

Neuropsychiatric Lupus Symptoms Are Common

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DESTIN, FLA. — Neuropsychiatric manifestations of systemic lupus erythematosus occur in more than 80% of patients, and can pose particular challenges to clinicians caring for these patients.

Not only can such manifestations be difficult to distinguish from infectious or other nonimmunologically mediated processes, they can occur in the absence of serologic disease activity or other systemic manifestations, Dr. Robin L. Brey said at a rheumatology conference sponsored by Virginia Commonwealth University.

“The challenge to us in caring for patients complaining of some kind of neuropsychiatric manifestation ... is really, first and foremost, determining if it is related to lupus,” said Dr. Brey, professor of medicine and associate dean for research at the University of Texas Health Science Center, San Antonio.

The American College of Rheumatology has developed case definitions of several neuropsychiatric manifestations of lupus, including cerebrovascular disease, cognitive disorders, headaches, and movement disorders, among many others. Based on these case definitions, the prevalence of the manifestations in adults has been shown to be between 14% and 80%. Headaches, for example, occur in up to 61% of patients.

fMRI May Prove Useful for Lupus

Magnetic resonance imaging and resting ¹⁸fluorodeoxyglucose-positron emission tomography both show a high frequency of anatomic brain abnormalities in newly diagnosed lupus patients, Dr. Brey said.

The finding suggests that damage to the brain is apparent early in the course of disease, but the findings using these modalities are nonspecific. Functional MRI and other newer imaging modalities might prove to be better approaches to evaluating and following lupus patients with neuropsychiatric manifestations, she said.

For example, functional imaging is being used in an ongoing pilot study to help identify which networks are involved in the neuropsychiatric manifestations in lupus. Functional MRI is used to identify areas of increased oxygen metabolism after controls, patients with lupus and impaired cognition, and patients with lupus and normal cognition participate in a cognitive test involving spatial working memory.

“It’s like a stress test for the brain,” Dr. Brey said, noting that functional MRI appears to be a useful tool in this setting.

The findings could eventually help to identify sources of pathology and surrogate end points for trials of treatments for neuropsychiatric manifestations of lupus, she said.

There is some controversy over whether headaches should be included in this list, as they are common both in lupus and nonlupus patients, but studies suggest migraine with aura is especially likely to be a neuropsychiatric manifestation of lupus—a particular concern given the association between migraine with aura and increased stroke risk in some studies (RHEUMATOLOGY NEWS, August 2008, p. 8), and an important factor to evaluate for in general practice when treating lupus patients, Dr. Brey said.

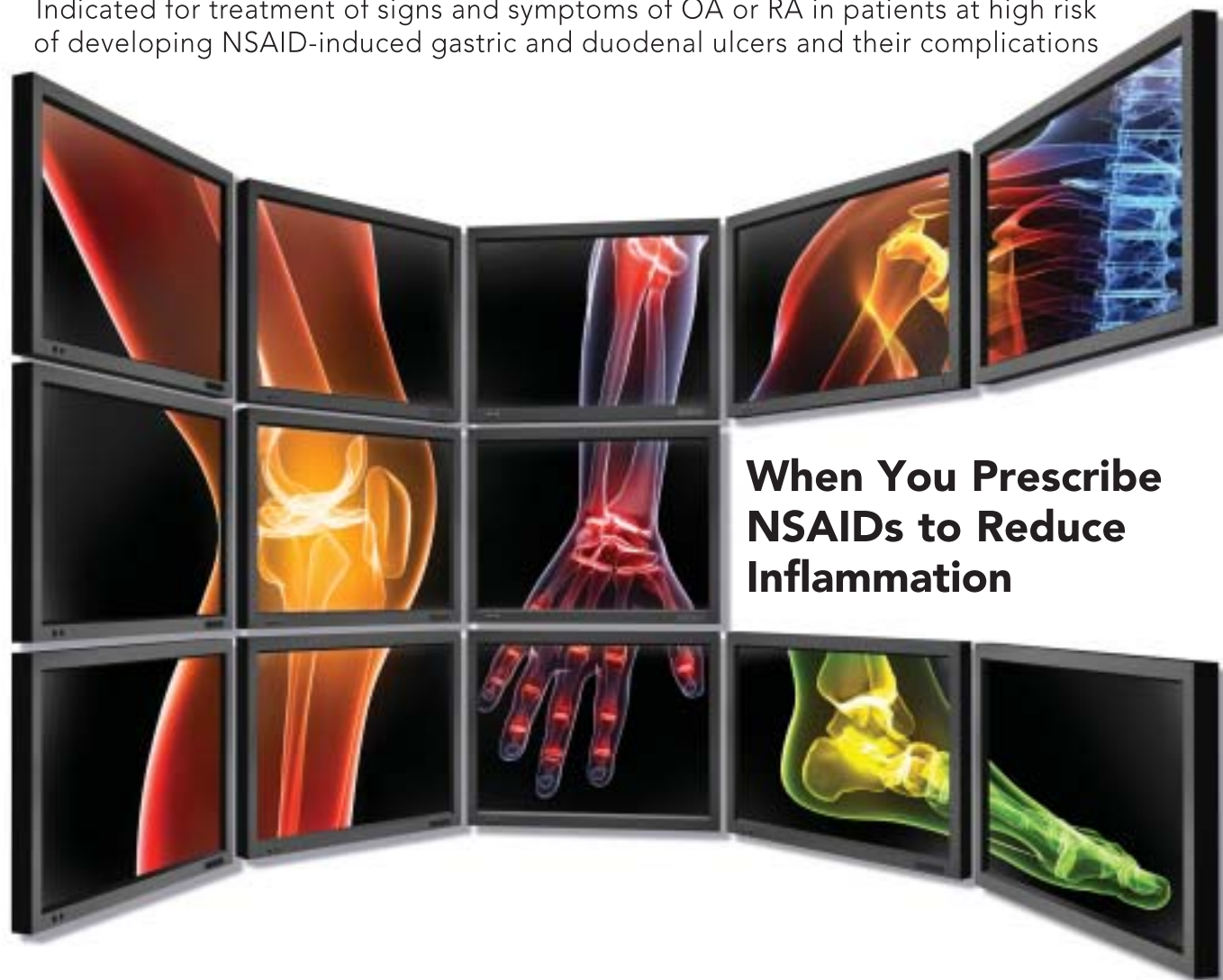
Other lupus-related manifestations, according to the ACR, include seizures, which occur in up to 18% of adults with lupus; cardiovascular disease, which occurs in up to 8%; and psychosis, which occurs in up to 5%. Cranial neuropathy and movement disorders occur only rarely—in about 2% and 1%, Dr. Brey said.

