EULAR Offers Guidance on SLE Monitoring

BY SALLY KOCH KUBETIN

New guidelines from the European League Against Rheumatism on the monitoring of patients with systemic lupus erythematosus offer advice for clinicians and design recommendations for observational studies.

The document includes recommendations on 10 components of patient monitoring. An appendix contains a core set of data to be collected in routine clinical practice. Having such standardized data would be a significant help to research, noted Dr. Marta Mosca of the University of Pisa (Italy) and her fellow authors. The panel included rheumatologists, internists, dermatologists, and a nephrologist, who arrived at the following recommendations after a systematic literature review and numerous consultations:

► **Patient assessment.** Every visit should include assessments of the patient's disease activity (using a validated index), quality of life (using history, either alone or in addition to a patient-completed measure such as a 0-10 visual analog scale), and comorbidities and drug toxicity. Organ damage should be assessed yearly.

► **Cardiovascular risk factors.** Cardiovascular disease, including related factors such as smoking, vascular events, physical activity level, oral contraceptive use, hormone therapies, and family history of CVD, should be assessed at baseline and monitored at least once a year thereafter. Similarly, lupus patients need yearly blood tests for cholesterol and glucose levels as well as blood pressure measurement and determination of either body mass index or waist circumference. Patients on glucocorticoids and other lupus patients at particularly high risk for CVD may require more frequent assessment.

► **Other comorbidities.** All patients with SLE should be assessed for osteoporosis risk factors, including adequate calcium and vitamin D intake, regular exercise, and smoking. They should be screened and followed for osteoporosis according to either of two existing sets of guidelines: those for postmenopausal women or those for patients on glucocorticoids or other medications that reduce bone mass, such as methotrexate. Cancer screening (including Pap smear) is recommended according to guidelines for the general population.

► **Infection risk.** Lupus patients should be screened for HIV, hepatitis C virus, and hepatitis B virus (especially before the start of immunosuppressive drugs); for tuberculosis (according to local guidelines, especially before the initiation of immunosuppressive drugs); and for cytomegalovirus. Lupus patients should receive inactivated vaccines for influenza and pneumococcus in accordance with guidelines for immunosuppressed patients issued by the U.S. Centers for Disease Control and Prevention. It is ideal to immunize when the lupus is inactive. The use of other vaccines should be considered on a case-by-case basis. To determine the exact risk for infection, lupus patients should be monitored for neutropenia, severe lymphopenia, and low IgG.

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► **Frequency of assessments.** Assessment every 6-12 months is adequate in patients with no disease activity, no organ damage, and no comorbidities. Preventive measures should be stressed during these visits. The committee found no data to suggest an optimal frequency of assessment in patients with lupus.

► **Laboratory assessment.** The committee recommended that baseline lab assessment include monitoring antinuclear antibody, anti–double-stranded DNA, anti-Ro, anti-La, anti-RNP, anti-Sm, antiphospholipid, C3, and C4. Reevaluation of antiphospholipid antibodies is necessary in previously negative patients prior to pregnancy, surgery, transplant, and estrogen-containing treatments, or in the presence of a new neurologic or vascular event. Before pregnancy, anti-Ro and anti-La antibodies also should be monitored. Remeasurement of anti-dsDNA and low levels of C3 or C4 may support evidence of disease activity or remission.

At 6- to 12-month intervals, patients with inactive disease should have the following lab tests: complete blood count, erythrocyte sedimentation rate, C-reactive protein, serum albumin, serum creatinine (or EGFR), urinalysis, and urine protein:creatinine ratio. Any patient on a specific drug treatment should have that drug monitored as well.

► **Mucocutaneous involvement.** Cutaneous manifestations include lupus erythematosus (LE)-specific lesions, including acute cutaneous LE (CLE), subacute CLE, chronic CLE, and intermittent CLE lesions, and LE-nonspecific lesions. Many conditions may mimic LE and therefore may require an evaluation by an experienced dermatologist as well as a skin biopsy for histologic analysis. Follow-up rebiopsy is recommended if the lesions' clinical morphology changes, or if there is no response to treatment.

► **Kidney.** Patients with a persistently abnormal urinalysis or raised serum creatinine should have urine protein:creatinine ratio tests, urine microscopy, and renal ultrasound, and should be considered for biopsy referral. Patients with established nephropathy should have protein:creatinine ratio and immunologic tests, urine microscopy, and blood pressure evaluations at least every 3 months for the first 2-3 years. Patients with established chronic renal disease should be followed according to the U.S. National Kidney Foundation guidelines for chronic kidney disease (www.kidney.org).

