Redistribution on the Thallium Scan in Myocardial Sarcoidosis: Concise Communication

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Resting and redistribution thallium studies were performed in four young patients with sarcoidosis to evaluate the possibility of myocardial involvement. In each case the resting scan showed marked defects that resolved on the redistribution studies. In a different patient population, these results would have implied significant coronary artery disease.


The principal roles of thallium scanning have been in the detection of coronary artery disease and of acute myocardial infarction. In the former, the images obtained after the patient has been stressed are compared with images obtained after redistribution of the initial injection (1) or with those of a separate resting study (2–4). Berger et al. (5) have shown evidence, however, that analyzing the combination of a rest study and redistribution can provide evidence for coronary artery disease if quantitative analysis of the data is performed.

Many conditions other than coronary disease can cause abnormalities in the resting thallium study. These conditions include scar from a previous myocardial infarction (6), congestive cardiomyopathy (7), and infiltration of the myocardium by tumor or sarcoidosis (8,9).

We have studied a small group of young patients with sarcoidosis to determine whether redistribution occurs when resting defects are present on the initial thallium scans. If the resolution of the resting abnormalities occurred, this would diminish the specificity of the rest/redistribution combined study for the detection of coronary artery disease.

METHODS

Patient selection. Thallium rest/redistribution scans were performed in four women who were between 26 and 34 years of age. One subject (G.A.) had clinical evidence of myocardial dysfunction; the other three were asymptomatic. Cases being examined to determine whether myocardial involvement was present.

Thallium scanning. Each patient received an intravenous administration of 2 mCi thallium-201 chloride after an overnight fast. Immediate images of the heart were obtained in the anterior, 30°, 45°, and 70° left anterior oblique (LAO) projections (6 min per view). For quantitative analysis, data were stored using a 128 X 128 matrix in a minicomputer.* After a delay of 4 hr, the patients had repeat 6-min images obtained in the same projections.

Quantitative analytical technique. In each resting study, the projection that most clearly showed a defect was chosen, and in it two regions of interest were marked with the light pen: one over the abnormal area and the other over the most nearly normal part. Corresponding areas were established in the analogous redistribution image. As both studies were obtained for equal acquisition times, any change in the observed counting rate per unit area represented a true change in the concentration of the thallium in the myocardium. Each patient had at least two abnormal and two normal regions ana-

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lyzed for changes in counting rate. Background subtraction was used before the visual inspection of the images but not before the quantitative analysis. The photographs were also made without benefit of background subtraction. Polaroid images were made at the time of the initial data collection, but interpretation was made using the computer display, with background subtraction. The subtraction was adjusted by the viewer and averaged approximately 25% of the peak left-ventricular activity.

Data analysis. Student's t-test for paired data was used to determine the significance of the washouts observed from the normal and abnormal areas when the rest and the redistribution studies were compared. This test was also used to document the significance of the observed difference in counting rates between normal and abnormal areas, for both the rest and redistribution studies.

CASE REPORTS

Case 1. G.A. is a 26-year-old black women who 1 yr before admission noted fatigue, a 10-pound weight loss, and intermittent right visual field defects that resolved spontaneously. Four months before admission she noted arthralgias, nonexertional squeezing chest pain lasting approximately 10 min, and night sweats. Three days before admission she developed severe dyspnea, including orthopnea and paroxysmal nocturnal dyspnea. On admission she was found to be in severe congestive heart failure with bilateral pleural effusions. Past medical history revealed a cyst of the left breast 7 yr previously and a uterine curettag 3 yr previously.

Chest examination showed a displaced PM1, S1 and S2 of equal intensity, and a summation gallop. A grade 2/6 holosystolic murmur was present at the apex. Her electrocardiogram revealed sinus tachycardia, an indeterminate QRS axis, low voltage, PVCs, and nonspecific ST-T abnormalities. Chest radiograph showed an enlarged cardiac silhouette with pulmonary vascular congestion and bilateral pleural effusions. M-mode and two-dimensional echocardiograms revealed a small pericardial effusion, an enlarged left atrium, and abnormal regional wall motion involving the apex and posterolateral wall. The overall ejection fraction was thought to be reduced.

A radionuclide equilibrium gated wall-motion study revealed an enlarged left ventricle with posterolateral dyskinesis and an ejection fraction of 50%. Cardiac catheterization showed elevated right- and left-heart pressures with normal coronary arteries. The posterolateral wall and apex were felt to be hypokinetic, and an intracavitary defect was noted on the ventriculogram.

