Fever of Unknown Origin? Ask About House Pets

BY GREG MUIRHEAD
Contributing Writer

MAUI, HAWAII — "Ask about pets in every febrile patient you see" was one of the take-home messages from Dr. Jay M. Lieberman as he discussed infections you can get from your pets.

And in particular, he said, "Consider cat-scratch disease in any patient with fever of unknown origin who has contact with cats—particularly if they're kittens."

He presented several cases of children with prolonged fevers who remained without a diagnosis, despite extensive evaluations, until the possibility of cat-scratch disease was entertained and a history of contact with kittens was obtained. The diagnosis of cat-scratch disease often can be made from the history and physical examination, and serologies may not be reliable, Dr. Lieberman said at a meeting sponsored by the University Children's Medical Group and the American Academy of Pediatrics.

Cat-scratch disease can be transmitted to humans by kittens, older cats, and sometimes dogs.

DR. LIEBERMAN

Kittens are more likely to cause cat-scratch disease than are older cats. The disease is caused by *Bartonella henselae*, and approximately 40% of cats are bacteremic with the organism, explained Dr. Lieberman, professor of clinical pediatrics at the University of California, Irvine.

Cat-scratch disease is transmitted to humans through scratches, licks, or bites from kittens, less often from older cats, and sometimes from dogs.

A primary papule may be seen 3-12 days after inoculation time, followed 7-60 days (average 12-14 days) later by regional lymphadenopathy that may suppurate or regress over 2-4 months. Lymphadenopathy usually involves the nodes that drain the site of inoculation. Fever occurs in half of patients, and malaise, anorexia, and headache also may occur.

The area around the nodes may be noninflamed but can be warm, tender, and erythematous, Dr. Lieberman said at the meeting, which also was sponsored by California Chapter 2 of the AAP. As many as 30% of nodes will suppurate spontaneously.

Atypical presentations of cat-scratch disease included prolonged fever/fever of unknown origin, granulomatous hepatitis, conjunctivitis with preauricular adenopathy (Parinaud's oculoglandular syndrome), encephalopathy/encephalitis, osteomyelitis, and ocular disease.

Although patients may be treated with rifampin or gentamicin or trimethoprim-sulfamethoxazole (TMP/SMZ), or a combination of anti-infectives, Dr. Lieberman does not routinely recommend their use. "In general, we have not treated our patients with antimicrobial therapy," he said. "Most patients do not require specific therapy, and the illness resolves on its own."

One prospective randomized trial of azithromycin vs. placebo found a significantly greater decrease in lymph node size in azithromycin-treated patients at 30 days, but there was no significant difference thereafter (Pediatr. Infect. Dis. J. 1998;17:447-52).

Dr. Lieberman then discussed other infections that can be acquired from pets:

► **Dog- and cat-bite wound infections.** Approximately 5%-15% of dog bites lead to infections, as do 20%-50% of cat bites. *Pasteurella* species, short gram-negative coccobacilli that are part of the normal flora of cats and dogs, are isolated from 75% of infections from cat bites and 50% of infections from dog bites. *Pasteurella* organisms are not susceptible to cephalexin or dicloxacillin, he said.

To help prevent infection from bites, wounds should be cleaned, debrided, and closed. Bite wounds should be reevaluated in 1-2 days. When indicated, there may be a need for tetanus and/or rabies prophylaxis.

Antibiotic prophylaxis is indicated for puncture wounds (including all cat bites), bites over tendons, joints, and bone; bites on the face and/or genitals; bites involving an immunocompromised person; and bites that cannot be well cleaned and debrided. Antibiotic prophylaxis, when indicated, may be used for 48-72 hours.

COURTESY DR. SHERIF EMIL

Lymphadenopathy usually involves the nodes that drain the site of inoculation. Fever occurs in half of patients.

Amoxicillin-clavulanate is the antibiotic of choice for prevention or treatment of animal bite wound infections, he said. Alternatives include a combination of cephalexin or dicloxacillin and penicillin V or a combination of clindamycin and trimethoprim-sulfamethoxazole.

► **Rat-bite fever.** This is "caused by *Streptobacillus moniliformis*, an unusual gram-negative pleomorphic rod. It is normal oral flora in rats and can be excreted in rat urine. Humans are infected after a bite or scratch—or kiss—from an infected rat, or after handling a rat or ingesting food or water contaminated with rat excreta," explained Dr. Lieberman.

