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Massive necrotizing myocarditis in a young patient with idiopathic hypereosinophilic syndrome

IMAGING

CASE REPORT

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ABSTRACT

A 27-years-old female with multiple autoimmune disorders presented to our cardiology unit for acute chest pain and worsening dyspnoea. Admission blood tests revealed increased serum levels of high-sensitive cardiac troponin, eosinophilic count and C-reactive protein. Laboratory findings, low QRS voltages by ECG, mildly reduced left ventricular systolic function in the context of pseudohypertrophy, mild and diffuse late gadolinium enhancement associated with markedly increased native T1 and T2 mapping levels assessed by echocardiography and cardiovascular magnetic resonance imaging, raised the suspicion of massive eosinophilic myocarditis, subsequently confirmed by histological examination of endomyocardial biopsy. Prompt initiation of immunosuppressive treatment allowed swift regression of myocardial inflammation and full recovery of left ventricular systolic function within one month. After ruling-out clonal myeloid disorder, lymphocyte-variant and reactive hypereosinophilia, the young lady was eventually diagnosed with idiopathic hypereosinophilic syndrome. This case report turns the spotlight on the role and importance of advanced multi-modality cardiovascular imaging for raising clinical suspicion of acute eosinophilic myocarditis, guiding diagnostic work-up and monitoring response to treatment.

KEYWORDS

eosinophilic myocarditis, hypereosinophilic syndrome, echocardiography, cardiovascular magnetic resonance, endomyocardial biopsy

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A 27-year-old lady presented with acute chest pain and worsening dyspnoea. She was apyretic and hemodynamically stable. Cardiovascular and respiratory examinations were unremarkable. Laboratory testing revealed an increase of high-sensitive cardiac troponin I (hs-cTnI) concentration (1,435 pg/mL), eosinophilic count (1,600/μL) and C-reactive protein (CRP, 16 mg/L). She reported previous history of atopic dermatitis, alopecia universalis and genetic susceptibility to celiac disease, as she tested positive for haplotype HLA-DQ2 in the absence of anti-tissue transglutaminase and anti-gliadin antibodies. Moreover, she showed an inherited thrombotic predisposition owing to heterozygous mutation of both factor V (G1691A variant) and prothrombin (G20210A variant) genes. Family history was suggestive of susceptibility to autoimmune disorder, with her mother affected by type 1 diabetes and

psoriasis, and her brother by celiac disease. Given the clinical suspicion of myocarditis and the presence of frequent and complex premature ventricular contractions (PVCs), the patient was admitted to our cardiovascular intensive care unit. Transthoracic echocardiography documented mildly impaired left ventricular ejection fraction (LVEF, 52%) and reduced global longitudinal strain (GLS, -13%, mechanical dispersion [MD], 53 ms), pseudohypertrophy of the left ventricle (LV) (maximum wall thickness, MWT 14 mm), markedly increased LV filling pressures (average E/E′ 20) and mild circumferential pericardial effusion (Fig. 1A–C). Standard 12-lead ECG demonstrated sinus tachycardia, low QRS. voltages in limb leads and T-wave inversion in inferior leads (Fig. 1D). Cardiovascular magnetic resonance (CMR) imaging confirmed the presence of diffuse LV pseudohypertrophy and mildly impaired LV systolic function (Fig. 2A), revealed homogeneous signal hyperintensity by T2-weighted STIR (Fig. 2B), markedly increased T2 mapping (70 ms, Fig. 2C), native T1 mapping (1570 ms, Fig. 2D) and extracellular volume (ECV, 45%) in keeping with diffuse oedema, showed biventricular, diffuse, mild late gadolinium enhancement (LGE) (Fig. 2E) and ruled-out presence of