Children with lupus have also been found to exhibit neuropsychiatric manifestations, and both children and adults tend to exhibit the manifestations early, she noted.

Studies show that between 28% and 40% of adults, and 11% of children, exhibit such manifestations at the time of lupus diagnosis, with up to 26% of children experiencing neuropsychiatric manifestations within one year of diagnosis.

Among the most common complaints are those associated with cognitive dysfunction. A subcortical pattern of complaints involving impairments in complex attention, cognitive processing speed, and memory retrieval is known as cognitive inefficiency,

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- NSAIDs may cause an increased risk of serious cardiovascular thrombotic events, myocardial infarction, and stroke, which can be fatal. This risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk.

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- NSAIDs cause an increased risk of serious gastrointestinal adverse events including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Elderly patients are at greater risk for serious gastrointestinal events.

ARTHROTEC is contraindicated in patients with hypersensitivity to diclofenac or to misoprostol or other prostaglandins and in patients who have experienced asthma, urticaria, or other allergic-type reactions after taking aspirin or other NSAIDs. Severe, rarely fatal, anaphylactic-like reactions to diclofenac sodium have been reported.

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Long-term administration of NSAIDs has resulted in renal papillary necrosis and other renal injury. Administration of NSAIDs may cause a dose dependent reduction in prostaglandin formation. Elevations in ALT and/or AST, and rare cases of severe hepatic reactions have also been reported. Transaminases should be monitored within 4-8 weeks after initiating treatment with diclofenac and should be measured periodically in patients receiving long-term therapy.

NSAIDs can cause serious skin adverse events such as exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis, which can be fatal.

which can be very bothersome for patients and vexing for physicians to treat, she said.

This pattern is similar to that seen in HIV dementia, with a great deal more energy than normal required to perform cognitive functions. Some researchers believe this contributes to the fatigue experienced by many lupus patients, she noted.

Risk factors for the development of lupus-related cognitive dysfunction include Hispanic ethnicity, higher depression scores, higher damage scores and acute disease activity scores, consistent prednisone use, and persistently positive antiphospholipid and antiribosomal antibodies. Effects of neuropsychiatric

manifestations may include decreased quality of life and increased lupus-related organ damage—both of which have been linked with these manifestations in adults.

Mortality may also be increased in those with these manifestations. In one study, the mortality rate over 20 years in children with lupus who experienced neuropsychiatric manifestations was 45%, compared with 17% in those without such manifestations.

Possible neuropathological/pathophysiological explanations for neuropsychiatric manifestations in lupus patients include microangiopathy, the presence of autoantibodies, intrathecal production of proinflammatory cytokines, atherosclerosis,

complement activation in brain blood vessels, loss of integrity of the blood-brain barrier, Dr. Brey said.

As with the many other clinical manifestations of lupus, there are numerous possible causes. Given the varying manifestations, no single diagnostic test is sensitive or specific for identifying lupus-related neuropsychiatric manifestations.

“Essentially, it takes an individualized approach, and it really, truly does depend on the complaint that the patient comes in with,” she said.

Appropriate assessment for clinical care might include immunoserologic testing, brain imaging (see box on prior page), and

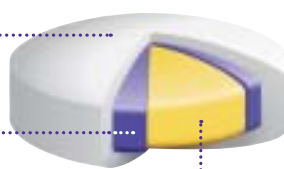
neurophysiological, psychiatric, and neuropsychological assessments, she said. However, infection must always be considered; lupus is not always to blame.

Treatments are the same as those used to treat other serious lupus manifestations—corticosteroids, azathioprine, cyclophosphamide, and mycophenolate mofetil. Symptomatic treatments may also be useful, such as for headaches, seizures, and stroke, and these appear to work as well in lupus patients as in those without lupus. Nonpharmacologic treatments may also be useful, such as stress management, lifestyle changes, psychotherapy, and cognitive rehabilitation. ■



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