Skin, Heart Meds Join List Of Lupus-Inducing Drugs

BY NANCY WALSH
New York Bureau

NEW YORK — The contemporary use of minocycline for acne and hydralazine for heart failure is expanding the spectrum of drug-induced lupus, and physicians need to heighten their index of suspicion for these as well as for other types of drug-induced lupus.

Minocycline-induced lupus was first reported in the early 1990s, and more than 250 cases have now been reported to the World Health Organization. There is a 5:1 female-to-male predominance. The clinical features include fever, morning stiffness, myalgias, polyarthralgias, and symmetric arthritis.

It is also characterized by large vessel vasculitis, and in more than 60% of patients, antineutrophil cytoplasmic antibodies are present and antihistone antibodies are not. This is in contrast to "classic" drug-induced lupus, in which antihistone antibodies are prominent.

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DR. FRANKS

Other autoantibodies also can be seen in minocycline-induced lupus, including antinuclear antibody (ANA) and anti–double-stranded DNA, said Dr. Andrew G. Franks Jr., of the department of dermatology at New York University Medical Center, New York.

"The likelihood of developing a lupus-like syndrome is elevated 8.5-fold with minocycline, so many clinicians are moving away from using minocycline for acne and rosacea and switching to doxycycline, which doesn't have this effect. I haven't used minocycline for 5 years," he said.

Hydralazine, which had fallen out of favor as an antihypertensive, has regained popularity as part of combination therapy for heart failure in African Americans following the benefits seen in the African-American Heart Failure Trial (N. Engl. J. Med. 2004;351:2049-57).

Younger physicians might not be familiar with the association of hydralazine with drug-induced lupus, Dr. Franks said. The drug is one of the "big five" causes of classic drug-induced lupus, along with procainamide, isoniazid, quinidine, and phenytoin, but more than 100 drugs have been implicated in the 15,000-20,000 cases reported in the United States annually.

Classic drug-induced lupus is characterized by flulike symptoms and significant musculoskeletal involvement, with most patients being ANA and antihistone antibody positive. "Patients starting hydralazine or any drug in the big five should have a baseline test for ANA, although that is somewhat controversial," Dr. Franks said.

The third main type of drug-induced lupus is subacute cutaneous lupus erythematosus (SCLE), which also is associated with an ever-widening variety of agents, including the thiazide diuretics, antifungals, calcium channel blockers, and ACE inhibitors. There also have been reports involving statins, leflunomide, and tumor necrosis factor inhibitors.

Clinically, SCLE can be difficult to sort out, he said, with targetoid lesions mixed with papulosquamous or annular lesions. The presentation can also resemble erythema multiforme or toxic epidermal necrolysis, with disadhesion of the epidermal layer and sloughing of the skin. "Patients with this subtype have very high morbidity and mortality."

An audience member asked what happens when the offending drug is withdrawn. Dr. Franks explained that the situation is different from that with an allergic reaction, where the process should resolve in a week or two. "It can sometimes take months for this to remit, and some patients require additional therapy, but 95% of patients ultimately do remit," he said at a rheumatology meeting sponsored by New York University.

Another audience member asked what to do if a patient's baseline ANA is positive, and whether that represents a contraindication to hydralazine therapy, for example. "That is why I said doing a baseline ANA is controversial," Dr. Franks replied. "A number of groups do not suggest doing this, but clearly autoantibodies and a loss of tolerance precede the development of lupus, so one could be prudent and repeat the ANA yearly and see if it turns positive and the titer starts rising."

No single mechanism has been identified to explain the variety of drugs associated with drug-induced lupus or the varied clinical and laboratory manifestations. Hypotheses include the possibility that the drugs can act as haptens or antigens that drive an immune response, or as immune system modulators that permit development of self-directed responses (Semin. Arthritis Rheum. 2007 Dec. 31 [doi:10.1016/j.semarthrit.2007. 10.001]).

Dr. Franks reported having no financial relationships to disclose. ■

CLINICAL GUIDELINES FOR FAMILY PHYSICIANS

Diagnosis and Treatment of Low Back Pain

BY NEIL S. SKOLNIK, M.D., AND KELLY L. GANNON, D.O.

