Impact of cardiac magnetic resonance imaging for assessment of Churg-Strauss syndrome: a cross-sectional study in 20 patients

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ABSTRACT

Objective. *To examine the diagnostic contributions of cardiac magnetic resonance imaging (CMRI) with delayed-enhancement (DE) in patients with Churg-Strauss syndrome (CSS).*

Methods. *We consecutively recruited 14 men and 6 women (mean age: 50±14 years) with CSS (mean disease duration: 4.5±3.6 years) and investigated them independently of the presence/absence of cardiac manifestations. Cardiac manifestations included heart failure in 6 patients, angina pectoris in 1, isolated ECG abnormality in 1, and isolated echocardiography and ECG abnormalities in 1. T1-weighted sequences were recorded after gadolinium injection to study myocardial DE.*

Results. *CMRI abnormalities were found in 13/20 patients, including all 9 patients with myocardial manifestations, and 4 of the 11 asymptomatic patients. DE was centromyocardial in 6 patients, subepicardial in 4, and subendocardial in 3. Most enhanced lesions were in the anteroseptal or lateral walls. Patients with myocardial symptoms and DE had higher transmyocardial wall DE scores (mean: 9.4 vs. 3.7, respectively; p=0.01) and lower left ventricular ejection fractions (mean: 42% vs. 59%; p=0.001) than asymptomatic patients with DE.*

Conclusion. *CMRI with DE enabled the detection of myocardial involvement in CSS patients with or without clinical symptoms. The clinical relevance of CMRI abnormalities in patients without clinical, echocardiographic and ECG signs of cardiac involvement remains unknown and needs to be evaluated in future studies. It seems premature to intensify treatment or to prescribe systematically steroids and cytotoxic agents based on the presence of isolated CMRI anomalies.*

Introduction

Churg-Strauss Syndrome (CSS), a rare necrotizing vasculitis first described in 1951, is characterized by asthma, eosinophilia and extrapulmonary manifestations. Myocardial abnormalities are found during >50% of autopsies of CSS patients (1). Cardiac manifestations comprise pericarditis, restrictive or dilated cardiomyopathy, myocarditis, arrhythmias and sudden death (2-7). Symptomatic cardiomyopathy carries a poor prognosis (8), is responsible for nearly 50% of the deaths (9), and requires combined therapy with steroids and immunosuppressants, usually cyclophosphamide. In a study on 96 patients (10), the 78-month survival rate was 90% in the absence, *vs.* 30% in the presence of symptomatic cardiac manifestations, highlighting the importance of identifying cardiac involvement early during the course of the vasculitis. CSS is considered to be an antineutrophil cytoplasm antibody (ANCA)-associated vasculitis but, recently, it was shown that different phenotypes could be observed according to the presence or absence of ANCA, thereby suggesting different pathogenic mechanisms (11). Cardiomyopathy was more frequently seen in ANCA-negative patients, while renal manifestations were observed more often in ANCA-positive patients (11, 12).

Cardiac magnetic resonance imaging (CMRI) provides considerable morphological and functional information on a variety of diseases including systemic and inflammatory diseases (13-15). Histological assessment of myocardial delayed-enhancement has been correlated with local fibrosis and active myocarditis (16, 17). Because MRI is a sensitive tool to detect cardiac involvement, we used it to investigate symptomatic and asymptomatic CSS patients to assess its ability to visualize abnormalities and to

describe their relationships with clinical manifestations and outcome.

Patients and methods

Between March 2004 and February 2006, 20 consecutive patients followed in our hospital's Department of Internal Medicine were recruited independently of their CSS phase (active or remission), the presence/absence of cardiac manifestations and treatment regimen. CSS had been diagnosed according to the American College of Rheumatology classification criteria (18). The following information was collected for all patients: sex, age, cardiovascular risk factors (cholesterol level, hypertension, tobacco use, diabetes, family history of coronary artery disease), CSS duration, its clinical manifestations, history of cardiovascular manifestations, cardiovascular symptoms at the time of CMRI, and ECG, echocardiographic and chest roentgenographic observations. ANCA were sought in sera from all patients by immunofluorescence and enzyme-linked immunosorbent assay (ELISA).

