

Subendocardial Ischemia and Myocarditis in Systemic Lupus Erythematosus Detected by Cardiac Magnetic Resonance Imaging

To the Editor:

A 47-year-old woman with systemic lupus erythematosus (SLE) was referred for evaluation of persistent chest pain, characterized as pressure-like substernal pain, associated with shortness of breath and palpitations, worse with exertion, but also occurring at rest, not related to food or body positioning. Medications included hydroxychloroquine, candesartan, and intermittent methylprednisolone for SLE flares, most recently treated 4 months prior to the current office visit. Vital signs, physical examination, and echocardiogram were normal. Computed tomography angiography demonstrated normal coronary arteries without evidence of plaque or calcification. However, an adenosine stress cardiac magnetic resonance imaging (CMRI) perfusion study demonstrated nearly circumferential subendocardial hypoperfusion (Figures 1A, 1B) without evidence of abnormality on T2 or delayed enhancement (DE; Figure 2, A1 and A2) and with a calculated left ventricular ejection fraction (LVEF) of 70%. Selective left coronary

angiography, as part of the research protocol, demonstrated no obstructive coronary artery disease (CAD; Figure 3). Coronary reactivity testing showed an abnormal coronary flow reserve of 1.35 (normal > 2.5) in response to intracoronary adenosine, consistent with microvascular coronary dysfunction. Therapy with low-dose aspirin, statin, and carvedilol was initiated, with improvement in chest pain symptoms.

In connection with a microvascular coronary dysfunction research protocol, the patient underwent a second adenosine stress CMRI perfusion study 13 months after the initial CMRI and coincidentally at the time of an SLE flare. CMRI again showed the nearly circumferential subendocardial perfusion abnormalities (Figures 1C, 1D). There were also new patchy enhancement areas on T2 and DE scans consistent with myocarditis (Figure 2, B1 and B2). The calculated LVEF was slightly lower at 64%. The patient was clinically stable and troponin levels were not checked. Although not checked with regard to the timing of the scans, erythrocyte sedimentation rate and C-reactive protein throughout that year were consistently elevated, 40–48 mm/h (normal 0–15) and 1.5–2.3 mg/dl (normal < 0.8), respectively. She was treated with methylprednisolone and experienced relief of her SLE flare. A followup adenosine CMRI 8 months after

