

IMAGING 360°

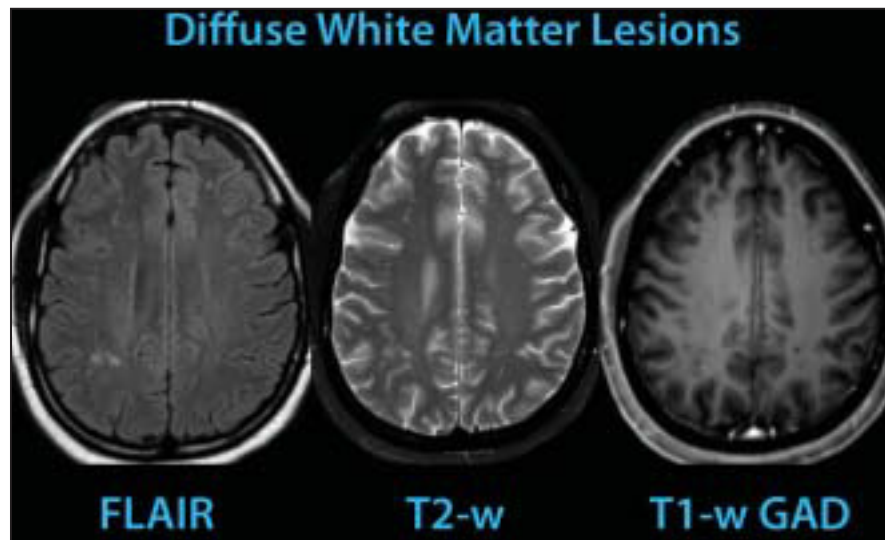
Neuropsychiatric Systemic Lupus Erythematosus

Neuropsychiatric systemic lupus erythematosus (NPSLE) is a diagnostic challenge, requiring both rheumatologic and neurologic assessments. Diagnosis is complicated by the number of forms the disorder can take. The American College of Rheumatology has described case definitions and diagnostic criteria for 19 central/peripheral nervous system syndromes observed in SLE (*Arthritis Rheum.* 1999;42:599-608). Diagnosis relies on a combination of clinical assessment, laboratory tests, neuropsychological evaluation, and imaging.

"The problem with neuropsychiatric systemic lupus erythematosus in general is that you have to figure out if the symptoms are related to the lupus," said Dr. Patricia C. Cagnoli, a rheumatologist at the University of Michigan in Ann Arbor. "We don't have any specific imaging technique that can tell you that." An important element of diagnosis is ruling out other causes of the symptoms: SLE-mediated organ dysfunction, infection, medication side effects, metabolic abnormalities, or an unrelated condition. Imaging can play an important role in ruling out other causes.

The diagnostic approach also depends in part on the presentation. Are the symptoms focal/acute or more diffuse? For example, in the case of acute symptoms, CT can help rule out ischemic strokes, large tumors, and massive bleeds—the most acute and urgent conditions that would require immediate treatment or surgery. "The CT scan will reveal the most obvious abnormalities," said Dr. Cagnoli. In addition, CT has the advantages of ready availability—CT equipment is in almost every emergency department—and of being quick to perform. If a patient has more diffuse symptoms, infection should be ruled out first with a lumbar puncture in addition to imaging.

"MRI is probably the cornerstone imaging technique to use in the diagnosis of neuropsychiatric lupus," said Dr. Cagnoli.



NPSLE lesions can be seen on MRI with fluid attenuated inversion recovery (FLAIR), as well as on T2-weighted MRI and T1 MRI with gadolinium contrast.

Multiple imaging sequences and intravenous administration of contrast are employed to accurately delineate abnormal areas in the brain. "More often than not, MRI will reveal several lesions that were not detected by CT scanning." These areas of new injury are likely capable of responding to treatment and healing in ways that cannot be seen by CT.

MRI also frequently identifies small bright spots in the subcortical white matter that are of uncertain significance and are sometimes referred to as "unidentified bright objects" or UBOs.

"Most of the patients with neuropsychiatric lupus will have these hyperintense white matter lesions, but so do apparently normal individuals. Their presence arouses suspicion, but you cannot be certain whether they are related to lupus," she said.

