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Case Report

CASE REPORT

Spontaneous coronary artery dissection in cardiac sarcoidosis

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Abstract

Cardiac sarcoidosis (CS) is increasingly recognized as a cause of diverse cardiac manifestations. Spontaneous coronary artery dissection (SCAD) has emerged as an important cause of acute coronary syndrome especially among young females. The prevalence of sarcoidosis in the causal spectrum of SCAD has not been described before but sarcoidosis is cited as a potential yet rare cause of SCAD. We aimed to examine the frequency and characteristics of SCAD in CS. Searching two prospective CS registries with 481 CS patients, we found only one case of manifest SCAD. She is a 61-year-old female previously diagnosed with endomyocardial biopsy confirmed CS. She presented with chest pain and elevated troponin. Coronary angiogram revealed two-vessel SCAD. Fluorodeoxyglucose positron emission tomography scan showed likely reactivation of CS. The patient was treated with dual antiplatelet therapy and immunosuppression. Repeat angiogram showed complete resolution of the coronary lesions.

INTRODUCTION

Spontaneous coronary artery dissection (SCAD) is defined as separation of the artery wall layers (intima, media and adventitia) without traumatic or iatrogenic cause [1]. Pathologically, SCAD can result from either an intramural hemorrhage in the arterial wall from ruptured vasa vasorum or intimal tear. SCAD is associated with arteriopathies that lead to inflammation, degeneration and stress in the arterial walls; fibromuscular dysplasia; systemic inflammatory diseases; connective tissue diseases; coronary spasm; pregnancy-hormonal related factors; etc [1, 2].

Typically presenting as an acute coronary syndrome (ACS), SCAD is often managed conservatively [1–5]. Smaller proportion of patients manifest with ventricular arrhythmias, sudden cardiac death or transmural ischemia in which case revascularization is needed [1–4]. In a recent study of 326 patients with ACS, SCAD accounted for 4% of ACS [6], but in younger females the prevalence of SCAD can be as high as 35% [1]. Although the detection rate of SCAD has increased in the last decade given increased awareness and improved endovascular imaging techniques, namely, intravascular ultrasound and optical coherence tomography [6], SCAD is likely still underdiagnosed due to misinterpreting intramural hematoma as spasm or atherosclerotic plaque during angiography and misdiagnosing young female's chest pain as non-cardiac [3].

Sarcoidosis is a systemic, granulomatous inflammatory disease, which can manifest with solely cardiac symptoms [7]. The four most common manifestations of cardiac sarcoidosis (CS) are heart block, ventricular arrhythmias, heart failure and sudden cardiac death. Granulomas can involve any part of the heart, including the coronary arteries [4, 5, 8–10]. In the literature,

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Table 1: CS registry patient characteristics

	Finnish CS Registry (MIDFIN)*	Ottawa CS Registry*
Age at diagnosis (mean ± SD, min–max), years	53 ± 12 (18–85)	55 ± 10 (29–74)
Gender, female N (%)	283 (71%)	31 (39%)
Presentation, N (%)		
Clinically manifest**	401	48
Heart block	193/401 (48%)	27/48 (56%)
Ventricular arrhythmia	47/401 (12%)	8/48 (17%)
LV dysfunction	57/401 (14%)	9/48 (19%)
Aborted SCD	15/401 (4%)	0
Fatal SCD	38/401 (9%)	0
Other	51/401 (13%)	4/48 (8%)
Clinically silent***	0	32
Follow-up time (median, range), months	43 (0.1–306)	48 (11–97)

CS = cardiac sarcoidosis, LV = left ventricle, SCD= sudden cardiac death, SCAD = spontaneous coronary artery dissection.

*Prospective clinical registries of CS patients in Finland and Ottawa region. MIDFIN also includes autopsy data on all patients with CS as a likely cause of death. All autopsies included examination of the coronary arteries. The Ottawa data is part of the Multi-center Canadian/Japanese Cardiac Sarcoidosis Cohort Study (CHASM-CS NCT01477359)

**Clinically manifest CS; patients who presented with cardiac symptoms and were diagnosed with CS based on cardiac imaging and cardiac or extra-cardiac histology.

***Clinically silent CS; patients who presented with extra-CS and were found asymptomatic cardiac involvement on imaging screening.

sarcoidosis is listed among the potential differential etiologies of SCAD, yet its frequency in the causal spectrum of SCAD has not been described before [1, 2]. Here we present a case of relapsing CS presenting with SCAD. Further, we report results from two prospective CS registries to demonstrate the rarity of SCAD in CS.