Because CSS affects small-sized vessels, the main coronary arteries are usually normal, so only patients with clinical manifestations consistent with coronary artery disease underwent coronary angiography. Pregnant women and patients for whom CMRI was contraindicated were not included.

Cardiac involvement was considered to be present when the patient had or previously experienced cardiac insufficiency and/or the echocardiogram showed heart enlargement and/or abnormal cardiac function, motion abnormality and/or abnormal ECG signs defined as follows: complete right or left bundle branch block, bifascicular block, third-degree atrioventricular block, ventricular tachycardia or pathological Q or ST abnormalities and/or elevated cardiac troponin I or brain natriuretic peptide (BNP)/N-terminal-proBNP.

Isolated pericardial effusion was not considered cardiac involvement, because only myocardial involvement was reported to have prognostic value in CSS (10). The local ethics committee (Comité de Protection des Personnes, Paris, Cochin) approved the study.

Cardiac magnetic resonance imaging protocol

CMRI was performed with a 1.5-T imager Avanto 76 × 32 SQ (Siemens Medical Solutions, Erlangen) using a dedicated cardiac, ECG-triggered, phased-array coil. After gradient-echo localizers, T2-weighted images were obtained with a breath-hold short-axis inversion recovery, black blood fast spin-echo sequence using the following parameters: repetition time: 1400 ms (function of RR interval), echo time: 47 ms, inversion time: 170 ms, 90° flip angle, a 340-mm field of view (function of patient), 256 × 154 matrix, an 8-mm section thickness, and 4-mm interslice gap. Functional examinations (Cine-MRI) were performed using a breath-held, short-axis segmented steady-state free precession sequence, with coverage of the whole left ventricle and a single slice per breath-hold. Imaging parameters were as follows: repetition time: 2.8 ms; echo time: 1.17 ms; 80° flip angle; 256 × 256 matrix; 380-mm field of view; 6-mm section thickness; 8-mm interslice gap. Gadolinium-DOTA-enhanced acquisitions were obtained with a left ventricular (LV), short-axis gradient-echo pulse sequence for 50 cardiac cycles during the first-pass of gadolinium-DOTA (perfusion scanning with 5 images per cycle, intravenous bolus of 0.1 mmol/kg, at 5 ml/s) followed by an LV short-axis inversion recovery prepared gradient-echo sequence, 1 slice per breath-hold, 5 slices for delayed phase, 10 min after a second 0.1-mmol/kg bolus of gadolinium-DOTA for delayed-enhancement imaging, using the following parameters: repetition time: 1200 ms (function of RR interval); echo time: 1.4 ms; the inversion time to null normal myocardium was determined with a dedicated scouting; 30° flip angle; a 380-mm field of view (function of patient); 256 × 128 matrix; and 6-mm section thickness; with no interslice gap. Additional 4-chamber or long-axis views were obtained as needed.

Endocardial borders were outlined on end-diastolic and end-systolic short-axis cine images with dedicated software (Argus). Volumes and LV ejection fraction (LVEF) were derived by summation of endocardial contours.

Analysis of magnetic resonance images

The processed and enhanced hard copy images were analyzed side-by-side by 2 radiologists and 1 cardiologist with expertise in contrast-enhanced CMRI, blinded to all information, including the date of the investigation and patient's name. The myocardium was studied using the17-segment model (19). The extent of delayed-enhanced tissue within each segment was graded using a 5-point scale (20) scored as follows: 0 indicated no hyperenhancement; 1, hyperenhancement of 1-25% of the tissue; 2, hyperenhancement of 26-50% of the tissue; 3, hyperenhancement of 51-75% of the tissue; 4, hyperenhancement of 76-100% of the tissue. The CMR images were interpreted as abnormal when the readers independently noted the same abnormal delayed-enhancement presence, distribution and localization. A segmental perfusion defect was considered to be present when the signal intensity was attenuated in a myocardial region on first-pass perfusion CMR images >10 s after contrast-medium injection, compared with the enhancement of the normal myocardium. Myocardial hyperintensity in T2-weighted short T1 inversion recovery sequences was considered to be present when described independently by the experts. Pericarditis was deemed present when pericardial effusion and/or pericardial hyperenhancement on delayed-enhancement images and/or pericardial thickness ≥4 mm were seen. Interpretation differences among the experts were resolved by consensus.

