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The Conundrum of Cervical Adenopathy

Two new studies may help identify the pathogen for cervical adenopathy in children, an often frustrating condition with numerous and divergent potential causes.

Most of us are comfortable treating certain presentations, such as tender, erythematous, anterior cervical lymphadenitis, for which the cause should be *Staphylococcus aureus* or *Group A streptococci* (GAS). We usually prescribe antibiotics and expect improvement within 10 days. A second presentation with a simple disposition is the nontender, unilateral, submandibular node with a purplish color and thinning of the skin over it. Usually, swelling has been present for weeks but has only recently developed the new color and thinning skin. This latter condition is usually nontuberculous mycobacterium (NTM) and is cause for referral to a surgical colleague.

BY CHRISTOPHER J. HARRISON, M.D.

But we have less certainty when predicting the cause of firm, unilateral, nontender adenopathy persisting after the usual 10-day course of antibiotics for initially tender adenitis, or when the child presents initially with nontender, unilateral, soft, mobile cervical adenopathy. Such nodes will often resolve spontaneously if we simply observe them for another 2-3 weeks. Those that don't are often the result of NTM. During the added observation, we often begin a diagnostic quest for such diverse causes as Epstein-Barr virus, *Bartonella* species, tuberculosis, NTM, *Toxoplasma*, or in some areas *Histoplasma*.

If our diagnostic quest is unrevealing and the node persists beyond 4-6 weeks, we usually refer for surgical excision to obtain histopathologic evaluation, plus cultures for mycobacteria, fungi, and conventional bacteria. Where available, fine-needle aspiration can fulfill the same objective. However, parents may become frustrated with the "tincture of time" approach and the slow pace before deciding on surgical referral. Two recent studies offer hope that we can make more rapid and accurate decisions.

A Dutch group reviewed the sensitivity and specificity of tuberculin skin testing (TST) in identifying NTM in Netherlands-born children (median age 48 months) with cervicofacial lymphadenopathy. Of these, 15 had immigrant parents, but none had traveled to TB-endemic areas (Clin. Infect. Dis. 2006;43:1547-51).

A total of 112 received a diagnosis of an NTM, confirmed by culture, polymerase chain reaction testing, or both. The infections were caused by *Mycobacterium avium-intracellulare* in 83 patients, by *M. haemophilum* in 21, and by other NTM species in eight. Nonmycobacterial lymphadenopathies were present in 46 of the children, including *Bartonella henselae* in 20, streptococcal infections in 14, staphylococcal infections in 11, and tuberculosis in one.

Using a cutoff of 5 mm of induration to define a "positive" NTM result, the TST's overall accuracy in detecting NTM was 0.84 (sensitivity, 70%; specificity, 98%; positive predictive value, 98%; and negative predictive value, 64%). Although 10-mm induration is the usual cutoff for *M. tuberculosis*, this study's data suggest that a 5–10-mm cutoff can predict NTM in previously healthy children with cervical lymphadenopathy, particularly where endemic TB is not common.

In my practice, I have used 5-10 mm of TST induration to strengthen my sense that NTM was the agent for nontender, unilateral cervical adenopathy of greater than 2 weeks' duration. This study increases my confidence with this approach.

In general, because community-acquired methicillin-resistant *S. aureus* has become more common, my algorithm is to first use 10 days of clindamycin, for antistaphylococcal and -GAS coverage. If the node persists but is asymptomatic and stable in size, I begin a work-up during a 2-4–week observation period before considering surgical referral. Unlike adults, in whom nonpainful neck masses are cancer until proven otherwise, prepubertal children rarely have this presentation for cancer, and so we can wait to see if slow resolution occurs.

My work-up includes serology, TST, and a chest x-ray (CXR). The CXR might show hilar adenopathy, histoplasmosis, or—rarely—tumor. Serology seems helpful only in the approximately 10% of these cases that turn out to be something other than NTM, such as *Toxoplasma, Bartonella*, or *Histoplasma*. Unfortunately, this work-up plus observation usually adds up to 6-8 weeks before surgical referral.

Clinical clues can sometimes hasten this process. If the node develops that rock-hard or adherent feel to palpation, I refer earlier to rule out the rare cancerous node. If the node breaks down to drain, or evolves into the purplish node noted above, prompt referral is warranted because of likely NTM.

Barring those or other new clues, can we more quickly feel confident in earlier surgical referral? The Dutch data suggest that we could postpone serologic evaluation until after a TST and perhaps a CXR. Here's how I would proceed, based on the size of the TST induration:

► **Less than 5 mm and normal CXR.** Proceed with serology and use standard observation before surgical referral.