CASE REPORT

The baseline characteristics of the two CS registry populations are shown in Table 1. A total of 481 patients were followed for a median follow-up was 3.7 years with a total of ≈1800 years of patient follow-up. There was a single report of SCAD from the Ottawa registry and none from the Finnish registry, which included 38 patients with sudden cardiac death as the first manifestation of CS.

A 61-year-old female with no conventional CV risk factors initially presented with ventricular tachycardia and intermittent complete heart block and was diagnosed with cardiac and pulmonary sarcoidosis in July 2012. Cardiac magnetic resonance imaging, whole body fluorodeoxyglucose positron emission tomography (FDG-PET) and chest CT findings were consistent with active sarcoid inflammation in myocardium, lungs and mediastinal and hilar lymph nodes. Endomyocardial biopsy confirmed sarcoid granuloma in one of the six biopsy samples taken. Echocardiography showed low normal LVEF of 50% with mild inferior hypokinesia. Coronary angiography showed no significant stenoses in July 2012. The patient was treated with Prednisone 50 mg with tapering doses and Methotrexate 15 mg weekly started a few months later. Dual chamber ICD was implanted for secondary prevention and she subsequently had multiple appropriate ICD shocks. She also developed persistent atrial fibrillation in July 2014. FDG-PET scan in November 2014 showed no active CS (Fig. 1A). At that time, she was only on Prednisone 5 mg daily which was needed due to adrenal insufficiency diagnosed while on steroid taper in 2013. Echocardiography in February 2015 showed LVEF of 50–55%.

In November 2015, she presented with 7/10 retrosternal chest pain that persisted for an hour. Troponin I rose from 0.127 up to 2.206 (reference limit <0.045 ug/L) and CK peaked at 77. Chest CT showed no evidence of pulmonary embolism or aortic dissection. She underwent coronary angiography that revealed a 90% distal circumflex lesion (LCX) and 90% diffuse right posterior descending artery lesion that were consistent with SCAD. There was intramural dye hang-up in the distal LCX due to coronary wall tear (Fig. 2A). The patient was hemodynamically stable and no coronary procedures were done.

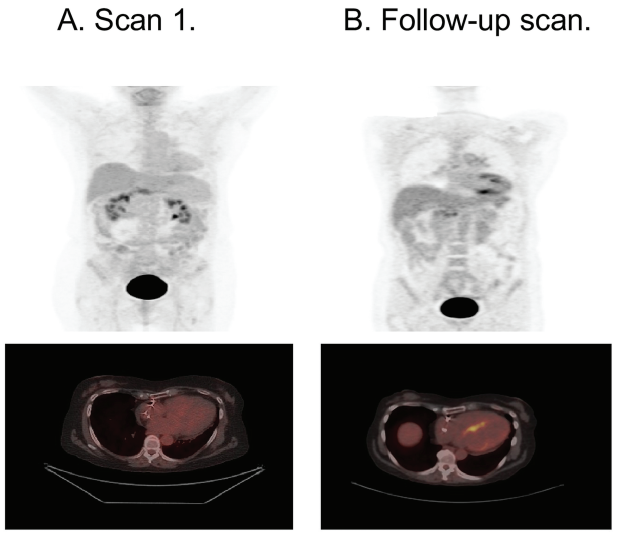

Figure 1: Whole body FDG-PET images (upper panels) and 4HC transaxial views of fused FDG-PET/CT thorax images (lower panels). Scan 1A upper panel: no cardiac or mediastinal FDG uptake. Scan 1A lower panel: no FDG uptake. Scan 1B upper panel: increased FDG uptake in mediastinal and hilar lymph nodes, basal to mid inferior wall and basal to mid anterior wall. Scan 1B lower panel: increased FDG uptake in the basal to mid inferior septum and lateral wall.

A FDG-PET scan (preceded by similar sarcoid diet preparation as in previous scans) showed increased FDG uptake in inferior and septal walls, being most prominent in the septum, not following the coronary territories and an inferior perfusion defect (Fig. 1B). The FDG-PET findings were best in keeping with recurrent active sarcoidosis and treated as such although

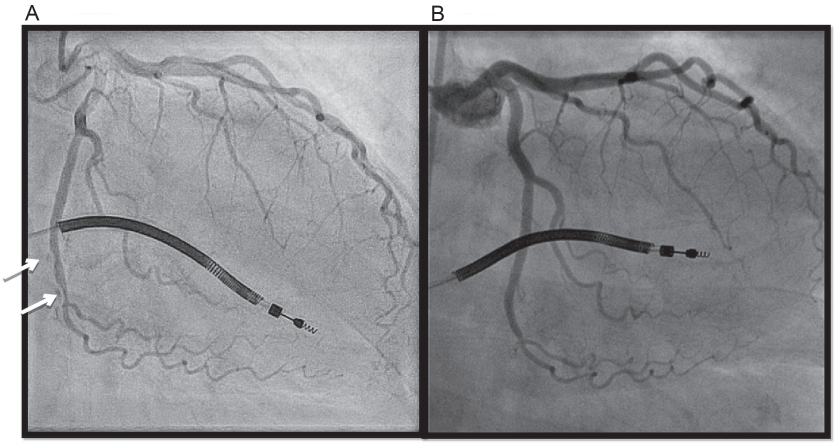

Figure 2: (**A**) Showing mural dye hung-up in the distal LCX due to mural hematoma. (**B**) Showing complete resolution of the LCX lesion.