Statistical analysis

All statistical analyses were performed using StatView software (Abacus Concept, Berkeley, CA). Among the patients with CMRI abnormalities, symptomatic patients were compared to asymptomatic patients. The number of involved segments, the mean myocardial delayed-enhancement score, and patients' LVEF were analyzed in each group using a nonparametric test (the Mann-Whitney U-test or Fisher's exact test, when appropriate). The mean $p<0.05$ was considered to be statistically significant.

Table I. Demographic and clinical characteristics of the 20 CSS patients investigated with CMRI*.

Patient	Age (yr) sex	CSS duration before CMRI (yr)	History of clinical CSS symptoms†	Manifestations at time of CMRI	Cardiovascular risk factors	Outcome	Treatment
1	51 F	<1	Sinusitis, mononeuritis multiplex, cardiac insufficiency, eosinophilia and vasculitis on NMB, pericarditis	QS, V1–V3, cardiac insufficiency wall-motion abnormalities on echocardiography	None	Relapse: asthma, eosinophilia	Steroids, CY, local treatment
2	36 F	7	Sinusitis, cardiac insufficiency, pericarditis, pulmonary infiltrates, eosinophilia in myocardial and pericardial biopsies	None	None	Complete remission	Steroids, CY
3	55 M	5	Gastritis, cardiac insufficiency, extravascular eosinophilia, pulmonary infiltrates	cardiac insufficiency	HT/high CH	relapse	Steroids, CY, local treatment for asthma
4	55 M	10	Sinusitis, purpura, mononeuritis multiplex, vasculitis and eosinophilia on NMB	None	HT/high CH	Complete remission	Steroids, CY
5	31 M	10	Sinusitis, central nervous system, angina pectoris, pulmonary infiltrates, myalgia, extravascular eosinophilia	wall-motion abnormalities on echocardiography	High CH	Complete remission; persistent hemiparesis	Steroids, CY, local treatment for asthma
6	59 F	<1	Myalgia, mononeuritis multiplex, sinusitis	None	None	Complete remission	Steroids
7	53 M	7	Sinusitis, mononeuritis multiplex, pulmonary infiltrates, purpura, extravascular eosinophilia	None	None	Complete remission	Steroids, CY, interferon
8	18 F	<1		Sinusitis, mononeuritis multiplex, purpura, myalgia	None	Complete remission	Steroids, local treatment for asthma
9	51 M	4	Sinusitis, mononeuritis multiplex, purpura	QS D3; VF	None	Complete remission	Steroids
10	67 M	4	Myalgias, diarrhea, cardiac insufficiency	LBBB/ cardiac insufficiency; wall-motion abnormalities on echocardiography	Smoking/HT	Relapse 1: asthma, eosinophilia; relapse 2: heart failure, eosinophilia	Steroids, CY, local treatment for asthma
11	49 M	4	Vasculitis and eosinophilia on NMB, purpura, mononeuritis multiplex, sinusitis	None	High CH	Complete remission	Steroids, CY then methotrexate; local treatment for asthma
12	56 M	4	Extravascular eosinophilia, sinusitis	None	HT/high CH	Complete remission	Steroids
13	56 F	<1		Vasculitis and eosinophilia on NMB, mononeuritis multiplex	HT	Relapse: mononeuritis multiplex	Steroids, CY
14	58 M	5	Purpura, mononeuritis multiplex, esophageal involvement, vasculitis and eosinophilia on NMB	None	Diabetes	Complete remission	Steroids, CY then azathioprine; local treatment for asthma
15	30 M	13	Sinusitis, purpura, cholecystitis, glomerulonephritis, mononeuritis multiplex, diarrhea	None	HT/high CH/FH	Complete remission; chronic renal failure (dialysis)	Steroids, CY then methotrexate; local treatment for asthma
16	53 M	5	Sinusitis, pulmonary infiltrates	RBBB, wall-motion abnormalities on echocardiography	Diabetes	Complete remission	Steroids; local treatment for asthma
17	73 M	1	Sinusitis, glomerulonephritis, myalgia, vasculitis on NMB	Aortic insufficiency, QS V1–V2	High CH	Complete remission	Steroids, CY, local treatment for asthma
18	71 M	<1	Pulmonary infiltrates, extravascular eosinophilia	None	HT/high CH/diabetes	Complete remission	Steroids, local treatment for asthma
19	34 F	3	Sinusitis, mononeuritis multiplex, pulmonary infiltrates, extravascular eosinophilia	None	None	Relapse: chest pain, mononeuritis multiplex	Steroids then CY
20	61 F	<1	Sinusitis, mononeuritis multiplex, cardiac insufficiency, pulmonary infiltrates, extravascular eosinophilia, myalgias	Sinusitis, mononeuritis multiplex, cardiac insufficiency, diffuse inverted T waves	None	Complete remission	Steroids, CY, local treatment for asthma

