Migraine Raises Thrombotic Event Risk in SLE

Frequent headaches with aura were tied to a higher risk of stroke, but Raynaud's phenomenon was not.

BY BRUCE JANCIN
Denver Bureau

PARIS — Migraine is an independent risk factor for stroke and other arterial thrombotic events in patients with lupus, but Raynaud's phenomenon is not.

The increased thrombotic risk conferred by migraine in patients with systemic lupus erythematosus (SLE) is of similar magnitude in migraineurs with and without aura, said Dr. Simone Appenzeller, a rheumatologist at McGill University, Montreal.

Speaking at the annual European Congress of Rheumatology, she reported on 327 patients prospectively followed for an average of 5 years since being diagnosed with SLE. One hundred of the 327 met International Headache Society diagnostic SLE criteria for migraine, including 38 who had migraine with aura.

When they were diagnosed with SLE, 5.5% of patients had a history of stroke or other arterial thrombotic events. During follow-up, 11.9% of participants experienced such events. Migraine proved to be independently associated with 4.3-fold increased odds of arterial vascular thrombotic events in a multivariate analysis adjusted for known thrombotic risk factors, including hypertension and diabetes, as well as for the presence of lupus anticoagulant, antiphospholipid antibodies, family history of cardiovascular events, and the use of aspirin or oral anticoagulants.

In addition, migraine was independently associated with a 9.8-fold rise in the odds of antiphospholipid antibodies being present. More frequent migraine with aura was linked to a higher risk of thrombotic events. However, duration of migraines was not.

The Raynaud's study involved 748 SLE patients, including the 327 from the migraine study. Their median age was 25 years, and 690 were women. Two hundred and fifty subjects (33%) had Raynaud's phenomenon. During a median 7 years of follow-up, 16% of the SLE patients developed arterial vascular thrombotic events. Another 6% had a history of such an event at baseline, when they were diagnosed with SLE.

In a multivariate model adjusted for common thrombotic risk factors, neither the presence nor duration of Raynaud's phenomenon independently predicted arterial thrombotic events. This finding is of particular interest because Raynaud's phenomenon is the result of small-artery ischemia. If Raynaud's doesn't predispose to arterial thrombotic events in patients with SLE, it suggests that the pathophysiologic basis of such events lies chiefly elsewhere.

The presence of the antiphospholipid syndrome was associated with an adjusted 9.8-fold increased rate of a history of arterial thrombotic events at the time SLE was diagnosed, and with a 5.7-fold greater rate of such events during the follow-up period than in unaffected patients with SLE.

Dr. Appenzeller noted that the mechanism by which migraine leads to stroke and other ischemic vascular events is likely to prove complex. She offered some hypotheses: Migraine and ischemic vascular events could be linked by genetic factors; drugs prescribed for migraine might predispose to such events; migraine might directly cause ischemic events; the headaches might adversely effect endothelial function in ways predisposing to vascular events even during migraine-free periods; and/or migraine may be associated with an increased prevalence of the major risk factors for stroke and other vascular events.

With regard to this last possibility, she noted that in several studies of the migraine/stroke association in individuals without SLE, the link tends to be strongest in the absence of traditional cardiovascular risk factors, and the association diminishes with advancing age. These findings suggest that the mechanism by which migraine increases thrombotic risk is independent of the standard major cardiovascular risk factors, which become more potent in older populations. ■

Selenium May Help Clarify Racial Differences in HT

BY SHARON WORCESTER
Southeast Bureau

NEW ORLEANS — Reduced serum selenium is an independent predictor of hypertension, according to an analysis of data from the third National Health and Nutrition Examination Surveys.

The findings from this and other studies, that serum selenium concentrations are reduced in African Americans, compared with those in with whites, may in part explain the increased incidence of hypertension in African Americans, Dr. Chizobam Ani said in a poster at a meeting sponsored by the International Society on Hypertension in Blacks.

Serum selenium is an essential component in substances shown to mediate the incidence of cardiovascular disease, such as glutathione peroxidase and homocysteine. In 9,881 nonpregnant participants aged 40 years and older, researchers noted significant differences in serum selenium concentrations between African Americans and whites at the highest and lowest quartile concentrations, reported Dr. Ani of Charles Drew University of Medicine and Science, Los Angeles.