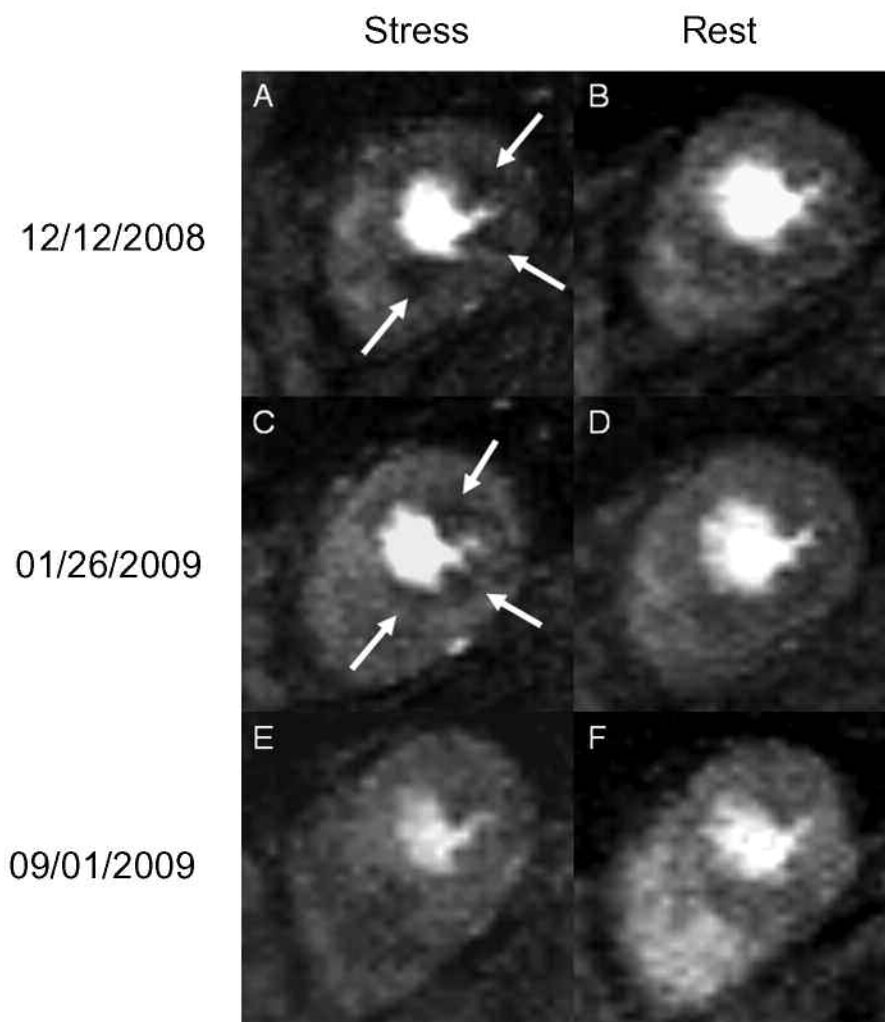


Figure 1. First-pass perfusion images through the short axis, 2-chamber views. The images show normal myocardial enhancement at rest (B, D, F) and the circumferential area of subendocardial hypoperfusion, marked by arrows during stress (A, C). Images A and B were taken prior to evaluation; C and D during an SLE flare; and E and F after medical management. Compared to previous scans, and following antiischemic therapy, the stress perfusion image (E) does not show any areas of hypoperfusion.

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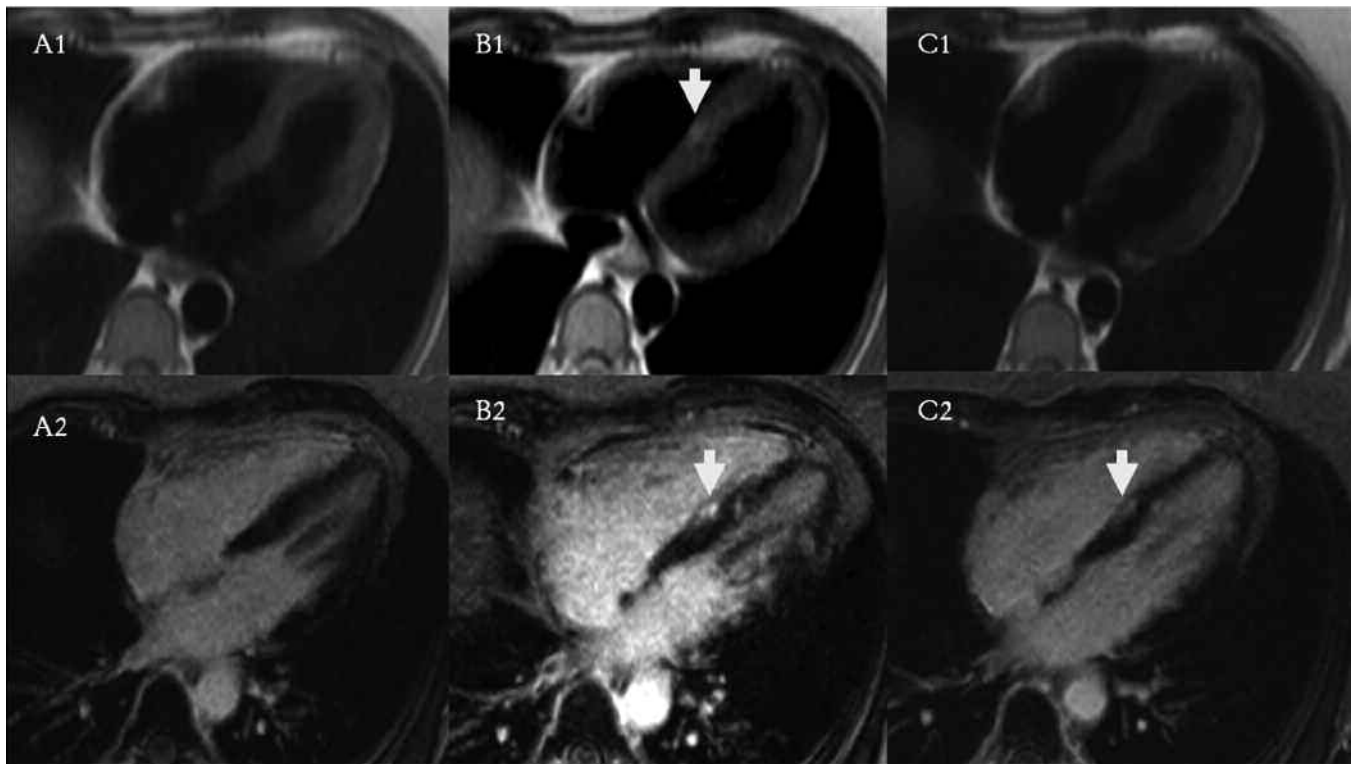