However, these lesions are not specific to NPSLE. It's theorized that "one of the mechanisms in lupus is demyelination, which is the same type of lesion in multiple sclerosis," Dr. Cagnoli noted. It's not uncommon for patients to have small white-matter lesions on MRI that are considered to be areas of possible demyelination. In fact, patients are often

referred to Dr. Cagnoli's group to help determine if patients have MS or lupus with CNS involvement. There are some more specific findings for MS: The lesions tend to be bigger, to coalesce, and to progress quickly.

"Still, we find ourselves with the neurologists going back and forth many, many times—is it SLE or MS?" Imaging is only part of the picture. "It's the rest of your physical assessment, your clinical impression, your laboratory evaluation that will tell you, in the end, what it is," she said.

Researchers are starting to use more functional MRI techniques, such as MR spectroscopy, diffusion-weighted imaging, and diffusion tensor imaging (DTI). "What we are trying to determine with those techniques is which patients really have functional abnormalities that the structural MRI is not showing us."

Researchers are seeing important differences with these techniques, particularly with spectroscopy and DTI. When comparing structural and functional MRI, "you have a normal conventional MRI and you see already evidence of neuronal loss or brain injury in the functional MRI," said Dr. Cagnoli, who is



NPSLE hyperintense white matter lesions are seen in more detail above.

also the associate director of the Michigan Lupus Program.

The researchers hope to use these techniques to identify patients with pre-clinical NPSLE-type lesions, in order to begin treatment as early as possible. "Eventually, our hope is that we might be able to treat these patients sooner rather than later," she said. "One of the problems we have with [NPSLE] is trying to identify those patients" who require earlier and more aggressive treatment, "as opposed to those patients who can benefit from a more conservative approach."

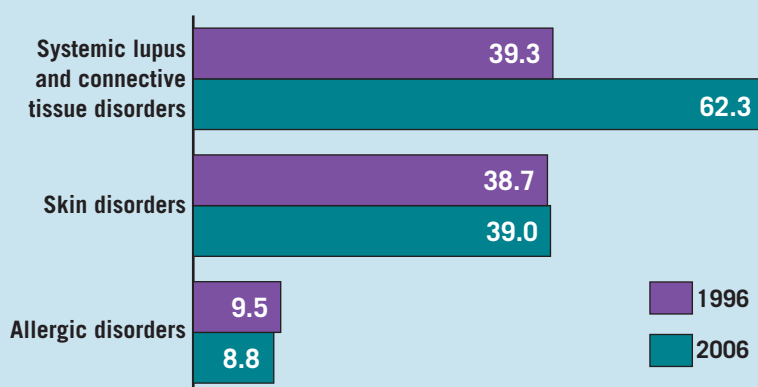
NPSLE requires treatment not just for the neuropsychiatric symptoms, with antipsychotics for psychosis as an example, but also for the underlying SLE, with immunosuppressants and high doses of corticosteroids. "So you treat the symptom—psychosis is the symptom in this case—but also the underlying mechanism, which is the lupus," Dr. Cagnoli said.

The researchers also hope that imaging will shed more light on the underlying mechanism of neuropsychiatric lupus.

For now, though, imaging is only one part of the multipronged diagnostic approach to NPSLE.

—Kerri Wachter

DATA WATCH

Lupus-Related Visits Rose 59% From 1996 to 2006
(in millions)

Note: Based on data for visits to hospital outpatient departments and office-based providers from the Medical Expenditure Panel Survey.
Source: Agency for Healthcare Research and Quality

FDA Approved Biologic for CAPS in Children and Adults

Canakinumab, an interleukin-1 beta blocker administered subcutaneously every 8 weeks, was approved in June as a treatment for cryopyrin-associated periodic syndromes (CAPS) in adults and in children aged 4 years and older.

The approved indication includes familial cold autoinflammatory syndrome and Muckle-Wells syndrome, which are among the rare genetic syndromes that fall under CAPS.

Canakinumab was shown to be safe and effective in a small, three-part, 48-week study of patients with CAPS who were aged 9-74 years. At 8 weeks, 97% of

those who had received one dose of canakinumab had a complete clinical response; during the following 24-week randomized withdrawal period, 81% of those randomized to a placebo experienced disease flares, compared with none of those who remained on treatment. Nasopharyngitis, diarrhea, influenza, headache, and nausea were the most common adverse events reported by patients treated with canakinumab, according to the prescribing information.

Canakinumab will be marketed under the trade name Ilaris by Novartis Pharmaceuticals Corp.

—Elizabeth Mechatie