There is an incubation period of 2-10 days, followed by rapid onset of fever, chills, headache, and myalgia. Rash may develop 2-4 days after the onset of fever. The rash usually is maculopapular, often including the palms of hands and soles of feet, and it may evolve into petechiae, purpura, and vesicles. About half of patients develop an asymmetric septic polyarthritis. Dr. Lieberman described three children with rat-bite fever seen at his hospital over the past several years, all of whom presented with fevers, polyarthritis, and the characteristic rash, which was most prominent on the soles of the feet.

The treatment of choice is penicillin G.

► **Salmonellosis.** About 3% of U.S. households have reptiles, most commonly lizards, snakes, and turtles. Tortoises are chronic, intermittent shedders of *Salmonella*, and the Centers for Disease Control and Prevention estimates that more than 70,000 reptile-associated U.S. cases of salmonellosis occur each year, Dr. Lieberman said. Reptiles should be kept out of child care centers and households in which children are younger than 5 years or immunocompromised people live, he noted.

Dr. Lieberman disclosed that he is a consultant and a member of the speakers' bureaus for GlaxoSmithKline, Sanofi Pasteur, and Merck & Co. ■

Fever Plus Abdominal Pain May Indicate CSD Complication

BY BRUCE JANCIN
Denver Bureau

ASPEN, COLO. — Hepatosplenic cat-scratch disease is a diagnostic possibility worth bearing in mind in a child with fever of unknown origin and prominent abdominal pain, Dr. Karen Dahl said a conference on pediatric infectious diseases sponsored by Children's Hospital, Denver, and the University of Colorado.

"Hepatomegaly is seen about half the time in these patients. Splenomegaly is even less common. Typically, liver function tests are normal. So it's a little bit of a silent disease except for the pain they may have, which may cause you to pursue ultrasound for other possible diagnoses," noted Dr. Dahl, chief of the pediatric infectious disease division at Helen DeVos Children's Hospital, Grand Rapids, Mich.

The literature suggests that children with hepatosplenic cat-scratch disease (CSD) benefit from prompt antimicrobial therapy, which shortens the duration of fever, although these are retrospective nonrandomized studies, she added.

Dr. Dahl noted that in one series of 19 patients with hepatosplenic CSD with serologically confirmed *Bartonella henselae* infection, 13 had microabscesses of both liver and spleen, while the remaining 6 were evenly divided between those with lesions of one organ or the other. None of the patients had a solitary lesion.

All 19 patients had an elevated erythrocyte sedimentation rate. Thirteen presented with abdominal pain, mostly left-sided, although the chief complaint in all 19 patients was fever of 1-4 weeks' duration. Only five patients had lymphadenopathy. None had the classic CSD inoculation site papule.

All patients were treated with gentamicin, rifampin, and/or trimethoprim/sulfamethoxazole in various combinations. Defervescence occurred within 1-5 days after starting therapy, even in patients with prolonged fever. The fastest response was seen with rifampin monotherapy at 15-20 mg/kg per day (Clin. Infect. Dis. 1999;28:778-84).

The largest published CSD treatment study involved 268 patients with a mixed bag of disease manifestations. Fourteen antimicrobials, including various cephalosporins and penicillins, were identified as being of little or no value in the retrospective study.

Indeed, only four agents were deemed effective by investigators: rifampin, ciprofloxacin, gentamicin, and trimethoprim/sulfamethoxazole. Response rates ranged from a high of 87% with rifampin to 58% with trimethoprim/sulfamethoxazole (Pediatr. Infect. Dis. J. 1992; 11:474-8).

However, azithromycin wasn't among the drugs included in this study. And it so happens azithromycin showed significant efficacy in the only randomized double-blind placebo-controlled trial ever conducted in CSD. The study, which involved 29 patients with CSD chronic lymphadenopathy, showed 7 of 14 patients who received a 5-day course of azithromycin had a significant reduction in lymph node size within 30 days, compared with 1 of 15 on placebo (Pediatr. Infect. Dis. J. 1998;17:447-52).

These studies—all of which are old, small, and/or uncontrolled and retrospective—highlight the shortcomings of the CSD literature.

"In some ways you can't go wrong with cat-scratch disease; the literature will support you no matter what you choose to do," Dr. Dahl quipped. "The most important thing is to keep your index of suspicion high if you live in an area where cat-scratch disease is common. Don't necessarily exclude cat-scratch because there's no lymphadenopathy or they don't tell you they've been scratched by a kitten. Your serologic diagnosis will be very useful." ■