SCIENTIFIC LETTER

Patterns of myocardial inflammation and scarring in sarcoidosis as assessed by cardiovascular magnetic resonance

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Sarcoidosis is a multisystemic disease. Cardiac involvement has a strong impact on the patient's prognosis but is difficult to detect in vivo. This is reflected by the high rate of unexpected cardiac sarcoidosis in postmortem studies. In a study of patients with necropsy proven cardiac sarcoidosis, it was established or suspected before death in only 45%, with cardiac involvement being fatal in 67%.¹ Cardiac sarcoidosis is mostly identified by impaired systolic left ventricular (LV) function, a feature of more advanced disease.

Cardiovascular magnetic resonance (CMR) detects tissue inflammation and fibrosis. The focus of our study was to identify cardiac tissue changes in patients with systemic sarcoidosis by using CMR.

PATIENTS AND METHODS

Between 1999 and 2003, we studied 31 patients with proven systemic sarcoidosis (mean (SD) age 46 (2) years; 19 men). Twelve patients (48 (4) years; 10 men) had evidence for cardiac involvement as defined by typical symptoms and documented arrhythmias. In eight patients with chest pain, risk factors for coronary artery disease, or age above 30 years, coronary artery disease was excluded by coronary angiography. The remaining four patients were three men and one woman (25, 30, 29, and 30 years old, respectively). All of them were non-smokers, had a normal serum lipid profile, and had no family history of coronary artery disease. We also investigated 19 patients with sarcoidosis and without cardiac symptoms (45 (3) years; 15 men). Sarcoidosis was confirmed by biopsy in all cases, taken from either the lungs ($n = 27$) or the skin ($n = 4$).

Nine healthy subjects served as controls (38 (8) years, seven men).

We used a dedicated cardiovascular MRI system (Signa CV/i, 1.5 T; GE Medical Systems, Milwaukee, Wisconsin, USA) with a four element phased array coil or with a body coil. To visualise inflammatory myocardial tissue changes, we assessed global and focal myocardial contrast enhancement in T1 weighted multislice fast spin echo images obtained before and within the first four minutes after application of 0.1 mmol/kg gadolinium-diethylenetriaminepentaacetic acid (Gd-DTPA) (Magnevist; Schering AG, Berlin, Germany), as described elsewhere.²

For the detection of scar tissue, we assessed delayed contrast accumulation with a multislice T1 weighted inversion recovery prepared gradient echo sequence (short axis, inversion time individually optimised, repetition time 5.5 ms, echo time 1.4 ms, slice thickness 10 mm, and no gap) 15 minutes after an additional administration of 0.1 mmol/kg body weight Gd-DTPA.

We studied cardiac function with a steady state free precession gradient echo cine sequence (contiguous set of short axis images, slice thickness 10 mm, no gap, and three long axis images). CMR was performed at baseline and in the patients with suspected cardiac involvement after six and 12 months.

Global and focal early relative enhancement was quantified as previously described². Focal scar lesions were identified by visual assessment. LV volumes, mass, and function were quantified by manually tracing the LV endocardial and epicardial borders at end diastole and end systole.

All values are presented as mean (SD). A probability value of $p < 0.05$ was considered significant. Data were analysed with the t test by standard software (StatView 4.5; Abacus Concepts, Berkeley, California, USA).

RESULTS

As defined by the inclusion criteria, all patients with sarcoidosis with suspected cardiac involvement had ventricular arrhythmias (bigeminy, trigeminy, or both); eight had atrial arrhythmias (two with atrioventricular bundle branch block), five had atrial fibrillation or atrial flutter, and one had atrial tachycardia and dyspnoea (six were in New York Heart Association functional class II, five in class III, and one in class IV).

Functional analysis showed normal values in all patients. No significant difference in the preserved LV ejection fraction between all groups was observed. We detected wall motion abnormalities in two patients and a posterior aneurysm in one patient. Global relative enhancement did not differ between volunteers and sarcoidosis patients without suspected cardiac involvement (1.9 (0.3) v 2.5 (0.2), not significant) but was significantly increased in patients with suspected cardiac involvement compared with patients without cardiac involvement (5.5 (1.0) v 2.5 (0.2), $p < 0.0002$). Focal areas of relative enhancement were detected in eight patients with suspected cardiac involvement (9.2 (2.8) v 3.0 (0.3) in volunteers, $p < 0.002$).

Follow up after six and 12 months in 12 patients showed a normalisation of relative enhancement during steroid treatment in 10 patients, according to an improvement of the clinical status in these patients. Focal delayed enhancement was present in three patients. In two of them the LV ejection fraction did not normalise and a clinical worsening was recognised during tapering off of steroids. Figure 1 shows the incidence of each pathological finding.

DISCUSSION

We showed that CMR can visualise myocardial contrast enhancement in patients with sarcoidosis and preserved LV function. This study confirms earlier reports on early contrast enhancement in myocardial inflammation and in patients with sarcoidosis.^{2–5} Global relative enhancement was not altered in patients with proven sarcoidosis but without evidence for cardiac involvement but was significantly higher in patients with evidence for cardiac involvement. The incidence of delayed enhancement was low.

Our results extend the existing knowledge on CMR in sarcoidosis by three new aspects: firstly, we used quantitative global relative enhancement data to reduce investigator dependent bias. Secondly, we included patients with preserved

Figure 1 Incidence of pathological findings. DE, delayed enhancement; LVEF, left ventricular ejection fraction; RE, relative enhancement.

LV function. Thirdly, we assessed the incidence of late enhancement. Remarkably, patients with delayed enhancement had an impaired prognosis—that is, worsening of the ejection fraction over time and symptoms during tapering off of steroids.

In summary, the presented method potentially improves the diagnostic capabilities for early assessment of myocardial sarcoidosis. It has the potential to identify the type of myocardial injury (inflammation or fibrosis) and thus provide means for earlier detection and better understanding of the disease.

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REFERENCES

- Perry A, Vuitch F. Causes of death in patients with sarcoidosis: a morphologic study of 38 autopsies with clinicopathologic correlations. *Arch Pathol Lab Med* 1995;**119**:167–72.
- Friedrich MG, Strohm O, Schulz Menger J, et al. Contrast media-enhanced magnetic resonance imaging visualizes myocardial changes in the course of viral myocarditis. *Circulation* 1998;**97**:1802–9.
- Mahrholdt H, Goedecke C, Wagner A, et al. Cardiovascular magnetic resonance assessment of human myocarditis: a comparison to histology and molecular pathology. *Circulation* 2004;**109**:1250–8.
- Schulz-Menger J, Strohm O, Dietz R, et al. Visualization of cardiac involvement in patients with systemic sarcoidosis applying contrast-enhanced magnetic resonance imaging. *Magma* 2000;**11**:82–3.
- Vignaux O, Dhote R, Duboc D, et al. Detection of myocardial involvement in patients with sarcoidosis applying T2-weighted, contrast-enhanced, and cine magnetic resonance imaging: initial results of a prospective study. *J Comput Assist Tomogr* 2002;**26**:762–7.

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