*CMRI: cardiac magnetic resonance imaging; CSS: Churg–Strauss syndrome; CY: cyclophosphamide; ECG: electrocardiogram; F: female; FH: family history of coronary artery disease; high CH: high cholesterol; HT: hypertension; LBBB: left bundle branch block; RBBB: right bundle branch block; NMB: neuromuscular biopsy.
†All but patient 13 were asthmatic.

Results

Patient characteristics

The demographic, clinical, biochemical and radiologic characteristics of the 14 men and 6 women included in the study are summarized in Tables I and II. Mean age (± standard deviation) was 50 ± 14 years and mean CSS duration at the time of CMRI was 4.5 ± 3.6 years. Cardiovascular risk factors were present in 12 patients. Nine (45%) patients had CSS-associated cardiac manifestations, including heart insufficiency in 6 and angina pectoris in 1. Two clinically asymptomatic patients had an abnormal ECG and/or echocardiogram: 1 had only ECG abnormalities and the other had both ECG and echocardiographic abnormalities. Coronary angiograms of 6 patients and exercise stress tests, obtained for 5 patients with suspected coronary artery disease (angina pectoris and/or cardiac insufficiency and cardiovascular risk factor and/or segmental wall motion abnormalities on echocardiogram) were normal. Six (30%) patients were ANCA-positive. BNP or NT-proBNP was elevated in 6 patients who experienced cardiac insufficiency. All 3 patients with high cardiac troponin I levels had markedly elevated BNP or NT-proBNP. Asymptomatic patients had normal myocardial involvement, and BNP/NT-proBNP and cardiac troponin I concentrations within their normal ranges.

Cardiac magnetic resonance imaging

CMRI results are summarized in Table III. Delayed-enhancement lesions were seen in 13 patients, including the 9/9 patients with cardiac manifestations, and in 4/11 of the asymptomatic patients. Patients with myocardial delayed-enhancement on CMR images did not have more cardiovascular risk factors than patients without CMR abnormalities (8/13 *vs*. 4/7 patients, *p*=non-significant (NS)). The presence of cardiovascular risk factor(s) was not predictive of CMRI abnormality.

Most enhanced lesions were located in the anterior or lateral wall (segments 1, 7, 8 and 12) and were centromyocardial in 6 patients and subepicardial in 4, with nodular or diffuse patchy distributions. In 3 other patients, delayed enhancement was subendocardial, consistent with endomyocardial fibrosis in 1 and with segmental vascular distribution in 2. It should be noted that the coronary angiograms of these last 2 patients were normal.

T2-hyperintensity was associated with delayed enhancement within the same myocardial territory in 6 patients (4 symptomatic and 2 asymptomatic patients). Perfusion defects were also found in first-pass sequences of 7 patients (5 symptomatic and 2 asymptomatic patients). Without an endomyocardial biopsy, the significance of these abnormalities remains unclear.