Figure 2. Delayed enhancement images, 4-chamber views. B2 demonstrates interventricular patchy enhancement (arrow) on cardiac MRI performed during an SLE flare and active chest pain. Appearance is typical for myocarditis and a new finding compared to the baseline scan A, with some residual involvement after resolution of the SLE flare and medical treatment (C2). The finding of myocarditis is supported by a patchy enhancement (arrow), consistent with myocardial edema and active inflammation on T2-weighted images without fat saturation. No active inflammation is noted on a followup scan (C1).

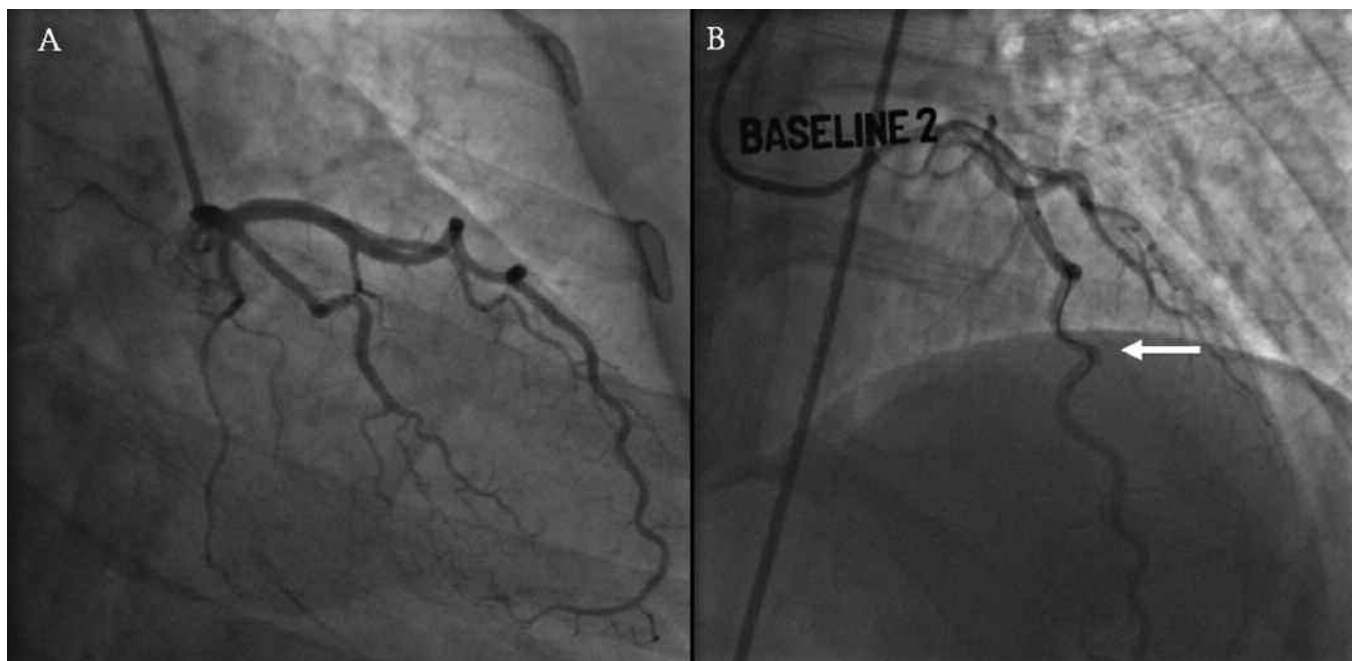


Figure 3. Selective left coronary angiography demonstrating normal left anterior descending (LAD) and left circumflex arteries and their branches (A). Coronary reactivity testing performed with the Volcano FloWire in the mid-LAD (arrow; B) demonstrated abnormal coronary flow reserve consistent with microvascular coronary dysfunction.

resolution of the flare revealed resolved subendocardial perfusion abnormalities (Figure 1, E and F), LVEF 68%, and improvement in patchy enhancement (Figure 2, C1 and C2).

Ischemic heart disease in patients with SLE, a leading cause of morbidity and mortality, has a complex pathogenesis that is incompletely understood^{1,2}. While pericarditis is the most commonly cited cardiac manifestation of SLE, other cardiac manifestations, such as myocarditis, also occur. Diagnosis of SLE myocarditis is challenging as it is typically detected only after clinically significant decreases in myocardial function are seen, and the gold standard for diagnosing myocarditis is endomyocardial biopsy. Advancements in CMRI techniques facilitate the noninvasive diagnosis of myocarditis³. Inversion recovery fast-gradient echo sequence, as used in this case, allows selective suppression of normal myocardial signal and thus maximizes contrast between normal and enhancing myocardium.

SLE myocarditis is an immune complex-mediated process. At the cellular level, the presence of inflammation leads to cardiomyocyte membrane rupture, which allows contrast agent to diffuse into the cells and results in contrast enhancement. The most frequent pattern observed is presence of patchy and small areas of myocardial hyperenhancement in both acute and chronic myocarditis, typically observed in the midwall and subepicardial myocardium⁴. The relatively small volume of cardiomyocytes involved and patchy distribution of cellular injury mean that DE observed in myocarditis may not be as bright as that seen in myocardial infarction⁵.