less likely they could have reflected post myocardial infarction stunning/hibernation. Methotrexate was restarted, Prednisone dose was increased to 20 mg daily and Clopidogrel 75 mg and ASA 81 mg were initiated. Coronary angiography was repeated in April 2016 and showed complete resolution of the right coronary artery and LCX lesions (Fig. 2B). Kidney and peripheral vasculature was normal. The appearance of the coronaries and natural history were considered consistent with SCAD with spontaneous healing. Since the SCAD in November 2015, the patient has been stable with no arrhythmias, chest pain or heart failure exacerbations. Last echocardiography in November 2017 showed LVEF of 47% and TnI has been negative (<15 ng/L).

DISCUSSION

From two prospective CS registries involving 481 patients, we found only a single case of SCAD. We believe that this is the first report of CS presumably contributing to SCAD occurrence in a living patient. It demonstrates a two-vessel SCAD in a biopsy-confirmed CS patient, most likely as a presentation of relapsing disease. Although the likelihood of coincidence of the two rare conditions is minimal, it cannot be ruled out definitely. The SCAD diagnosis was based on angiogram findings. In the CS registries, patients did not routinely undergo angiography at initial diagnosis; however, theses were performed depending on particular presenting features, e.g. for cardiomyopathy, ventricular arrhythmias or chest pain. The patient in this report had a normal coronary angiogram at initial presentation. Further, in the post-mortem-diagnosed patients, the coroner studied the coronaries with no signs of SCAD in any of the 38 patients.

The two previous case reports described autopsy cases with histopathological proof of sarcoidosis affecting the coronary arteries [4, 5]. The first case was a postpartum female with multi-vessel chronic and acute SCAD leading to sudden death caused by arrhythmia [4]. The second case was an acute SCAD causing cardiac tamponade and death secondary to previously undiagnosed CS in a male [5].

The vascular involvement in CS can be complex. It is now apparent that CS entails tissue level changes beyond focal areas of granuloma and scar [11, 12]. Early radionuclide studies showed perfusion abnormalities with reverse distribution (i.e. the presence of a perfusion defect at rest that decreases or disappears under stress, contrary to what happens in ischemia) in systemic sarcoidosis patients, implying a microvascular dysfunction mechanism, hypothesized to be due to focal reversible vasoconstriction in arterioles adjacent to sarcoid granulomas [13]. On the other hand, a recent study demonstrated normal myocardial blood flow at rest but reduced hyperemic blood flow parameters locally in inflamed myocardium and in advanced disease even outside the inflamed regions [12]. Although somewhat contradictory at a mechanistic level, these findings suggest a diffuse impairment of coronary circulation in some patients with CS. In keeping with this, from histopathological studies, it is known that the granulomas can locally afflict the coronaries with granulomas found within atherosclerotic plaques [10], in the arterial media and in the adventitia, but also wider spread vascular inflammation similar to vasculitis has been reported [5, 8, 9]. Furthermore, one possible link between CS and SCAD is the collagenolytic and cytotoxic effect of eosinophils. In the two previous case reports, autopsy showed infiltrates of eosinophlis and mononuclear cells at the involved areas [4, 5]. Periadventitial eosinophilic infiltrates have also been observed in autopsies of peripartum women [14]. It is believed that these eosinophilic granules cause breakdown of the medial–adventitial layer via lytic substances, predisposing the artery to dissection. However, it is unclear whether the eosinophilic granules cause SCAD or are reactive to a nonspecific response to vascular injury in SCAD.

CS is increasingly recognized as a cause of diverse cardiac manifestations. Sarcoidosis has been previously introduced as one of the differential diagnoses of SCAD, yet its prevalence in the causal spectrum of SCAD has not been described before. This report shows that manifest SCAD in CS is rare (1/481 cases from two large CS registries). Physicians should be aware that CS can present with SCAD. Also importantly, our case showed that reactivation of active CS can present with SCAD.

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None.

CONFLICT OF INTEREST STATEMENT

No conflicts of interest.

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CONSENT

Patient consent obtained.

GUARANTOR

Riina Kandolin, University of Ottawa Heart Institute.

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