LV dysfunction (defined as LVEF <45%) was observed in 5 patients (all were symptomatic). The mean LVEF evaluated with CMRI was 51.6±13.3%. Patients with CSS-associated myocardial involvement and CMRI abnormalities had more involved myocardial

Table II. Biochemical and radiologic characteristics of the 20 CSS patients investigated with CMRI*.

Patient	Eosinophils/ml at onset/time of CMRI	ANCA	BNP at time of CMRI†	Troponin I at time of CMRI†	Echocardiography findings	Coronary angiogram	Abnormal CMRI
1	10,000/510	None	BNP 234	0.05	Septal and lateral hypokinesis	ND	Yes
2	19,000/780	None	NT 606	<0.04	Normal	Normal	Yes
3	6,625/490	None	NT 143	<0.04	Normal	Normal	Yes
4	9,000/354	Anti-MPO+	BNP 11	<0.04	Normal	NS ECG	Yes
5	8,000/588	None	BNP 19.1	<0.04	Anterior hypokinesis	Normal	Yes
6	1081/0	Anti-MPO+	BNP 3.7	<0.04	Normal	ND	Yes
7	7,440/600	None	NT 16	<0.04	Normal	Normal	No
8	6,500/150	None	NT 64	<0.04	Normal	ND	No
9	2,477/393	Anti MPO+	ND	ND	Normal	ND	Yes
10	12,500/510	None	BNP 343	0.11	Dilated cardiomyopathy	Normal	Yes
11	1,794/520	None	NT 25	<0.04	Normal	ND	Yes
12	2,000/450	None	ND	ND	Normal	NS ECG	Yes
13	2,424/9	Anti-MPO+	NT <10	<0.04	Normal	ND	No
14	1,500/170	None	NT 54	<0.04	Normal	ND	No
15	6,000/260	Anti MPO+	BNP 48	<0.04	Normal	NS ECG	No
16	1,590/270	None	BNP 3.4	<0.04	Apicoseptal hypokinesis	NS ECG	Yes
17	1,180/190	Anti-MPO+	NT 3011	0.04	Aortic insufficiency, global hypokinesia	Normal	Yes
18	5,470/756	None	NT 7	<0.04	Normal	ND	No
19	4,000/220	None	NT 50	<0.04	Normal	NS ECG	No
20	8,000/136	None	NT 20,761	0.3	Endomyocardial fibrosis	ND	Yes

*ANCA: antineutrophil cytoplasm antibodies; BNP/NT-proBNP: brain natriuretic peptide/N-terminal-proBNP; CMRI: cardiac magnetic resonance imaging; CSS: Churg-Strauss syndrome; MPO: myeloperoxidase; NCA: normal coronary angiogram; ND: not done; NS ECG: negative stress ECG.
†Normal values: troponin I <0.15 ng/ml; BNP <60 ng/l; NT-pro BNP <300 pg/ml.

Table III. CMRI observations in 20 patients with Churg-Strauss syndrome.

Patient	Delayed-enhancement localization (17-segment model)	Delayed-enhancement localization (myocardial wall)	Transmural delayed-enhancement score	Delayed-enhancement pattern	LVEF (%)	T2 hyperintensity
1	1,2,8,7	Subepicardial	12	Nodular/patchy	31	Yes
2	12,8	Subepicardial	5	Nodular/patchy	45	No
3	1,7,8,12	Centromyocardial	9	Nodular/patchy	48	Yes
4	14,15	Centromyocardial	3	Nodular/patchy	60	No
5	1,7,6,12,15,16	Subendocardial*	14	Bandlike	45	No
6	5	Centromyocardial	2	Nodular/patchy	52	Yes
7	–	–	–	-	59	No
8	–	–	–	-	68	No
9	10,12,8	Subepicardial	7	Nodular/patchy	60	Yes
10	3,4,8,9,10,14,15	Centromyocardial	19	Nodular/patchy	17	No
11	1,5,4,7	Centromyocardial	4	Nodular/patchy	49	No
12	3,9	Centromyocardial	6	Nodular/patchy	65	Yes
13	–	–	–	–	65	No
14	–	–	–	–	58	No
15	–	–	–	–	61	No
16	3	Subepicardial	3	Nodular/patchy	–	No
17	5,11,1,7	Subendocardial*	9	Bandlike	38	No
18	–	–	–	–	68	No
19	–	–	–	–	50	No
20	13,14,16,17	Subendocardial†	7	Bandlike	52	Yes

