Form a Network

Uveitis *from page 1*

The tendency for some physicians not to use systemic immunotherapy can't be blamed on ignorance, said ophthalmologist Steven Foster, M.D., of Cambridge, Mass. "In public meetings with other uveitis experts, they all know how to talk the talk, and they do talk the talk. The pity is, there are significant numbers who don't walk the walk," he said.

In the 95 years since an association between anterior uveitis and juvenile idiopathic arthritis (JIA, formerly called juvenile rheumatoid arthritis) was first noted, effective treatments have been sought.

The uveitis associated with JIA is often silent at first, and children can experience a great deal of permanent vision loss before it's noticed. For this reason, patients with JIA are routinely advised to have frequent ophthalmologic exams.

In the treatment of any degree of uveitis, the ideal is to have a network of cooperating physicians including a rheumatologist, an ophthalmologist, and possibly a pediatrician, Dr. Lehman said. "I can't do a slit-lamp exam. I can't evaluate how well the eye disease is or isn't doing. I'm dependent on the ophthalmologist. And they don't like having to deal with these potentially toxic medicines. That's not what they're trained to do. They like having me take care of that for them."

Recent reviews in both the rheumatologic and ophthalmologic literature confirm that steroid eyedrops may be useful in the short term to put out the fire of a uveitis inflammation. Long-term management, however, requires systemic immunosuppression (Curr. Opin. Rheumatol. 2002;14:542-7, Surv. Ophthalmol. 2003; 48:489-502, Curr. Rheumatol. Rep. 2003;5:477-81).

Among traditional immunosuppressants, methotrexate is typically the first-line agent, and it has a good evidence base of randomized, placebo-controlled trials to support its use in anterior uveitis in children. Low-dose cyclosporine is a reasonable alternative, but the evidence for its use in children is a bit weaker. Azathioprine (Azasan) and mycophenolate mofetil (Cellcept) may be other alternatives, but they have even less evidence for their efficacy against uveitis in children with JIA.

Studies of chlorambucil have been equivocal, with some seeming to demonstrate efficacy and others failing to do so. The drug is usually avoided because of potential side effects that include sterility and bone marrow suppression in addition to infections and oncogenicity.

More recently, much attention has been focused on the TNF-α inhibitors. Etanercept (Enbrel) appears to be ineffective in uveitis, but results with infliximab (Remicade), adalimumab (Humira), and daclizumab (Zenapax) have been more promising.

"Methotrexate is slower and probably causes more side effects with a little bit less efficacy than the biologics," Dr. Lehman said. "I think in the future the biologics may supplant methotrexate, but that is not currently the correct answer."

Ophthalmologist Gary N. Holland, M.D., takes a more nuanced position and favors avoiding formulaic approaches."I frequently use immunosuppression for kids with uveitis," said Dr. Holland of the Jules Stein Eye Institute, Los Angeles.

That said, "treatment should be individualized. When aggressive immunosuppression is called for, it should be started early."

But "not every child with uveitis is at the same risk for vision-threatening complications, and there needs to be an assessment of that risk in choosing treatment.

"If one could identify children with anterior uveitis who have a low risk of vision loss, one might treat them more conservatively," he said.

Ophthalmologists tend to look for evidence of white blood cells in the anterior chamber and to treat children who have such cells very aggressively. But Dr. Holland, working with Janet L. Davis, M.D., of the Bascom Palmer Eye Institute, Miami, demonstrated that flare, not the presence of cells, is associated with complications from uveitis.

If low-grade flare does turn out to be an independent predictor of good outcomes, patients with low-grade flare could be treated more conservatively. But while any ophthalmologist can measure cell counts in the anterior chamber, accurate flare measurements require laser flare photometry, a technology that is not widespread.

"I don't think that treatment should be chosen on [the basis of] diagnosis alone," Dr. Holland said. "I also don't think the choice of treatment is dependent on the level of vision or the laterality or the point in the course of the disease. An older idea was that you never use immunosuppression unless it was bilateral disease or the vision was less than 20/40. Waiting for a child to lose even a little vision is inappropriately conservative.

"The more severe the inflammation, the more likely you are to treat early with immunosuppressive agents," he continued. On the other hand, "if a child eventually makes his or her way to the treating ophthalmologist and has had very low-grade inflammation for a long time but has never developed complications and has good vision, then you've got time to reassess and see whether he or she responds to low-dose topical corticosteroids, and determine the subsequent course of disease."

Despite the use of TNF-α inhibitors and other forms of immunosuppression, the treatment of anterior uveitis in children with JIA remains an inexact science.

"Our understanding of the causes and pathogenesis of the various forms of uveitis is rudimentary," said pediatric rheumatologist Alan M. Rosenberg, M.D., of the University of Saskatchewan, Saskatoon.

"Consequently, with the limited knowledge we have, it is difficult to develop rationally conceived treatments that are as predictably effective and safe as we desire. Accessibility to more and different immunomodulatory agents does provide increasing opportunities to consider and evaluate their use in uveitis." ■

Once Rare, *K. kingae* Plays a Greater Role in Skeletal Infections

BY MIRIAM E. TUCKER
Senior Writer

Once considered an unusual cause of pediatric infection, *Kingella kingae* has emerged as potentially the No. 1 cause of septic arthritis in the child younger than 24 months of age, according to Mary Anne Jackson, M.D., chief of pediatric infectious diseases at Children's Mercy Hospital, Kansas City, and professor of pediatrics at the University of Missouri–Kansas City.