Patients with SLE often have recurrent chest pain that is typically attributed to pericarditis once a laboratory investigation for obstructive CAD is negative. Microvascular coronary dysfunction is prevalent in women with evidence of ischemia but without obstructive CAD, and has an adverse prognosis⁶. We recently described in a pilot study a 50% prevalence of abnormal adenosine stress myocardial perfusion by CMRI in the absence of obstructive CAD in 20 SLE patients with anginal chest pain⁷. Compared to controls, abnormal visual perfusion scores and myocardial perfusion reserve index (MPRI) were observed in patients with SLE; presence of SLE was a significant predictor of abnormal MPRI⁷. These findings are consistent with the hypothesis that anginal chest pain in patients with SLE who do not have obstructive CAD is due to myocardial ischemia, in turn likely due to microvascular coronary dysfunction.

CMRI can be a useful noninvasive tool for the evaluation of myocardial ischemia and myocarditis in patients with SLE. Our case further demonstrates that chest pain in patients with SLE, when not related to obstructive CAD or pericarditis, can alternatively be due to microvascular coronary dysfunction and/or myocarditis. Further research using CMRI in patients with SLE is warranted.

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Supported by contracts from the National Heart, Lung and Blood Institutes, nos. N01-HV-68161, N01-HV-68162, N01-HV-68163, N01-HV-68164, RO1-HL-073412-01, and grants U0164829, U01 HL649141, U01 HL649241. Grants from the Gustavus and Louis Pfeiffer Research Foundation, Danville, NJ; The Women's Guild of Cedars-Sinai Medical Center, Los Angeles, CA; The Ladies Hospital Aid Society of Western Pennsylvania, Pittsburgh, PA; QMED Inc., Laurence Harbor, NJ; the Edythe L. Broad Endowment, Cedars-Sinai Medical Center; and the Barbra Streisand Women's Cardiovascular Research and Education Program, Cedars-Sinai Medical Center.

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J Rheumatol 2012;39:2; doi:10.3899/jrheum.110812