Think Rat Bite Fever in Those With Joint Pain, Rash

BY DOUG BRUNK
San Diego Bureau

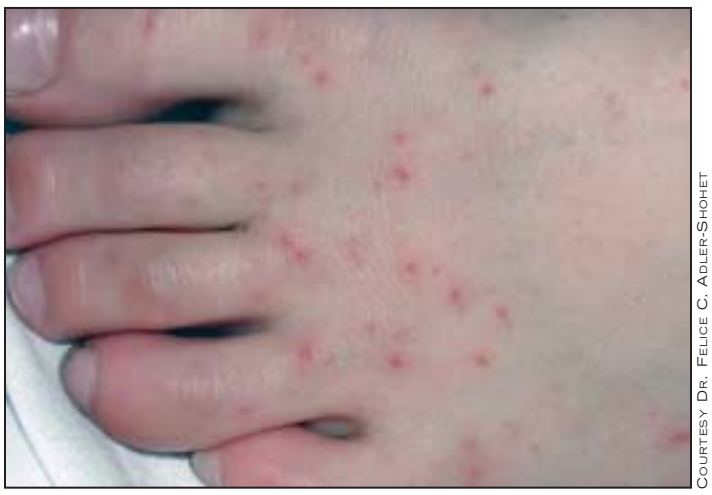
LAS VEGAS — If a child presents to your office with fever, chills, muscle pain, joint swelling/pain, and a skin rash and has a pet rat, consider rat bite fever, Dr. Jay M. Lieberman advised at a meeting sponsored by the American Academy of Pediatrics' California Chapters 1, 2, 3, and 4 and the AAP.

In the summer of 2002, one of his colleagues at Miller Children's Hospital in Long Beach, Calif., consulted on a 6-year-old boy who was admitted with a 3-day history of fever as high as 103 and petechial and pustular lesions on his feet. He had initially complained of left ankle pain and refusal to walk and then had diffuse pain of the left knee, elbow, and wrist.

The boy's lab tests were normal except for a low blood platelet count (146,000/mcL of blood). Liver function tests also were normal. The family was from Pennsylvania and had been living in southern California for 2 months. The patient had a pet rat that the family had acquired several weeks before the onset of his symptoms.

"This boy liked to kiss his rat," said Dr. Lieberman, chief of pediatric infectious diseases at the hospital.

The history of the pet rat prompted Dr. Lieberman's colleague to review the medical literature on rat bite fever, and it became apparent that the boy had a classic presentation of the disease. Rat bite fever is caused by *Streptobacillus moniliformis*, a bacterium that is found in the normal oral flora of rats and can be excreted in rat urine.



COURTESY DR. FELICE C. ADLER-SHOHET

Petechial and pustular lesions appeared on the foot of this 6-year-old boy who liked to kiss his pet rat.

Humans can become infected with *S. moniliformis* after a bite or scratch from the infected rat, from handling it, or by ingesting food or water contaminated with rat excrement.

The incubation period ranges from 2 to 10 days and patients present with a flu-like illness, including an abrupt onset of fever, chills, headache, and myalgia. A rash may develop 2-4 days after the onset of fever.

The rash "is usually maculopapular, predominantly involves the palms and soles, and may evolve into petechia, purpura, and vesicles," said Dr. Lieberman, who also is a professor of pediatrics at the University of California, Irvine.

Penicillin G is the treatment of choice, and the boy improved rapidly once on the regimen. Untreated, the infection may have a relapsing course for 3 weeks or more with a case fatality rate as high as 10%.

Dr. Lieberman said the case underscores the importance of asking about pets in every febrile patient and considering the possibility of rat bite fever in acutely ill patients with rat exposure.

According to the textbooks, "children inhabiting crowded urban dwellings or rural areas infested with wild rats" are at risk. Half or more of wild rats carry the organism in their nasopharynx, Dr. Lieberman explained.

According to the Centers for Disease Control and Prevention, two people died from rat bite fever in 2003 (MMWR 2005;53:1198-202). One of the victims, a previously healthy 19-year-old woman in Washington, was pronounced dead upon arrival at a hospital emergency department after being ill for 3 days. She had lived in an apartment with nine pet rats, and *S. moniliformis* was identified from the liver and kidney on autopsy. ■

Micafungin as Effective as Other Antifungals for Candida Infections

BY TIMOTHY F. KIRN
Sacramento Bureau

SAN FRANCISCO — Two head-to-head comparison trials of micafungin found that it was as effective as older antifungals in treating invasive candidiasis, according to presentations at the annual Interscience Conference on Antimicrobial Agents and Chemotherapy.

Micafungin, a member of the class known as echinocandins, was approved in the United States in 2005 for treatment of esophageal candidiasis and for prophylactic treatment of patients undergoing bone marrow transplantation.