► **Neuropsychiatric manifestations.** Neurologic (central, peripheral, or autonomic) involvement occurs frequently in SLE. The most frequent syndromes observed are headache, mood disorders, seizures, cognitive impairment, and cerebrovascular disease. The assessment of neurologic symptoms is difficult; no specific instrument has been evaluated in clinical practice. Thus, the guidelines recommend that patients should be monitored by clinical history. Cognitive impairment may be assessed by evaluating memory, attention, concentration, and word-finding difficulties (Ann. Rheum. Dis. 2009 Nov. 5 [doi:10.1136/ard.2009.117200]).

► **Eye assessment.** The incidence of retinopathy among SLE patients who are treated with antimalarial drugs is low (0.5%). Risk factors are age older than 60 years, presence of macular degeneration, retinal dystrophy, obesity, liver disease, renal insufficiency, duration of therapy longer than 5 years, daily dose of hydroxychloroquine greater than 6.5 mg/kg, or chloroquine greater than 3 mg/kg. Recommendations on screening for antimalarial retinopathy include a baseline eye assessment according to published guidelines (Ophthalmology 2002;109:1377-82). Thereafter, in low-risk patients, no further testing is required for the next 5 years; after the first 5 years of treatment, eye assessment is recommended yearly. In high-risk patients, an eye assessment is recommended yearly. In addition, an eye assessment may be required if there are symptoms suggesting eye involvement by lupus.

In most cases, anything left out of these recommendations should be considered part of standard good clinical practice, the authors noted. ■

SLE Presents Differently Before and After Age 50 Years

BY DOUG BRUNK

SAN DIEGO — Although an estimated 80% of patients with systemic lupus erythematosus acquire the disease before age 50 years, beware of ruling out the potential for diagnosing new cases in older patients.

"It certainly can happen," Dr. Bevra H. Hahn said at the annual meeting of the North American Menopause Society. "It's not rare, so it's okay to let it cross your mind."

The clinical presentation of SLE that develops before the age of 50 differs from that of disease that occurs later in life, said Dr. Hahn, chief of rheumatology at the University of California, Los Angeles. SLE that develops before age 50 is marked by development of nephritis, anti-DNA antibodies, malar rash, and/or discoid lupus. This relatively early-onset form of SLE causes less organ damage in general. Mortality in this patient population "is primarily from active lupus or from infections that relate to being sick and having immunosuppressive therapies," Dr. Hahn said.

SLE that develops after age 50 is marked by cardiac and pulmonary problems. "I see a lot of patients who present with heart failure or with pericarditis, or arrhythmias, and they have a strongly positive antinuclear antibody, so it's fine to screen for ANA in that situation," she said.

Compared with their younger counterparts, patients who develop SLE after age 50 are also more likely to have arthritis, Sjögren's syndrome, and a high damage index. "Their mortality is more from coronary artery disease or stroke, some from infection, and less of it from antilupus medications," said Dr. Hahn. "For this group, preventive care is very important for the coronary artery disease."

Several clinical studies have demonstrated that the antimalarial drug hydroxychloroquine reduces damage over time. "In general, we think most people should be on [hydroxychloroquine] if there is not a contraindication," she said. The major problem with the drug is its potential for associated retinal damage, which occurs only rarely, Dr. Hahn added.

Dr. Hahn's approach to treatment involves first determining whether the disease threatens life or organs. If the disease is mild, she will consider agents to lessen pain, fatigue, and rash, including NSAIDs; topical agents, such as steroids or tacrolimus; sunscreen with SPF 50; antimalarials, such as hydroxychloroquine at a dosage of 200-400 mg/day or quinacrine dosed at 100 mg/day; DHEA (dehydroepiandrosterone) dosed at 100-200 mg/day; or low-dose prednisone.

She cautioned that the use of NSAIDs "can bump creatinine levels and cause aseptic meningitis in patients with lupus. It's not common, but it happens."

For women with severe lupus, she prescribes agents that confer a survival benefit with as few adverse effects as possible. "The three phases of treatment for severe SLE are 'induce improvement, maintain improvement, and prevent damage,' " she said. For these patients, high-dose prednisone "saves lives. It causes cataracts, osteoporosis, and diabetes, but it really is life saving."

For patients with severe lupus, consider antimalarials and the cytotoxic agents mycophenolate mofetil, azathioprine, and cyclophosphamide. Other agents showing promise include rituximab and belimumab.

Dr. Hahn had no relevant financial disclosures to make. ■