*Two patients with subendocardial DE had normal coronary angiographies. †Another patient with subendocardial DE had typical endomyocardial fibrosis. LVEF: left ventricular ejection fraction.

segments (3.8 *vs*. 2.2, *p*=NS), a higher mean transmyocardial delayed-enhancement score (9.4 *vs*. 3.7, *p*=0.01) and a lower mean LVEF (42% *vs*. 59%, *p*=0.001) than asymptomatic patients with CMRI abnormalities.

CMRI detected pericarditis in 10 (50%) patients, associated with myocardial delayed enhancement in 7 and isolated in the other 3. Echocardiography had visualized pericarditis in only 7 patients (no. 1, 2, 6, 13-15, 20). So, CMRI diagnosed pericarditis in 3 more patients (no. 5, 9, 10).

Six patients had LV echographic abnormalities: segmental or global hypokinesis in patients 1, 5, 10, 16 and 17 and endomyocardial fibrosis in patient 20. All of them had anomalies on CMR images.

Seven patients (no. 2, 3, 4, 6, 9, 11 and 12) with normal echocardiograms had myocardial delayed enhancement on CMR images. Compared to echocardiography, CMRI diagnosed cardiac involvement in CSS patients in 7 more patients.

Among the 6 ANCA-positive patients, 2 had symptomatic cardiac involvement and CMRI abnormalities, 2 were asymptomatic and had CMRI abnormalities, and 2 were asymptomatic and had normal CMR imaging. Symptomatic patients were not more frequently ANCA-negative than asymptomatic patients (respectively, 7/9 *vs*. 7/11; *p*=NS), as were patients with delayed-enhancement on CMR images (9/13 *vs*. 5/7; *p*=NS).

No asymptomatic patient with CMRI abnormalities (n=4) had elevated cardiac troponin I and/or BNP/NT-proBNP concentrations.

Outcome

Among the 20 patients included in this study, 5 (25%) experienced a CSS relapse during a mean follow-up of 2.2 years: 3 with known myocardial involvement (signs of heart disease and myocardial delayed enhancement) and 2 asymptomatic patients with normal CMRI at baseline evaluation. Patient 19, who was initially free of CSS-associated myocardial involvement, complained of chest pain at the time of the relapse, but ECG, echocardiography, cardiac troponin I and/or BNP/NT-proBNP levels and new CMRI were all normal; the chest pain was probably not of myocardial origin. Symptomatic patient 3, who had CMRI abnormalities at baseline, experienced a CSS relapse with no new cardiac symptoms but lesion progression was observed on new CMR images. The 3 others, patients 1, 10 and 13, had no new symptom(s) of cardiac disease. Among them, the 2 patients with known cardiac involvement still suffered from heart insufficiency and still had CMRI abnormalities on their second examinations but with no evidence of CMRI-detected lesion progression. Patients 4, 6, 11 and 12, whose cardiac involvement was limited to CMRI abnormalities, had no CSS relapse or appearance of cardiac symptoms during follow-up.

