4 New Things About Lupus

September 20, 2017 | Lupus [1]
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The latest studies explore new aspects of diagnosis, management, and comorbidities.

Up to 322,000 persons have definite or probable systemic lupus erythematosus (SLE). Persons of all ages are affected, including children. At greatest risk are women of childbearing age, 15 to 44 years; men are at lower risk. Minority and ethnic groups are affected more than whites.

SLE diagnosis may be challenging because the signs and symptoms are not specific. The diagnosis may be made too easily when only a positive blood test is used. Several recent studies have reported on new aspects of lupus diagnosis, management, and comorbidities. Read on for brief summaries of the latest research findings.

Posttraumatic Stress Disorder Provokes Lupus Risk

Harvard researchers conducted the first longitudinal study to examine whether trauma exposure and posttraumatic stress disorder (PTSD) are associated with increased risk of incident systemic lupus erythematosus (SLE) in civilian women. They ascertained incident SLE with 4 or more American College of Rheumatology criteria by self-report and confirmed it by medical record review, and they assessed PTSD and trauma exposure with the Short Screening Scale for DSM-IV PTSD and the Brief Trauma Questionnaire.

The 54,763 women in the study were categorized as having no trauma, trauma and no PTSD symptoms, subclinical PTSD (1 to 3 symptoms), or probable PTSD (4 to 7 symptoms). The investigators examined whether longitudinally assessed health risk factors (such as smoking, body mass index, and oral contraceptive use) accounts for increased SLE risk in women who have trauma exposure and PTSD compared with those who do not.

- Compared with women who had no trauma, probable PTSD was associated with increased SLE risk.
- Subclinical PTSD was associated with increased SLE risk, although this did not reach statistical significance.
- Smoking, body mass index, and oral contraceptive use slightly attenuated associations.
- Trauma exposure was strongly associated with incident SLE, regardless of PTSD symptoms.

The authors concluded that the study contributes to growing evidence that psychosocial trauma and associated stress responses may lead to autoimmune disease.

“We were surprised that exposure to trauma was so strongly associated with risk of lupus—trauma was a stronger predictor of developing lupus than smoking,” lead author Andrea L. Roberts, PhD,
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**Exercise is Good for Lupus Nephritis, Social Stress Not So Much**

Daily moderate exercise and stress management are underemphasized in the care of patients who have lupus nephritis because their potential roles in controlling the inflammatory response are poorly understood, researchers from The Ohio State University suggested.

To investigate these effects on murine lupus nephritis, they monitored disease progression with daily moderate exercise or social disruption stress induction in a mouse study. Social disruption stress induction of previously established social hierarchies was performed daily for 6 days. Daily moderate exercise consisted of treadmill walking at a 8.5 m/min pace for 45 minutes a day.

- Social disruption stress induction significantly enhanced kidney disease compared with age-matched, randomly selected control counterparts.
- Although 88% of nonexercised mice displayed significant renal damage by age 43 weeks, this was reduced to 45% with exercise.
- Daily moderate exercise also reduced histopathology in kidney tissue and significantly decreased deposits of C3 and IgG complexes.
- A macrophage-mediated inflammatory response was revealed that was significantly induced with social disruption stress induction and suppressed with daily moderate exercise, which also correlated with expression of inflammatory mediators.
- Social disruption stress induction induced IL-6, TNF-α, IL-1β, and MCP-1. Daily moderate exercise suppressed IL-6, TNF-α, IL-10, CXCL1, and anti-dsDNA autoantibodies.

The authors concluded that the data demonstrate that psychological stressors and daily moderate exercise have significant but opposing effects on the chronic inflammation associated with lupus nephritis.

“If we observe similar results in human studies, this could mean that stress reduction and a daily regimen of physical therapy should be considered as interventional strategies to be used alongside current medical treatment,” said study senior author Nicholas Young in a press release.

“We may have started to characterize an effective way to reduce inflammation and help people with lupus aside from conventional drug therapy,” he stated.

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**Mortality Goes Up, Functionality Goes Down After Stroke in Lupus**

Swedish researchers investigated mortality and functional impairment after stroke in patients with SLE.

In their study, they used nationwide registers to identify 423 persons with SLE and 1652 persons without SLE who had a first-ever ischemic or hemorrhagic stroke and monitored them until all-cause death or for 1 year.

The investigators estimated the hazard ratio for death after ischemic or hemorrhagic stroke and the risk ratio of functional impairment (dependence in transferring, toileting, or dressing) 3 months after ischemic stroke.

- One year after stroke, 22% of patients who had SLE died, compared with 16% of patients who did not have SLE.
- The risk of death was increased in patients with SLE after ischemic stroke and was attenuated after controlling for SLE-related comorbidities.
- Functional impairment at 3 months was increased in SLE by almost 2-fold.
- After hemorrhagic stroke, patients with SLE had an HR of 2.30 for death, which was increased even during the first month.

Mortality after ischemic stroke increases after the first month in patients with SLE, and functionality is worse at 3 months, the authors concluded. SLE is associated with all-cause death after hemorrhagic stroke even during the first month, suggesting a need for a shift of focus to patient functionality and prevention of hemorrhagic strokes.

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**Pulmonary Arterial Hypertension Linked with Lupus**

Pulmonary arterial hypertension (PAH) associated with connective tissue disease (PAH-CTD) is the second most common cause of pulmonary hypertension, and SLE is the second most frequent cause of PAH-CTD, according to French researchers.
Because SLE-PAH case series are rare, and SLE-PAH series in which the PAH diagnosis was based on right heart catheterization (RHC) are even rarer, they conducted a study of the characteristics and survival rates of patients with SLE-PAH proven by RHC who were enrolled in the French Pulmonary Hypertension Registry between June 2003 and June 2013 and compared them with those of patients who had SLE without PAH.

The patients with SLE-PAH in the study did not differ from the control group regarding age, sex, or duration of SLE at the time of the analysis but had a higher frequency of anti-SSA and anti-SSB antibodies.

- The delay between SLE diagnosis and PAH diagnosis was 4.9 years (range, 2.8 to 12.9 years).
- The 3- and 5-year overall survival rates were 89.4% and 83.9%, respectively.
- The survival rate was significantly better in patients with anti-U1-RNP antibodies. The presence of anti-U1-RNP antibodies appears to be a protective factor regarding survival.
- Anti-SSA/SSB antibodies may be a risk factor for PAH in patients with SLE.

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