On bivariate analysis, there was a significant association between serum selenium concentration and the prevalence of hypertension and other cardiovascular disease, including peripheral vascular disease, myocardial infarction, and congestive heart failure.

An analysis that controlled for known predictors of cardiovascular disease, including family history, diabetes, sociodemographic variables, and renal disease, showed a significant relationship between serum selenium and the prevalence of hypertension (odds ratio 1.30) and a significant interaction effect between ethnicity and serum selenium in individuals with hypertension (OR 1.10).

These findings are important because African Americans have higher rates of hypertension and mortality from heart disease and stroke than do whites and Hispanics in the United States, and because African American men have three times the risk of sudden death as do white men.

Based on the emerging understanding of the role of serum selenium in hypertension and cardiovascular disease, and the differing concentrations in African Americans and whites, Dr. Ani and his colleagues theorized that high serum concentrations of selenium might predict reduced levels of oxidate stress and vascular injury in certain ethnic groups that correlates with the incidence of cardiovascular diseases.

The current findings seem to support this theory of "differential oxidative protection for cardiovascular injury" in African Americans, compared with whites, he said in an interview. The findings are of interest because low serum selenium concentration is a modifiable risk factor, he said. ■

Unique Cardiac Risks in Systemic Sclerosis Need Early Intervention

BY BRUCE JANCIN
Denver Bureau

PARIS — Periodic cardiac evaluations should be a routine part of the management of all patients with systemic sclerosis, beginning "from the first day of the disease."

Cardiac problems in patients with systemic sclerosis (Ssc) were thought to occur mainly in those with the diffuse subtype of disease, not the limited cutaneous subtype. But with the use of contemporary cardiac evaluation tools, including tissue Doppler echocardiography, myocardial scintigraphy, and cardiac MRI, it has become apparent that coronary lesions occur early in the course of both subtypes—and are far more prevalent than previously realized, Dr. André Kahan said at the annual European Congress of Rheumatology. "I'd say they are present in close to 100% of patients," said Dr. Kahan, professor of rheumatology at René Descartes University, Paris.

If these cardiac abnormalities aren't treated early on, irreversible myocardial fibrosis can occur.

DR. KAHAN

Subclinical myocardial perfusion abnormalities, diminished coronary reserve, and reduced left and/or right ventricular contractility are common in patients with Ssc. The good news is that numerous studies by Dr. Kahan and others have demonstrated that these abnormalities are reversible with high-dose vasodilator therapy using calcium channel blockers or angiotensin-converting enzyme inhibitors. In addition, bosentan in standard doses has been shown to reverse the early abnormalities.

However, if these cardiovascular abnormalities aren't treated early, then fibroblasts become activated, collagen is deposited, and irreversible myocardial fibrosis occurs.

When clinical cardiac disease is present, as in 15%-25% of Ssc patients, all-cause mortality is sharply increased. The coronary disease in Ssc patients is completely different both in site and mechanism from that encountered in rheumatoid arthritis, systemic lupus erythematosus, or atherosclerotic heart disease in the general population. In those cohorts, the large coronary arteries are involved, whereas in Ssc, it is the small coronary vessels.

Vascular lesions in Ssc patients are vasospasm-induced ischemic reperfusion injuries. Not just the small coronary arteries are affected, but small arteries everywhere else in the body, too, including the digits, pulmonary circulation, and the kidneys. These vascular injuries and the resultant fibrotic changes lead to the major complications of Ssc.

Tissue-Doppler echo is now widely available in routine cardiology practice; it provides an excellent noninvasive means of assessing left and right ventricular function. It is far more sensitive than standard echocardiography and should be applied routinely in all Ssc patients undergoing periodic cardiac assessment, in Dr. Kahan's view.

Cardiac MRI is probably the method of choice for evaluating myocardial perfusion in these patients. Scintigraphy has excellent sensitivity, too, but the need to inject radioisotopes is a significant disadvantage over the course of years of repeated testing, he continued.

Diffuse myocardial perfusion abnormalities are common in Ssc patients. They can be detected at rest and induced by cold, high altitude, or exercise.

An audience member asked whether the aggressive exercise program he and his colleagues prescribe for their Ssc patients is a good idea. Dr. Kahan replied that his research in the mid-1980s showed that coronary reserve in Ssc patients is only half that of normal subjects, so he counsels his patients to stick to limited exercise relieved by liberal rest periods. "They must not exercise at too high a level because they may induce ischemia." ■