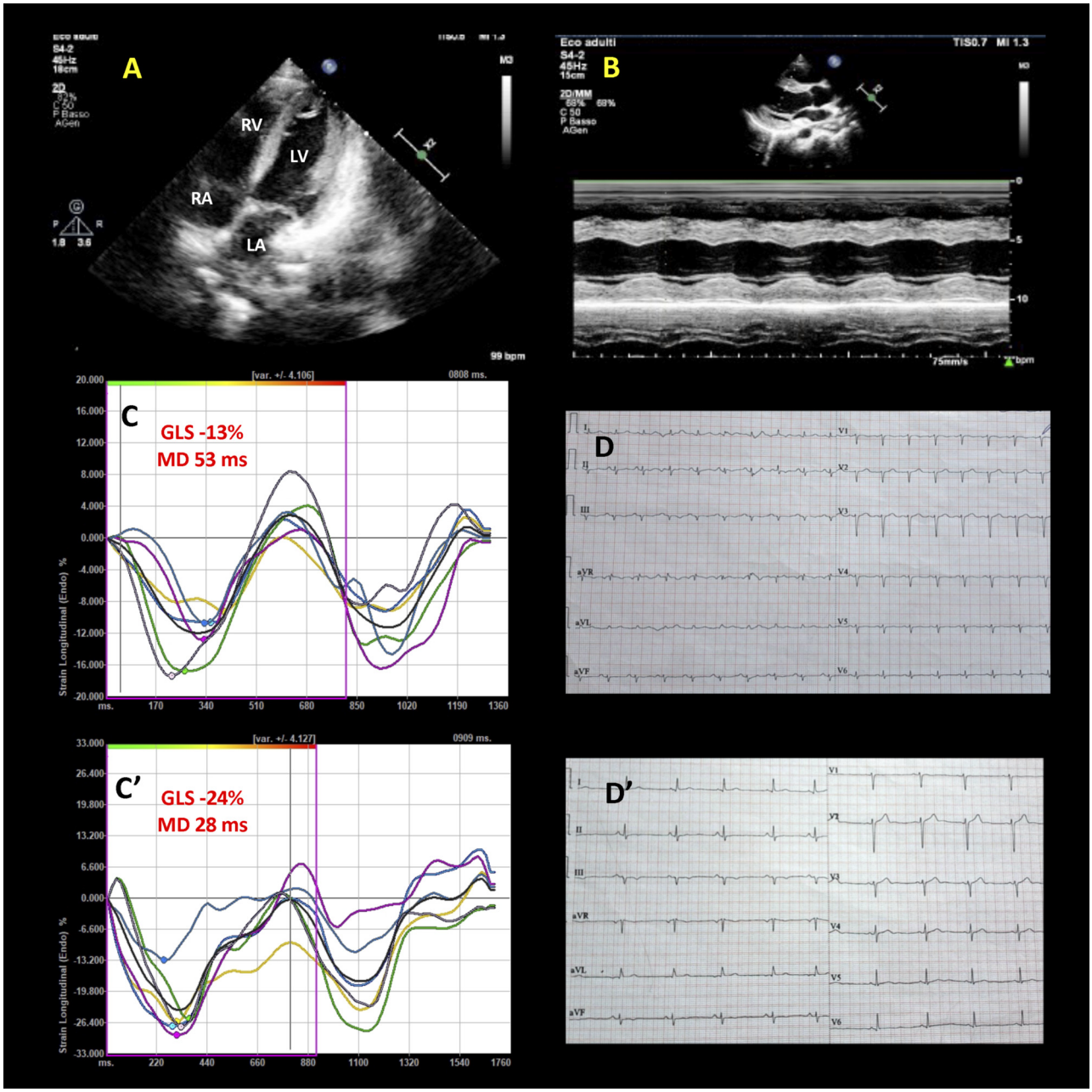

Fig. 1. Echocardiographic and electrocardiographic findings [A-B]. Transthoracic echocardiography: 2D 4-chamber view and M-mode imaging showing LV pseudohypertrophy and mildly impaired LV systolic function at presentation. [C-C'] Analysis of GLS and MD of longitudinal strain before and after immunosuppressive treatment. [D-D'] Standard 12-lead ECG before and after immunosuppressive treatment. GLS, global longitudinal strain; MD, mechanical dispersion; LA, left atrium; LV, left ventricular; RV, right ventricle

