Ask the Expert

Screening for Depression in Lupus

The high prevalence of major depression in individuals with systemic lupus erythematosus (SLE)—estimated in various studies to be between 11% and 40%—is likely explained by biologic effects of the illness and the psychosocial impact of the limitations imposed by the illness in combination, according to Dr. Fabiano Nery of the University of São Paulo in Brazil.

FABIANO NERY, M.D.

In a recent study, Dr. Nery and his associates evaluated 71 consecutive SLE patients for the presence and intensity of major depressive disorder, psychosocial stressors, functional disability, SLE disease activity, and cumulative damage, 16 (23%) met DSM-IV diagnostic criteria for a current major depressive disorder (Comprehensive Psychiatry 2007;48:14-19). Patients with major depression presented a trend toward having greater severity of SLE disease activity compared with those without major depression. Additionally, major depression was associated with life events and hassles, and depression severity was directly correlated with disease activity and with functional ability, said Dr. Nery.

In this month's column, Dr. Nery discusses the implications of these findings on the identification and management of lupus patients with depression.

Rheumatology News: In your opinion, does the evidence suggest this increased risk of depression in SLE is a function of the brain involvement characteristic of lupus or of the social/emotional upheaval associated with having a chronic disease?

Dr. Nery: Our results show that SLE patients with active disease have a greater risk of developing major depression than do SLE patients with inactive disease, even after we controlled for measures of environmental stress (i.e., life events) and biologic predisposition to major depressive episodes. This finding suggests that the disease activity is an additional risk factor for major depression in SLE patients, together with common risk factors for primary forms of depression.

Findings from several other studies have shown that autoimmune or inflammatory mechanisms may generate depressive symptoms in SLE patients. For instance, there are studies showing correlations between depressive symptoms and anti–glutamate receptor antibodies and associations between anti–ribosomal P antibodies and depression. To date, there is no clear symptom or sign that helps to differentiate between a primary depression and an autoimmune depression. Another potential confounder is the high doses of corticosteroids commonly used in SLE patients with active disease, which are known to cause mood disturbances.

Rheumatology News: How does the possibility of widespread or focal brain involvement in lupus affect the diagnosis of depression in these patients?

Dr. Nery: Depressive symptoms that are associated with overt neurologic symptoms or with severe cognitive disturbances and/or behavioral alterations are highly suggestive of brain involvement. General rules to diagnose organic forms of depression also apply here: There should be evidence from the history, physical examination, or laboratory findings that the depressive symptoms are a direct physiologic consequence of the SLE. In other words, evidence for a parallelism between the course of the depressive symptoms and the SLE disease activity, a lack of personal and familial history for major depression, and brain imaging techniques showing acute brain involvement would help to support a diagnosis of secondary major depression rather than a primary major depression.

Rheumatology News: Are the same drugs that are used in the general population for treatment of depression appropriate for lupus patients?

Dr. Nery: There is no consensus guideline about pharmacologic therapy for major depression in SLE patients. The general management of depression in SLE follows the rules of treatment of depression in patients without medical conditions, respecting the medical factors that are particular for SLE patients, such as interactions with concomitant drugs, pharmacokinetic properties of antidepressants with hepatic or renal metabolism, and so forth. Common antidepressants, such as selective serotonin reuptake inhibitors, might neutralize cytokine-induced depressive symptoms. In other words, they might act on pathways that lead to major depression that involve inflammatory alterations. Obviously, in those cases in which brain involvement is highly suspicious, the management should follow the rheumatologic clinical guidelines for treatment of neuropsychiatric lupus.

Rheumatology News: What should the clinical rheumatologist be on the lookout for in terms of diagnosing depression, and at what point should a psychiatric referral be made?

Dr. Nery: A routine screening for depression is highly recommended in SLE patients. To diagnose depression, a clinical rheumatologist should look for the presence of depressed mood or loss of interest or pleasure in the past 2 weeks. Additionally, diagnosis requires the presence of disturbances in sleep, appetite, and level of physical energy; decreased concentration; feelings of worthlessness or pathologic/excessive guilt and suicidal ideation. The diagnosis of depression can be challenging as some of these symptoms can be symptoms of SLE as well. Diagnosis ideally should not be delayed or denied because the clinician thinks the symptoms result from SLE or are a natural reaction to having SLE. In general, a psychiatric referral should always be made in case of suicidal ideation, severe agitation, delusions or hallucinations, and refractoriness to treatment. All SLE patients with depression, whether their depression is caused by any kind of brain involvement or not, need support and understanding to deal with the pain, losses, and disability caused by their condition. Support groups and psychotherapy should also be considered in the treatment of SLE patients with mood disorders. ■

Dr. Nery is a psychiatrist at the University of São Paulo (Brazil) Medical School.