► **Less than 5 mm and hilar adenopathy.** This can signify histoplasma, evolving NTM, or TB. If suspicion for TB is high because of social factors, obtain TST on family members. If family TSTs are negative and still no symptoms are present, then there are two options. First, one could do the serologies and, if they are negative, wait to reapply a TST in 4 weeks. Alternatively, referral for biopsy at this point could more rapidly identify the pathogen.

► **5-10 mm in size.** Referral for surgical excision is appropriate if the child is not ill, lives where TB prevalence is low, and has no known TB exposure and no BCG vaccination. Excision not only is usually curative, but also provides tissue for microbiologic or histologic diagnosis, rendering serology unnecessary.

I don't agree with the editorial that accompanied this study, in which the author argued for multidrug antimicrobial treatment (Clin. Infect. Dis. 2006;43:1552-4). In my view, unless the position of the node places the facial nerve in jeopardy from excision, surgery is simpler than trying to keep a patient on 3-6 months of multiple, relatively expensive drugs that have potential adverse effects and that children don't like to take. At least one-third of these children either can't tolerate the regimen or don't respond to it, and end up having surgery anyway. The rate of recurrence after surgery is lower, about 5%-8%.

► **Greater than 10 mm in size.** This is generally presumed to be either latent or—if the CXR is positive—active TB. An appropriate TB regimen can be started. Some NTM infections can cause that degree of induration, but these cases are traditionally treated as TB is ruled out. This is possible with node biopsy. Whether to start TB medications before biopsy depends on risk factors.

For this situation, the second article, from Japan, offers future hope for an additional nonsurgical test to reduce the uncertainty about whether the child with a 10-mm or greater induration actually has NTM or TB. The authors evaluated a whole-blood interferon- and enzyme-linked immunosorbent assay (the Quantiferon TB-2G test, made by Cellestis Ltd.) in 50 healthy volunteers, 50 patients with active TB, and 100 patients with known NTM. They also skin-tested each individual (Clin. Infect. Dis. 2006;43:1540-6).

Among the healthy students, TSTs were negative in 64% and the Quantiferon test was negative in 94%. In confirmed TB cases, 64% had greater than 10-mm TST and only 4% had negative Quantiferon results. With pulmonary *M. avium-intracellulare*, 60% had greater than 10-mm TST and only 7% had positive Quantiferon results. The Quantiferon's mean sensitivity was 86% and specificity 94%. Although the Quantiferon does cross-react with a few NTM species, it does distinguish between TB and *M. avium-intracellulare*, which is the most common NTM.

The Quantiferon is currently marketed only for adults, and I don't think we have the data to support its use in children just yet. But ongoing studies should produce pediatric data in the next few years. Hopefully, this targeted test will become the new generation TB skin test substitute. ■

DR. HARRISON *is professor of pediatrics and pediatric infectious diseases at Children's Mercy Hospitals and Clinics, Kansas City, Mo.*

Extended Corticosteroids Fail to Aid Bronchiolitic Infants

BY DEBRA L. BECK
Contributing Writer

TORONTO — In infant outpatients with bronchiolitis who received corticosteroids in the emergency department, continuation of therapy beyond the initial dose appeared to offer no additional benefit, according to Dr. Suzanne Schuh of The Hospital for Sick Children in Toronto.

"Most babies with bronchiolitis do not need corticosteroids," she said. "In fact, it's highly controversial, but one would wonder whether any of them need corticosteroids."

"It's often difficult to tell whether a baby has acute asthma or bronchiolitis. Sometimes you can get a hint from the family history, but often babies with bronchiolitis will be given corticosteroids" before a definitive diagnosis is reached, Dr. Schuh explained at the annual meeting of the Pediatric Academic Societies.

"We asked in infants [who were] ultimately determined to have asthma if a single dose of corticosteroid is just as good as a 5- or 6-day course, and the answer was 'yes,' " she said.

In a randomized, double-blind study, Dr. Schuh and her colleagues looked at infants with bronchiolitis given 1 mg/kg oral dexamethasone in the ED and discharged on four further daily doses (0.15 mg/kg per day) versus those discharged on placebo.

Eligible infants were between 2 and 23 months of age, had bronchiolitis, and had baseline Respiratory Disease Assessment Instrument (RDAI) scores of 6 or greater. Average age was 8 months in the single-dose group (n = 61) and 7 months in the multiple-dose group (n = 64).

The primary outcome was the proportion of randomized outpatients subsequently hospitalized or given bronchodilators or corticosteroids for dyspnea outside of protocol by day 6.

The rate of primary outcome did not differ significantly between groups: 14% in the single-dose arm and 12% in the multiple-dose arm. In the single-dose arm, 19% of patients had unscheduled medical visits by day 6, compared with 18% in the multiple-dose arm, a nonsignificant difference. RDAI scores decreased in both groups from baseline, but did not differ between groups at day 4 or day 6. ■