This fastidious organism, which is often resistant to clindamycin, colonizes the oropharynx of approximately 15% of healthy toddler children. The problem is, it is difficult to grow on culture, requiring an enhanced isolation methodology and a little longer than normal (4.4 days) to grow. Knowing when to think about *K. kingae* as a potential pathogen should help guide treatment decision making.

The typical case involves a previously healthy and fully immunized toddler with a recent upper respiratory infection (URI) who presents with a high spiking fever and irritability. The next day, the child is limping.

What tip-offs might suggest that *K. kingae* should be considered as a potential pathogen, and how might this impact therapeutic decision making?

For the most part, this organism is an important cause of skeletal infection only in those less than 2 years of age. Other information that may be helpful includes the fact that concomitant URI or stomatitis occurs frequently in such patients (over half in one study), suggesting a respiratory or buccal source for the infection. And this organism has a predilection for ankle involvement in cases of arthritis and calcaneal involvement in bone infection.

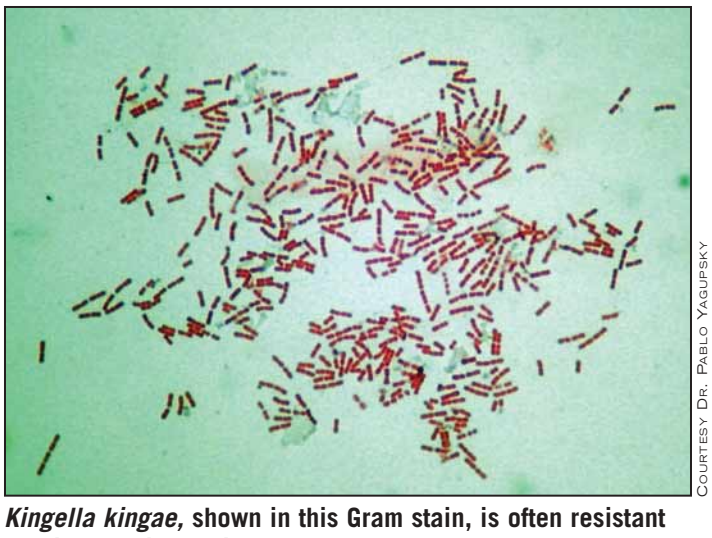
Since *K. kingae* is extremely hard to grow on culture, request that the orthopedic surgeon place some of the purulent fluid into a blood culture bottle, in addition to plating for routine culture, Dr. Jackson recommended. Over a decade ago, physicians were alerted to the importance of using BACTEC blood culture bottles to isolate *K. kingae* in toddlers with skeletal infection (J. Clin. Microbiol. 1992;30:1278-81).

In that study, the investigators analyzed culture records for the period 1988-1991 and compared the performance of routine culture versus use of blood culture bottle for the recovery of pathogens. A diagnostic joint tap was performed in 216 children. Of those, 63 specimens grew significant organisms. Both methods were comparable for recovery of usual pathogens, but *K. kingae* isolates were detected by the BACTEC system *only,* in 13 of 14 specimens.

Just how often *K. kingae* is the culprit in infant septic arthritis is not completely clear since many centers have not routinely used the above technique to enhance growth, she added.

In a study conducted in Atlanta between 1990 and 1995, where joint aspirates were inoculated into thioglycolate broth, rather than blood culture, gram-positive bacteria were identified in 47 of 60 children (78%) younger than 3 years of age with culture-positive hematogenous septic arthritis and acute or subacute osteomyelitis, while gram-negative organisms were identified in 13 (22%).

Of those, *K. kingae* was cultured in 10 (17%); all of these cases occurred in children between the ages of 10.5 and 23.5 months. (J. Pediatr. Orthop. 1998;18:262-7).



COURTESY DR. PABLO YAGUPSKY

***Kingella kingae,* shown in this Gram stain, is often resistant to clindamycin and is extremely hard to grow on culture.**

More recent evidence implicates *K. kingae* in a cluster of skeletal infection in one day care center in Minnesota. Three cases occurred among children aged 17-21 months attending the same toddler classroom. Within the same week, all affected children had onset of fever, and antalgic gait. They all had preceding or concurrent upper respiratory illness. *K. kingae* was isolated from clinical specimens.

A colonization study was performed in response to the Minnesota outbreak. The investigators demonstrated that 13% of children at the index day care center (and 45% in the room where the cluster occurred) were colonized in the nasopharynx with *K. kingae*.

Interestingly, no day care center staff or children less than 16 months old were colonized. They compared the nasopharyngeal colonization results with a control day care center. Similarly, 16% of toddler age children were colonized (Pediatrics 2005;116:e206-13).

As the importance of recognizing *K. kingae* as a pathogen in the infant with skeletal infection is increasingly appreciated, clinical decision making in cases of pediatric skeletal infection is becoming more complex. Dr. Jackson suggested taking a collaborative approach with an infectious disease specialist and an orthopedic surgeon in order to focus on early diagnosis, pathogen isolation, prompt surgical drainage, and appropriate antimicrobial therapy. ■