the patients were not tested but were determined to have an influenza-like prodrome.

One of the patients died, and two needed below-the-knee amputations.

In each of the cases, the only bacterial pathogen recovered from the patients was methicillin-resistant *Staphylococcus aureus* (MRSA), and the cases therefore provide further evidence that methicillin resistance is becoming more prevalent among community-acquired staphylococcus infections.

Cases of necrotizing pneumonia have been reported previously in Europe. A paper published in April in the *New England Journal*

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of Medicine reported 14 cases of MRSA necrotizing fasciitis, and another article in the same issue said that 8%-20% of MRSA isolates being collected by laboratories are not coming from the hospital.

An increase in the prevalence of MRSA has also been reported in California jails.

MRSA in the community is different from MRSA in the hospital, Dr. Bartlett said. Hospital-acquired MRSA generally has other resistance factors that make it resistant to trimethoprim/sulfamethoxazole, doxycycline, clin-

damycin, rifampin, and the quinolones.

Community-acquired MRSA tends to be susceptible to those agents, but it often has genes for encoding Panton-Valentine leukocidin, which is the presumed virulence factor for its necrotizing ability.

Leukocidin pulls in monocytes and macrophages and then lyses them, releasing cytokines.

"People have called this fatal attraction," Dr. Bartlett said.

Because the four necrotizing pneumonia patients had such bad outcomes despite treatment with antibiotics to which the organisms should have been susceptible, "I almost have the feeling we are going to have to do something different in these cases, such as [intravenous immunoglobulin]," he said.

"I'd like to tell you how to treat these, but I really don't know," Dr. Bartlett added. ■

Linezolid May Be Overused to Treat Staphylococcal Infections

BY TIMOTHY F. KIRN
Sacramento Bureau

SAN FRANCISCO — Linezolid is being used too often for staphylococcal infections when other options are available, William E. Dismukes, M.D., said at the annual meeting of the American College of Physicians.

For example, linezolid is being used increasingly often for treatment of methicillin-resistant *Staphylococcus aureus* (MRSA) pneumonia.

The drug is approved for the treatment of hospital-acquired MRSA pneumonia, and its use may be increasing largely in response to an article published in 2003 in the *Journal of the American College of Physicians*, said Dr. Dismukes, director of the division of infectious diseases at the University of Alabama, Birmingham.

In the paper, the authors combined data from two separate studies in which vancomycin and linezolid were used. They concluded that survival and clinical cure rates were both better with linezolid.

The survival rate was reported to be 80% with linezolid versus 63% with vancomycin. The clinical cure rate, defined as resolution of signs and symptoms at the end of treatment with improvement or no change in x-rays, was 59% for linezolid and 35% for vancomycin (*Chest* 2003;124:1789-97).

But not everyone is convinced, including Dr. Dismukes. "This paper has generated all kinds of controversy," he said.

In his opinion, the analysis is less than definitive because it included groups from two different trials, and there were only 160 MRSA patients. "You do get higher lung-tissue levels with linezolid," Dr. Dismukes said. "But I am skeptical."

Another use for linezolid that is becoming increasingly common is staphylococcal

endocarditis. There are anecdotal reports of successful treatments, but no clinical trial data. In contrast, much experience and data are available on use of nafcillin and gentamicin, or vancomycin with or without gentamicin, Dr. Dismukes said.

"I think we use too much of this drug for indications such as this for which there are no data," he said.

Linezolid is approved for complicated and uncomplicated soft tissue infections, both methicillin resistant and methicillin susceptible. But community-acquired MRSA infections are different from hospital-acquired MRSA, and so, for uncomplicated infections, cost is an issue.

Hospital-acquired *Staphylococcus aureus* that is methicillin resistant most often has a resistance pattern that includes resistance to other non- β -lactam antibiotics, because the gene that confers methicillin resistance most commonly comes as part of a cassette chromosome that contains other resistance determinants.

But that is not generally true of community-acquired MRSA, which is usually susceptible to doxycycline, trimethoprim/sulfamethoxazole, and quinolones, Dr. Dismukes said.

A single course of linezolid can cost over \$1,000, whereas in some of these cases trimethoprim/sulfamethoxazole would do, he said.

Moreover, adverse events do occur. Linezolid can cause bone marrow suppression, neuropathies with long-term use, and serotonin syndrome in patients on drugs such as selective serotonin reuptake inhibitors.

Dr. Dismukes commented that he has seen three cases of serotonin syndrome in patients taking linezolid during recent months. ■

Multifaceted Approach May Stunt Recurrent MRSA in Children

BY ROBERT FINN
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PORTLAND, ORE. — Recurrent infections with methicillin-resistant *Staphylococcus aureus* are common in children, and the effectiveness of the available treatments is "modest at best," Sarah S. Long, M.D., said at a conference sponsored by the North Pacific Pediatric Society.

Still, one must try something because repeated episodes of furunculosis are so common in children. *S. aureus* colonizes the nasal passages, and when a child picks her nose, the infection can spread to anything the child touches. Especially vulnerable are areas with microabrasions, such as the diaper area and any place the child has eczema, said Dr. Long of Drexel University, Philadelphia.

About 70% of the cases of *S. aureus* infection in her hospital are community acquired and methicillin resistant. Because of that, "you now have to consider the bacteriology of every case," she said.

Gone are the days when one could use amoxicillin/clavulanate because of its activity against staph and strep. Now once a furuncle is drained, "everybody deserves to have a culture" with susceptibility testing, Dr. Long said.

No one strategy against recurrent methicillin-resistant *S. aureus* (MRSA) has more than modest effectiveness. Nevertheless, she described the available strategies and how she might apply them.

► A repeat course of antibiotics is certainly indicated, but only after susceptibility testing to ensure that the an-

tibiotic will be effective. Dr. Long said she might try a third course of antibiotics if the infection recurred.

► Rifampin by itself gives unimpressive results, but it can reduce MRSA colonization. At about the third recurrence, Dr. Long would add oral rifampin, 10 mg/kg per day, toward the end of a course of antibiotics.

► Alternatively, the third recurrence may be the time to use mupirocin applied in the nasal passages twice a day for 2 weeks.

► By the fourth recurrence, Dr. Long will combine rifampin, mupirocin, and a course of antibiotics.

Additionally, there are several hygiene measures that physicians may wish to recommend to the parents.

► Shower the child using chlorhexidine (Hibiclens) once a day for 2 weeks, and then once every 3 days. This reduces the chance that *S. aureus* will colonize various sites on the skin. But one note of caution: Chlorhexidine can cause dry skin, and parents should keep an eye out for this.

► It's important to take aggressive care of diaper rashes, which can easily be complicated by MRSA infections.

► Have the parent empty and clean the bathroom thoroughly. Soap, toothpaste, toothbrushes, and cosmetics all are frequently contaminated by *S. aureus*. "Do a blitz on the bathroom," Dr. Long advised.

► Ensure that all family members use separate towels and washcloths because these are common vectors for the spread of staph infections. This precaution is critical for older children involved in sports, such as wrestling, where abrasions are commonplace. ■