Technetium-99m-HMPAO Brain SPECT in Systemic Lupus Erythematosus with Central Nervous System Involvement

TO THE EDITOR: We read with great interest the article by Lin et al. (1) about brain SPECT in systemic lupus erythematosus. After working for the past 2 years on a similar group of patients, we formed conclusions similar in some aspects, but different in others, which may be the result of a different methodological approach. We previously reported a part of our observations (2,3); the rest of this material is in preparation to be published.

We performed brain SPECT using a triple-head gamma camera, MRI and anticardiolipin antibody (ACA) assays in 66 systemic lupus erythematosus, 14 Sjögren’s syndrome, 12 diffuse scleroderma and 4 mixed collagenosis patients. In most, an acetazolamide stress test was performed 3 days later. SPECT results were compared with a group of 25 healthy volunteers. Brain SPECT was abnormal in 91% of systemic lupus erythematosus patients, with MRI abnormal in only 26%. Until that point, our observations are in agreement with those of Lin et al. (1). In our opinion, however, although visual interpretation may sometimes be superior to semiquantitative, some subtle changes may be overlooked in visual analysis, especially regarding intrahemispherical asymmetries. We found diffuse hypoperfusion of both frontal lobes when compared to HMPAO cerebellar uptake and healthy control subject indices in 30% of systemic lupus erythematosus, 50% of Sjögren’s syndrome and none of diffuse scleroderma patients. This correlated well with cognitive impairment assessed by psychometric tests.

Also, analysis of interhemispherical asymmetries revealed significant problems, which are underlined by the authors. We believe that the subtle changes seen on images of systemic lupus erythematosus patients require comparison to physiological asymmetries of a healthy volunteer database and visual interpretation is not sufficient. As in systemic lupus erythematosus, at least in our patient group, diffuse HMPAO uptake defects are more frequent than focal ones and comparison with healthy control subject results seem to be particularly important, especially in analyzing basal ganglia HMPAO uptake, where, even in healthy subjects standard deviation of interhemispherical HMPAO may be high (s.d. = 8.7% in our material). Therefore, basal ganglia SPECT results should be interpreted with caution. Another problem is ACA assay results. The authors did not find correlation with clinical findings. How did the correlation with SPECT images look? This is important because thombo-embolic brain infarcts are more frequent in ACA patients (4). This was consistent with our SPECT findings, where 9 of 12 patients with ACA had multiple focal HMPAO uptake defects (more than five per patient) resembling multi-infarct dementia.

Last, but not least, there is the problem of future guidelines in systemic lupus erythematosus brain research. What is the appreciable in Lin et al.’s (1) article is the size of the patient groups, subdivision to different pathological groups and insight into basal ganglia. The other interesting points seem to be cerebrovascularity in systemic lupus erythematosus, reversibility of cerebral blood flow (CBF) changes and comparison with other connective tissue diseases. Lin et al. (1) describe improvement in brain perfusion in a patient after methylprednisolone therapy. During control scanning after steroid therapy, we found brain perfusion improvement in 12 of 20 patients, no change in 6 and new hyperperfused areas in 2. Of 6 ACA-positive patients, none showed improvement. Another crucial point might be reactivity to acetazolamide-induced hypercapnia, as carbon dioxide is the most important physiological regulator of regional CBF redistribution. We found it altered (no change or paradoxical HMPAO uptake improvement in 48% of patients). In comparing systemic lupus erythematosus with the other connective tissue diseases, we found a pattern similar to systemic lupus erythematosus in mixed collagenosis, multifocal-defect pattern but not hypofrontality in Sjögren’s syndrome and little or no CBF changes in diffuse scleroderma. This may be related to different pathological mechanisms.

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should be considered as well since corticosteroids may result in cerebral atrophy (3), which changes the presentation of $^{99m}$Tc-HMPAO. The false-positive rates of CNS involvement in systemic lupus erythematosus patients could be high when comparing systemic lupus erythematosus patients with a long history of steroid use with normal healthy subjects.

Therefore, an age-matched control group with similar steroid history may be necessary when establishing a SPECT database for the clinical application of $^{99m}$Tc-HMPAO brain SPECT in systemic lupus erythematosus patients.

We did find some correlation between SPECT findings and anticoagulant therapy (83.3%). Of the 48 patients with positive SPECT findings, 20 (41.7%) had positive ACA assay results. Of the 24 patients with positive SPECT findings, only 4 (16.7%) had positive ACA assay results. There was a statistical difference, with a p value of 0.0292, using a Fisher exact test. Of the 24 patients with positive ACA assays, 20 (83.3%) had positive SPECT findings. This result is similar to Dr. Lass’s findings.