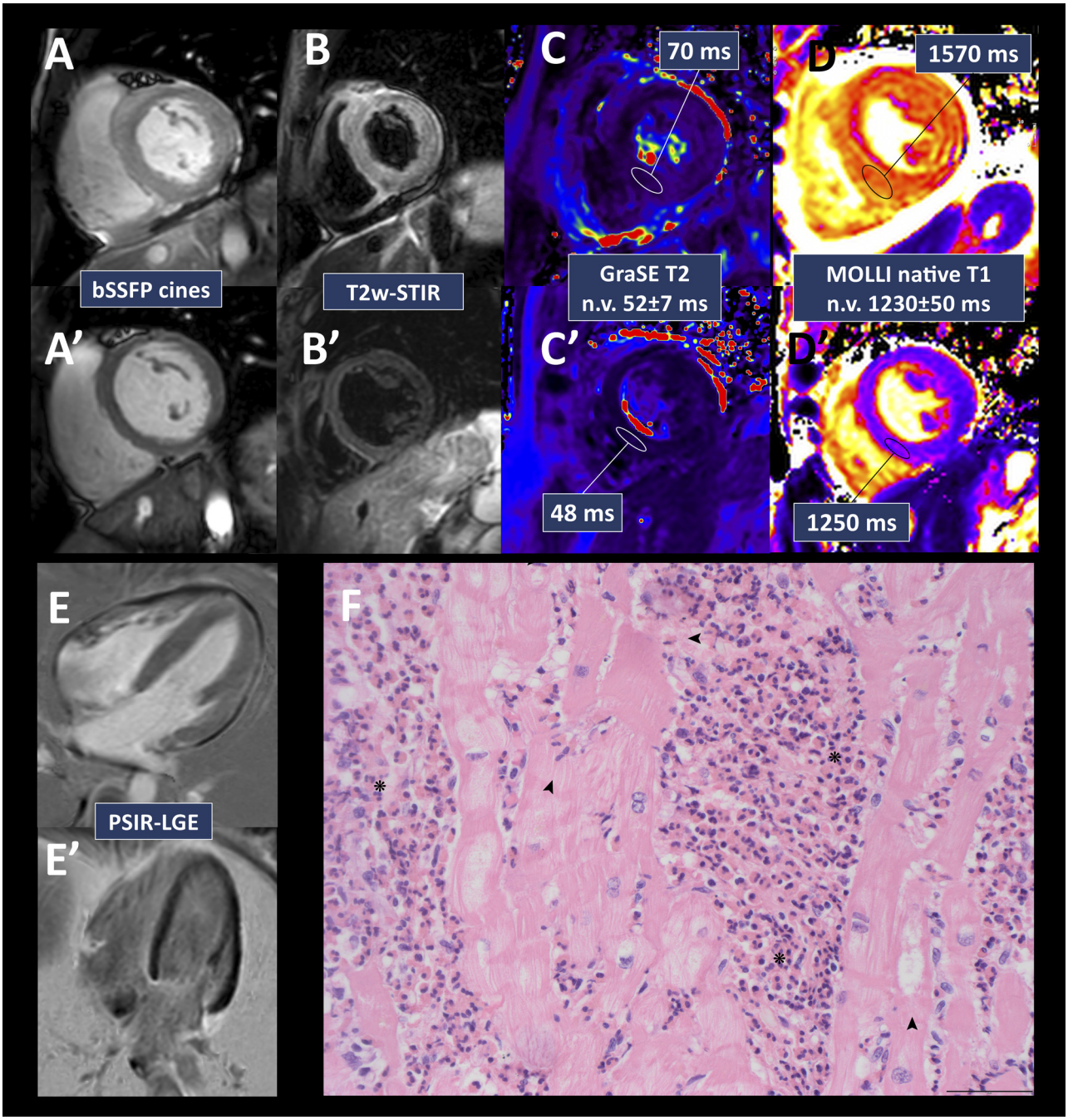

Fig. 2. Cardiac magnetic resonance imaging and endomyocardial biopsy. [A-A'] Balanced steady state free precession cine images before and after immunosuppressive treatment. [B-B'] T2-weighted short-tau inversion recovery (STIR) imaging before and after immunosuppressive treatment. [C-C'] Gradient spin echo (GraSE) T2 maps before and after immunosuppressive treatment. [D-D'] Modified Lock-Locker inversion recovery (MOLLI) native T1 maps before and after immunosuppressive treatment. [E-E'] Late gadolinium enhancement module before and after immunosuppressive treatment. [F] Histological examination revealing massive eosinophilic inflammatory infiltration (asterisk) and diffuse myocardial necrosis (arrowhead)

intracardiac thrombi by early and late enhancement sequences. Overall, clinical and CMR findings were in keeping with diffuse acute myocarditis with suspected extensive eosinophilic infiltrate underpinning the inflammatory process. Accordingly, endomyocardial biopsy (EMB) was immediately performed under echo guidance, and histological examination revealed massive eosinophilic inflammatory infiltration and diffuse myocardial necrosis, without evidence of replacement-type fibrosis (Fig. 2F, scale bar 50 µm). Treatment with prednisolone (1 mg/kg od), low-molecular-weight heparin at prophylactic dose and metoprolol (50 mg bid), was promptly initiated leading to rapid normalization of the eosinophilic count and abrupt reduction of PVCs, followed by progressive improvement of symptoms, LV systolic function and MWT (LVEF, 67%; GLS -24%; MWT 8 mm), reduction of LV mechanical

dyssynchrony (MD 28 ms) (Fig. 1C') and normalization of QRS voltages (Fig. 1D'). After one month, repeat CMR showed complete resolution of transient pseudohypertrophy (Fig. 2A'), oedema (Fig. 2B'–C'–D') and LGE (Fig. 2E'), also with normalization of ECV (27%). Subsequent diagnostic work-up, including bone marrow biopsy, serum protein electrophoresis, IgG subclasses, IgE, parasite testing and autoimmune serology, ruled-out clonal myeloid disorder, lymphocyte-variant hypereosinophilic syndrome and reactive eosinophilia, eventually leading to the final diagnosis of idiopathic hypereosinophilic syndrome. The patient had uneventful recovery, and she remained asymptomatic and recurrence-free at one-year follow-up.

Idiopathic hypereosinophilic syndrome is a rare but potentially serious cause of multi-organ damage, with frequent involvement of myocardial tissue [1]. EMB is the gold standard for the detection of cardiac involvement [2], and despite the suboptimal diagnostic yield, its invasiveness and possible complications, it does deliver unique diagnostic and prognostic significance [3]. This case clearly highlights the role and utility of advanced non-invasive cardiovascular imaging to raise clinical suspicion of acute eosinophilic myocarditis in the setting of peripheral eosinophilia, rule-out thrombotic complications, gauge the extent of myocardial inflammation, stratify the risk of arrhythmic events, guide invasive diagnostic procedures and monitor response to treatment [4–7].

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