Biopsy of the left-ventricular wall was performed under general anesthesia. It revealed diffuse involvement and near replacement of the posterolateral wall and apex by noncaseating granulomas.

The TI-201 resting study revealed a dilated cavity, right-ventricular activity, and defects at the apex and posterolateral walls of the left ventricle.

Case 2. E.Y. is a 31-year-old black woman who, 1 mo before admission, noted photophobia and bilateral red eyes after an upper-respiratory infection. Three weeks before admission she noted fatigue, with nausea, vomiting, headache, and blurring in the left eye. Two weeks before admission she noted left facial weakness with loss of sensation, a 10-pound weight loss, and intermittent fevers to 101°F. She had a hysterectomy 1-yr ago, and a family history of diabetes mellitus and organic heart disease.

Physical examination revealed bilateral papilledema, bilateral uveitis, and normal conjunctivae. Cardiac examination revealed a normal point of maximum impact and 1/6 systolic ejection murmur at the left sternal border. Neurological examination revealed a left peripheral facial palsy and slight ataxia of gait. Her electrocardiogram was normal. A chest radiograph showed bilateral hilar adenopathy with a right paraaortic node. Pulmonary function tests revealed mild obstructive airway disease. A lumbar puncture showed normal pressure, with ten lymphocytes and normal glucose and protein concentrations. A TCT scan of the head was normal. She had abnormal liver function tests, and a liver scan showed nonhomogeneous uptake and an enlarged spleen.

The patient was felt to have sarcoidosis. A resting study showed a defect in the anterior wall on the 70° left anterior oblique (LAO) projection and an apical defect on the anterior oblique.

Case 3. D.C., a 34-year-old black woman, had a diagnosis of sarcoidosis made by cervical node biopsy (noncaseating granulomas) 2 yr before admission. At that time, she presented with severe constitutional symptoms of 4 mo duration. She was recently admitted for E. coli urinary-tract infection, sepsis, the syndrome of inappropriate antidiuretic hormone. Her cerebrospinal fluid, showed increased cells and decreased glucose, with cultures negative for bacteria, fungi, and TB. She was felt to have sarcoid menigitis. On the current admission, she was found to have hepatosplenomegaly, lymphadenopathy, anemia, abnormal liver function tests, and an abnormal liver scan. She denied all cardiac symptoms.

Cardiac examination revealed a normal point of maximum impact and a 2/6 systolic ejection murmur at the left sternal border and apex. Examinations of the abdomen, extremities, and nervous system were unremarkable. Her electrocardiogram, chest radiograph, and echocardiograms (M-mode and sector) were also normal.

A TI-201 resting study revealed defects at the apex (anterior view) and septum (45° LAO).

Case 4. E.W. is a 25-year-old black woman with a history of sarcoidosis since 1977, most recently admitted
for fluid loss and hypokalemia. The diagnosis of sarcoidosis was established in 1977 by liver and renal biopsy, both of which revealed extensive noncaseating granulomas. The renal involvement resulted in a salt-wasting nephropathy that initially required dialysis. There were no cardiac symptoms except occasional palpitations and shortness of breath. Present medications include replacements of K, Ca, Na, and bicarbonate.

On physical examination her chest was clear. Cardiac examination revealed a normal point of maximum impact without any murmurs or gallop sounds. An electrocardiogram showed a sinus rhythm of 75/min and a prolonged Q-T interval. Chest radiograph and echocardiograms (M-mode and sector) were within normal limits. A Holter monitor revealed sinus rhythm, with premature atrial contractions and episodes of sinus tachycardia. A gated wall-motion tracer study revealed the left ventricle to be of normal size with an ejection fraction of 58% and normal wall motion. The resting TI-201 scan showed an inferior defect on the anterior view and a posterior defect on the 30° LAO.

RESULTS

Clear areas of diminished thallium concentration were seen in the resting study in each of the four patients.

In the anterior view, resting, Patient G.A. showed a large area of decreased activity involving the distal anterior wall and apex of the left ventricle (Fig. 1). The defect resolved in the redistribution image. The quantitative data are presented in Fig. 5A. The apical region of the left ventricle may normally have less activity per unit area than the other walls, but the ratio of the apex to the other walls should not change with time. Thus the patient’s defect is not likely to be due to anatomic variability.