The American College of Physicians and the American Pain Society have developed recommendations for diagnosing and treating low back pain in adults who have acute or chronic low back pain unrelated to major trauma. Low back pain is the second most common complaint-related reason for physician visits. Direct medical costs and indirect costs (lost work days) are substantial. Those seeking care usually show improvement in pain and disability and return to work in the first month; about a third report persistent pain 1 year after the initial episode (Ann. Intern. Med. 2007;147:478-91).

Guidelines are most useful when they are available at the point of care. A concise yet complete handheld computer version of this guideline is available for download, compliments of FAMILY PRACTICE NEWS, *at www.redi-reference.com.*

Evaluation

Patients with new-onset low back pain need a history and physical exam to be placed into one of three categories: nonspecific low back pain; back pain with associated radiculopathy or spinal stenosis; or back pain potentially associated with another specific spinal cause. Evaluation should include duration of symptoms, severity of baseline pain, risk factors for potentially serious conditions, symptoms suggesting radiculopathy or spinal stenosis, presence and severity of neurologic deficits, and psychosocial risk factors. Psychosocial factors and emotional distress are stronger predictors of low back pain outcomes than are physical findings and the severity or duration of pain. Psychosocial factors include depression, passive coping strategies, job dissatisfaction, higher disability levels, disputed compensation claims, and somatization. If the patient is presenting with low back pain that has lasted longer than a month, assess for a herniated disc or spinal stenosis.

Diagnosis

There is no need to routinely obtain imaging or other diagnostic tests in patients with nonspecific low back pain. Plain radiography is recommended for patients suspected of having a vertebral compression fracture. Diagnostic imaging and testing should be performed when severe or progressive neurologic deficits are also present, or when a serious underlying condition is suspected. The diagnostic imaging test of choice is MRI or CT, with a preference for MRI because there is less radiation and better visualization.

Imaging is suggested in those with persistent (longer than 4 weeks) low back pain and signs or symptoms of radiculopathy or spinal stenosis only if these patients are potential candidates for surgery or epidural steroid injection. MRI findings are often nonspecific. Decisions for interventions should be based on correlation between symptoms and radiographic findings, patient preference, surgical risk, and cost.

Treatment

The treatment plan should be tailored for the patient, who should be provided with evidence-based information about the expected course, advised to remain active, and informed about self-care options. Heat compresses for acute back pain, and a firm mattress for chronic back pain, are effective. Lumbar supports and cold compresses are not recommended.

The primary medication options for the relief of low back pain are acetaminophen or nonsteroidal anti-inflammatory drugs (NSAIDs). Opioid analgesics or tramadol are options in those with severe or disabling acute or chronic low back pain that is not controlled with acetaminophen or NSAIDs. If a patient does not respond to a time-limited course of opioids, then reassess and consider alternative therapies, further evaluation, or referral.

Skeletal-muscle relaxants have good evidence for efficacy for short-term relief, although they are associated with CNS adverse effects, mostly sedation. Tricyclic antidepressants are an option for pain relief, but SSRIs and trazodone have not been shown to be effective. Depression is common in patients with chronic pain and they should be assessed and treated appropriately.

Other medications include gabapentin and benzodiazepines, both for short-term relief. Evidence suggests that systemic corticosteroids for treating low back pain with or without sciatica are not effective.

For those patients who don't improve with self-care, consider adding nonpharmacologic therapies that have proven benefits. For acute low back pain, try spinal manipulation; for chronic or subacute low back pain, suggest intensive interdisciplinary rehabilitation, exercise, acupuncture, massage, yoga, cognitive behavioral therapy, spinal manipulation, or progressive relaxation. Herbal therapies (devil's claw, willow bark and capsicum) may be safe for acute exacerbations of chronic low back pain, although data are limited. Transcutaneous electrical nerve stimulation and intermittent or continuous traction in patients with or without sciatica have not been proved effective.

The Bottom Line

Low back pain is a common complaint. A history and physical examination are needed to classify patients into one of three categories. Psychosocial risk factors play an important role in recuperation. Diagnostic imaging or testing is not recommended for nonspecific acute low back pain. NSAIDs and acetaminophen are considered first-line therapy. Inform patients of their expected course, advise them to stay active, and provide them with self-care resources.

DR. SKOLNIK is an associate director of the family medicine residency program at Abington (Pa.) Memorial Hospital and is a coauthor of "Redi-Reference Clinical Guidelines." DR. GANNON is a third-year resident at Abington.

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