By Diana Mahoney, New England Bureau

Image of the Month

Conventional MRI has helped characterize the variety of neuropsychiatric systemic lupus erythematosus symptoms, including atrophy, focal or diffuse nonspecific white matter lesions, hemorrhage, infarcts, and demyelination. However, conventional MRI may be negative or nonspecific, even in symptomatic patients.

MR spectroscopy has found protein ratios that may represent inflammatory processes, demyelination, or cell membrane degradation, all of which involve microstructural changes that affect how water molecules move—the diffusivity.

Diffusion-weighted imaging (DWI), an MR-based technique, is sensitive to water's motion within extracellular space. DWI can diagnose and characterize abnormalities in brain tissue.

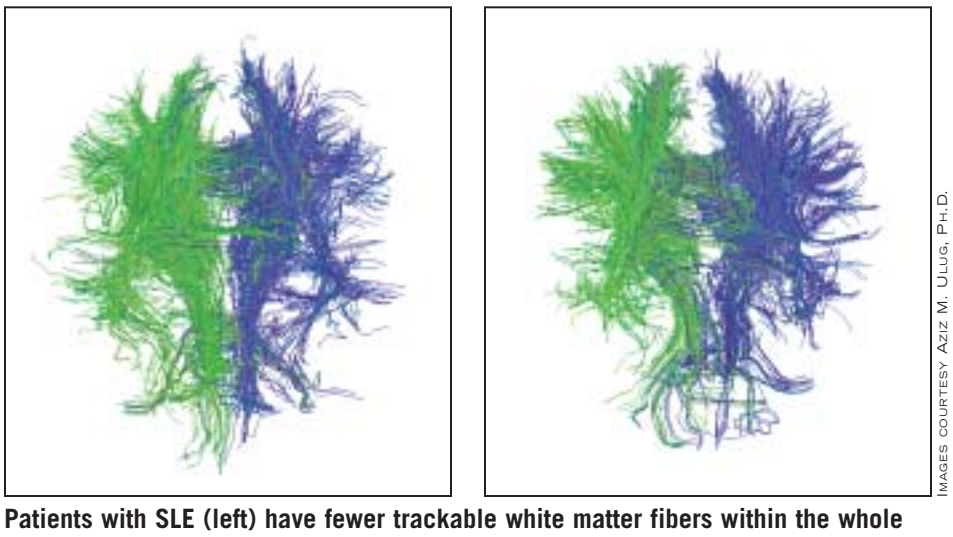
Diffusion tensor imaging (DTI) analyzes the directional diffusion properties of water and the integrity of organized tissue microstructures. It is often applied to white matter tracts to reveal tissue orientation and integrity.

Tractography lets researchers see the symmetry of brain water diffusion. Bundles of fiber tracts make the water diffuse asymmetrically in the major axis parallel to the direction of the fibers. The asymmetry is called anisotropy. A direct relationship exists between the number of fibers and the degree of anisotropy.

Aziz M. Ulug, Ph.D., of Cornell University, Ithaca, N. Y., and colleagues used these techniques to study 34 SLE patients and 29 age-matched controls. Participants underwent MRI (1.5 T), DWI, DTI, and tractography (Magn. Reson. Imaging 2007;25:399-405). Overall, 20 patients had an abnormal MRI finding: 3 showed volume loss inappropriate for age; 15 had focal or spreading nonspecific white matter disease; and 2 showed both volume loss and nonspecific white matter disease.

The D_{av} is average diffusion constant for all MRI pixels. The greater D_{av}, the more freely water diffuses. In SLE, there were regions where D_{av} was higher, versus controls. In the entire SLE group, D_{av} was higher in the anterior internal capsule, frontal lobe, and splenium of corpus callosum.

BD_{av} is the diffusion constant (D_{av}) measured from the entire brain. BD_{av} is is useful for diseases in which the insult is not focal or not exactly known. "In SLE patients, we find BD_{av} is increased compared to normals," said Dr. Ulug. "The disease [is] affecting a large portion of the brain (or entire brain). The BD_{av} value was increased in the patient group that [had] normal MRI findings, compared with controls. This means the BD_{av} measure is a very sensitive one that detects the disease or disease load in the brain before regular MRI."



IMAGES COURTESY AZIZ M. ULUG, PH.D.

Patients with SLE (left) have fewer trackable white matter fibers within the whole brain, compared with healthy controls (right), on DTI tractography.

Diffusion anisotropy in the anterior internal capsule was significantly decreased in the patient group, suggesting a preclinical impairment of axon integrity (contained in the anterior internal capsule and running to and from the frontal association cortex). Anisotropy in the anterior internal capsule for patients with normal MRI findings was lower than in patients with abnormal MRI findings. This suggests ractional anisotropy is a sensitive tool to detect early signs of disease involvement. Tractography in SLE patients showed fewer trackable fibers in the whole brain compared with controls, suggesting white matter damage, said Dr. Ulug.

—Kerri Wachter