New CMR images were obtained for 8 patients. Among them, 6 had CMRI abnormalities and 2 had normal CMRI at baseline. Images remained unchanged for 5 of the 6 with CMRI abnormalities and for 1 of the 2 patients with normal CMRI. CMR lesion progression was seen in 1 patient with a history of cardiac insufficiency but asymptomatic at the time of CMRI. CMRI abnormalities

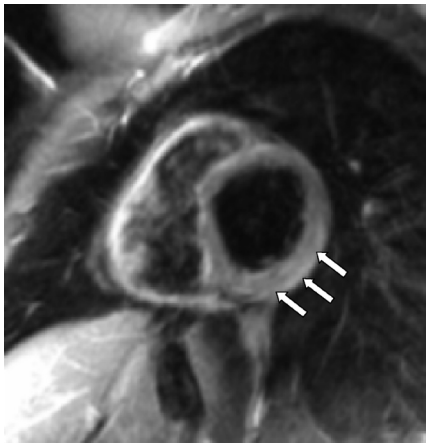

Fig. 1. Short-axis view. Two-dimensional inversion recovery, black blood fast spin-echo image (repetition time: 700 ms; echo time: 47 ms; inversion time: 170 ms) shows anterior myocardial T2-weighted hyperintensity consistent with edema.

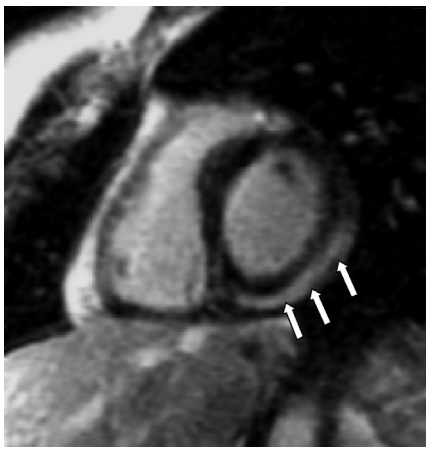

Fig. 3. Short axis view. Three-dimensional delayed-enhancement T1-weighted gradient-echo IR MR image (repetition time: 1.4 ms; echo time: 600 ms; inversion time: 250 ms) shows inferolateral myocardial delayed enhancement.

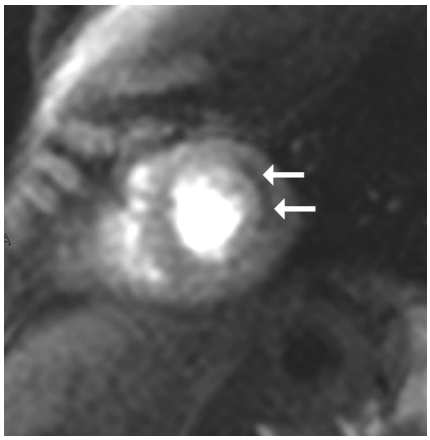

Fig. 2. Short axis view. First-pass 2-dimensional T1-weighted gradient-echo MR image (repetition time 175 ms; echo time: 1.01 ms) shows a defect in the anterolateral wall of the left ventricle.

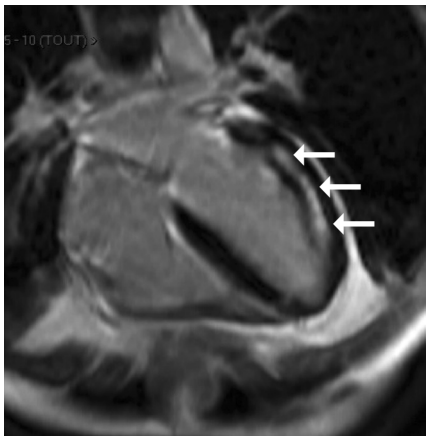

Fig. 4. Four-chamber view, three-dimensional delayed-enhancement T1-weighted gradient-echo IR MR image (repetition time: 1.4 ms; echo time: 600 ms; inversion time: 250 ms) shows lateral myocardial delayed enhancement.

appeared in 1 patient initially free of cardiac involvement without any evidence of CSS relapse or sign of cardiac involvement.

Discussion

Among our 20 CSS patients, the proportion with abnormal CMR images was higher than expected, based on their clinical manifestations of cardiac insufficiency. All patients with clinical manifestations of CSS-associated heart disease and/or ECG/echocardiography abnormalities had delayed enhancement, confirming the high sensitivity of this investigation to detect cardiac involvement in symptomatic patients. All patients with abnormal echocardiograms had CMRI-detected myocardial delayed enhancement. Seven patients with normal echocardiograms had CMRI abnormalities. CMRI seems to be more sensitive than echocardiogram for the assessment of cardiac involvement in CSS patients.