In Patient E.Y., a large anterior defect was seen in the anterior and 70° LAO views (Fig. 2); it resolved in a redistribution image. The quantitative data from the 70° LAO view are presented in Fig. 5B. In Patient D.C., a large septal defect was seen in the 45° LAO view; it resolved almost completely in the redistribution image (Fig. 3). The analysis of the thallium counting-rate data is presented in Fig. 5C. Patient D.C. also had an apical defect, seen in the anterior view, which underwent partial resolution. Patient E.W. had a large defect in the inferior and apical regions, best seen in the anterior view, and a septal abnormality seen in the 30° and 45° LAO views. Figure 4 shows the anterior views, with the quantitative data in Fig. 5D.

Analysis of the data showed a significantly lower concentration of thallium in the abnormal areas during the resting studies: (68.8 ± 4.64%) of the normal areas, p < 0.001. During the 4-hr redistribution period, the
activity in the normal areas decreased by (40.4 ± 11.0)%, and in the abnormal areas by (11.6 ± 9.4)%. Washout from the normal areas was highly significant (p < 0.01) and the washout from the abnormal area was probably significant (0.10 < p < 0.15). At the time of the redistribution study, the difference in the thallium concentration between normal and abnormal areas was only (2.65 ± 5.34)% (not significant).

**DISCUSSION**

Sarcoidosis is a multisystem granulomatous disorder that has been recognized for more than a century. In the general population, its incidence in blacks is ten times the average, and it is twice as frequent in female as in male blacks. No sex predilection is present in the white population. Cardiac sarcoidosis has been noted in 20–27% of autopsied patients with sarcoidosis (10,11). Most commonly affected are the upper septum including the conduction system, the right and left ventricular free walls, and papillary muscles (12,13). The atria, pericardium, and aorta may also be involved (14); with transmural involvement, aneurysm formation may occur (15).

Although 25% of patients with sarcoidosis have cardiac involvement at autopsy, only a small percentage have symptoms. Silverman noted that only four of 23 had definite symptoms for which no other cause could be found (11). Most commonly, atrial and ventricular arrhythmias and conduction disturbances, with Strokes–Adams syncope were noted (15,16). Less often, congestive heart failure and pericardial effusion are found. Sudden death is a particular problem in that two out of three patients with myocardial sarcoidosis die from this condition (17).

We began our series in the effort to determine the frequency of myocardial sarcoidosis in the patients seen at our hospital. The discovery of abnormal resting thallium scans in our first three unselected patients (G.A. was known to have cardiac sarcoidosis at the time of her study) was unexpected, but not statistically implausible, since cardiac involvement is frequent (25%) and the series is small. The fact that in all cases the defects underwent resolution on the redistribution study was, however, unexpected.

In an effort to obtain the full thallium study in one day, and thus avoiding a second injection of an expensive tracer, the redistribution thallium scan has become, in some institutions, a standard adjunct to the stress thallium study. Data have also been published showing that in some patients with coronary artery disease there are changes between rest and redistribution studies. This raises the possibility that, at least in some patients, the diagnosis of coronary artery disease can be made following a thallium injection at rest (5). Several groups have used this rationale to explain the presence of resting defects that “fill in” on a redistribution study in patients with severe coronary artery disease (5,21,22). The explanation of the findings in our four cases of myocardial sarcoidosis is not so clear. Myocardial sarcoidosis does not usually produce abnormalities of the main coronary arteries—indeed, one subject had normal coronary arteries documented during coronary arteriography. The two possibilities that appear most reasonable are (a) that sarcoidosis produces abnormalities of the microcirculation that (on thallium scanning) functionally mimic the abnormalities produced by severe lesions of the coronary arteries; or (b) that the extraction efficiency.
of thallium by the heart is reduced in the areas involved with sarcoidosis. We cannot, on the basis of our data, determine whether either of these theoretical mechanisms is applicable.

If a patient with myocardial sarcoidosis has a defect on the resting thallium study, the defect would presumably be present on a stress thallium study. If the stress study is compared with the resting study, the images could look the same and the implication would be that there was no evidence for exercise-induced ischemia. If the stress study is compared with a redistribution study, however, the impression might well be that of stress-induced ischemia. The findings in these patients document a problem with the specificity of the thallium scan when the redistribution images are being compared with initial images. Because we do not routinely perform a combined rest and redistribution study in an effort to diagnose coronary artery disease, we do not know what the sensitivity or specificity of such a technique would be in our hands. Thus we can not tell whether redistribution after a resting thallium injection is a finding of low specificity in a population with a low incidence of coronary artery disease.

**FOOTNOTE**

* MDS, Mugacart.

**REFERENCES**