We admire Dr. Lass’s work in the application of $^{99m}$Tc-HMPAO brain SPECT in various connective tissue diseases. The presentation of $^{99m}$Tc-HMPAO brain SPECT may be different in these diseases because of different pathological mechanisms. We will say that there is still a long way to go for the application of $^{99m}$Tc-HMPAO brain SPECT scan in connective tissue diseases.

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**Continuous Ambulatory Radionuclide Monitoring of Left Ventricular Function**

**TO THE EDITOR:** We read with interest the article by Mizuno et al. (1) and the accompanying editorial (2). Mizuno et al. (1) used an ambulatory left ventricular (LV) function monitoring device (the VEST system; Capintec, Inc., Ramsey, NJ) to compare changes in LV ejection fraction (LVEF) and LV end-diastolic and end-systolic volumes during supine and upright bicycle exercise in a group of 16 healthy volunteers. Although changes in heart rate and blood pressure were comparable in both exercises, the changes in relative end-systolic volumes and ejection fraction were significantly different. There was a fall in LVEF and an increase in relative end-systolic volumes during exercise in the supine position.

The authors explain this result as due to a limitation of the device in accurately tracking the changes in LV volumes during supine exercise, presumably related to the relative shift in detector position with deep breathing during exercise. Although this inference is logical, the clinical and practical implications of this finding need to be put in proper perspective. The major unrivaled advantage of the ambulatory LV function monitoring device (as its name implies) is its capability to monitor LV volumes and ejection fraction under a variety of ambulatory conditions. Supine exercise in clinical practice is not usually performed by choice, but rather due to a limitation of conventional gamma cameras, which require the patient’s chest to be still while equilibrium radionuclide angiography is performed. This is possible only when the patient is in the supine position. However, exercise in this position is often difficult, limited and somewhat unphysiological. This study was carried out in young, healthy volunteers who were able to attain similar peak heart rates and blood pressure (and, presumably, similar peak workloads as well) in the supine position compared to the upright position. However, in a significant proportion of patients, supine exercise attains only a submaximum workload compared to upright exercise. If it is possible to monitor LV function reliably in the upright position, this is the preferred exercise modality.

Therefore, the very purpose of the study by Mizuno et al. (1) is, to our minds, questionable from both a clinical and physiological perspective. Why bother studying a phenomenon with minimal relevance when a more appropriate manner of study exists?

It should also be noted that supine monitoring of LV function may still be accurate, reliable and acceptable for monitoring silent ischemia and for studying the effect of pharmacological intervention on LV function over a period of several hours. In prior studies in which we monitored LV function for the detection of spontaneously occurring, unprovoked myocardial dysfunction and during routine physical activities in the convalescent period in patients with myocardial infarction and unstable angina, some of the patients were monitored in the supine position (3,4). In the absence of exercise we did not encounter any specific problems with supine monitoring.

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**REPLY:** We thank Drs. Jain and Zaret for their interest in our recently published study (1). A continuous ambulatory radionuclide monitoring system (the VEST system; Capintec, Inc., Ramsey, NJ) is a new technique of continuously monitoring left ventricular ejection fraction (LVEF) using standard principles of electrocardiographic-gated radionuclide ventriculography. The VEST system makes it possible to monitor LVEF during stress tests and silent myocardial ischemia and to evaluate cardiac function in daily life (2–4).

In our article, we assessed the reliability of the VEST system during exercise (1). Sixteen healthy volunteer subjects underwent measurement of left ventricular (LV) performance with the VEST system during ergometer exercise in the upright and supine positions. No significant difference was shown in the baseline data at rest between the upright and supine positions. LVEF increased significantly, as we expected, during ergometer exercise in the upright position. On the other hand, LVEF decreased during exercise in the supine position. Thus, in the supine position during exercise, the VEST system may give false data due to unsatisfactory data accumulation. Since the detector of the VEST system may be too small, data collection is impaired during exercise in the supine position because the heart may shift with deep respiration. To measure LVEF with the VEST system, the detector should be located on the center of the LV cavity and should remain in that position regardless of the heart’s location relevant to the patient’s body position. However, the heart is suspended, not fixed, in a space of the mediastinum. Thus, the position of the heart is easily shifted by different body positions. It is quite possible that the accumulation of VEST data could be false in some cases, not only because of respiratory movement of the diaphragm but also by position changes (i.e., standing, sitting, supine, and right and left lateral decubitus positions). For example, during an