Intravenous micafungin at two different doses produced cure rates similar to those with caspofungin in an international trial with 593 adults who had candidemia or invasive candidiasis, said Dr. Robert Betts, a professor of medicine at the University of Rochester, New York.

The cure rates overall were 74% for the lower dose of micafungin (100 mg/day), 70% for the more typical dose (150 mg/day), and 71% for caspofungin, which was given as a 70-mg loading dose on the first day followed by 50 mg/day.

There were no significant differences between the treatments in adverse events, treatment discontinuation, or relapse, Dr. Betts said.

The only significant difference was in the treatment of patients with invasive candidiasis, for whom the lower dose of micafungin was more effective than the higher dose, with a cure rate of 75%, compared with 53%. By comparison, the caspofungin cure rate was 65% for invasive candidiasis.

Some nonsignificant differences were found for species of Candida other than *Candida albicans*: Caspofungin performed slightly better against *C. tropicalis* (75% success vs. 68%), and micafungin performed better against *C. glabrata* (86% vs. 67%) and *C. parapsilosis* (77% vs. 64%). Those results may deserve further investigation, Dr. Betts said.

"Micafungin at 100 mg a day appears to be the optimal dose in the treatment of invasive candidiasis or candidemia," he said.

In the second study, micafungin was compared with liposomal amphotericin B in 98 children with Candida infection, 91% of whom had candidemia.

Micafungin had an overall success rate of 72%, compared with 76% for liposomal amphotericin B. In patients with neutropenia, micafungin was effective in 85%, compared with 77% for amphotericin B. Neither of these differences was statistically significant, said Dr. Antonio Arrieta, an infectious disease specialist at Children's Hospital Orange County, Orange, Calif.

The majority of patients had a Candida infection other than *C. albicans*; the most common other species was *C. parapsilosis*. Micafungin treatment was successful in 80% of patients with *C. parapsilosis*, compared with 60% for liposomal amphotericin B, a difference that was not statistically significant.

No differences in treatment were found between children less than 2 years of age and older children, but the differences observed were mainly in the adverse effects, Dr. Arrieta said. Serious adverse events occurred in 4% of the patients treated with micafungin and 9% of the patients treated with liposomal amphotericin B. "I think the safety of [micafungin] is what has changed my practice," Dr. Arrieta said in an interview at the meeting.

Both studies were sponsored by the manufacturer of micafungin, Astellas Pharma. ■

Macrolide Resistance Is Common Cause of Breakthrough Bacteremia

SAN FRANCISCO — Drug resistance was a common cause of treatment failure in 26 patients with community-acquired pneumonia who developed bacteremia while being treated with macrolide antibiotics, Dr. Gavin Bayan Grant said at the annual Interscience Conference on Antimicrobial Agents and Chemotherapy.

Of the 26 patients who developed bacteremia while on erythromycin, clarithromycin, or azithromycin therapy, 21 (81%) had resistant organisms, compared with 15 (44%) of 34 patients who developed bacteremia after recent use of one of the macrolides (defined as 16-90 days before the bacteremia diagnosis) and 14% of 721 patients who had not been taking any antibiotics and developed bacteremia.

Macrolide antibiotics are standard therapy for outpatient treatment of pneumonia, and evidence that significant macrolide resistance occurs has been inconclusive, said Dr. Grant of the Centers for Disease Control and Prevention, Atlanta. The current findings provide further evidence that resistance can lead to treatment failure with macrolides, which may inform clinical decisions to change antibiotics in some patients, he said at the meeting, sponsored by the American Society for Microbiology.

Dr. Grant has no association with the companies that make macrolides.

After patient age, immunosuppression, chronic comorbidities, and residence in a long-term care facility were controlled for, patients failing macrolide therapy were 5 times more likely to have resistant organisms, compared with patients who developed bacteremia after recent macrolide use, and 26 times more likely to have resistance than patients with bacteremia who had not been taking antibiotics.

The study also found that clinicians who define macrolide resistance using a cutoff of a minimum inhibitory concentration (MIC) of at least 16 mcg/mL will miss a significant percentage of the treatment failures. "Failures often occur at macrolide MICs less than 16 mcg/mL," he said.

The laboratory-defined cutoff for pneumococcal resistance to erythromycin is 1 mcg/mL, but some researchers advocate the 16 mcg/mL cutoff as more likely to result in breakthrough bacteremia, he explained.

Comparison of isolates from all three patient groups found that breakthrough bacteremia occurred at a broad range of MIC values above 1 mcg/mL, not just at the higher levels of resistance, Dr. Grant said.

Among the patients who had MICs of 1 mcg/mL or greater, the distribution of MICs did not differ significantly between groups. An MIC of 16 mcg/mL or greater was seen in 39% of the group failing macrolide therapy and 6% of patients who developed bacteremia after recent macrolide therapy or not taking antibiotics.

—Sherry Boschert