More importantly, 4 of the 13 asymptomatic patients had CMRI abnormalities and, in these patients, the evidence of CSS-associated cardiac involvement was limited to these imaging abnormalities. Among the patients with CMRI abnormalities, symptomatic patients had significantly lower mean LVEF and higher mean myocardial delayed-enhancement score than asymptomatic patients. Symptomatic patients seemed to have more extensive CMRI lesions than asymptomatic patients. However, cardiac symptoms may only occur when a sufficient part of the myocardium has been affected by the vasculitis and causes markedly decreased LVEF.

The frequency of CMRI abnormalities observed in our study agrees with the reported percentage of myocardial involvement found during autopsy examinations of CSS patients (1). CSS can cause myocardial inflammation and fibrosis, both of which have already been visualized with CMRI (21, 22). Notably, delayed enhancement alone did not help distinguish between fibrosis and inflammation. Myocardial delayed enhancement has been correlated with histologically proven fibrosis and active myocarditis (16).

Distinguishing between myocardial inflammation and fibrosis might be of great importance, since the former reflects active disease which could require therapy, unlike fibrosis, which reflects irreversible sequela. T2-weighted triple inversion recovery sequences, which can detect myocardial edema (23), may help make this distinction. On our T2-weighted sequences, we observed hyperintensities in association with delayed enhancement within the same myocardial territory in patients 1, 3, 6, 9, 12 and 20 (Fig. 1), 3 of whom had CSS durations <1 year. Without endomyocardial biopsies, we cannot confirm that these abnormalities represented areas of active myocardial inflammation. Perfusion defects were also identified in first-pass sequences (Fig. 2) in 8 patients. Because coronary angiograms were not available for all patients and pharmacological stress tests were precluded by CSS-associated asthma, the meaning of these abnormalities remains unclear and will need to be pursued in future studies.

In the majority of our patients, the delayed-enhancement distribution was subepicardial or centromyocardial (Figs. 3 and 4), consistent with the expected distribution of nonischemic cardiomyopathy, as defined by Mahrholdt *et al*. (24). In patients 5, 17 and 20, delayed enhancement was band-like

and subendocardial, consistent with the distribution expected with vascular disease. In patient 20, this distribution was attributed to endomyocardial fibrosis. However, the perfusion defects in the other 2 might have been due to ischemia caused by microvasculitis, because their coronary angiograms were normal and perfusion defects were present on their first-pass sequences in the delayed-enhancement territory. Smedema *et al*. (4) previously described myocardial ischemia attributed to microvasculitis observed on CMR images from a 53-year-old woman with CSS who complained of palpitations; CMRI detected a perfusion defect and myocardial delayed enhancement in the septal wall, while her coronary angiogram was normal.

Anti-myeloperoxidase ANCA are present in approximately 40% of CSS patients (10-12). Sinico *et al*. (11) and Sablé-Fourtassou *et al*. (12) found that cardiac involvement was significantly more frequent in ANCA-negative than ANCA-positive patients: 22.4% *vs*. 5.7%, respectively (p=0.04) (10). In this study, CMRI detected anomalies independently of ANCA status. Indeed, ANCA-negativity was not more common in symptomatic (cardiac symptom(s) and/or CMRI abnormality) than asymptomatic patients.

The long-term follow-up of asymptomatic patients in whom fibrosis or myocardial inflammation was detected by CMRI is, at present, unknown. Further investigations are needed to determine the meaning and evaluate the prognosis of CMRI abnormalities and to decide whether such imaging findings should induce therapeutic intervention, specific to CSS or cardiac disease. Our 4 patients, whose CSS-associated myocardial involvement was limited to CMRI abnormalities, did not suffer CSS relapses or develop symptomatic heart disease during a mean follow-up of 2.2 years, but that observation period is probably too short. At this time, careful monitoring of cardiac manifestations is recommended because some CSS patients have had late heart failure and succumbed to sudden death, even months or years after vasculitis recovery.

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