


# Extrapulmonary sarcoidosis involving only the heart and guts: a case report

Shun Sasaki<sup>1</sup>, Takaharu Hayashi <sup>1\*</sup>, Emi Tateishi<sup>2</sup>, and Yoshiharu Higuchi<sup>1</sup>

<sup>1</sup>Department of Cardiovascular Medicine, Osaka Police Hospital, 10-31 Kitayamacho, Tennoji-ku, Osaka, Osaka 543-0035, Japan; and <sup>2</sup>Department of Radiology, National Cerebral and Cardiovascular Center, 6-1 Kishibe-Shimmachi, Suita, Osaka 564-8565, Japan

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## Background

The respiratory tract is the most commonly affected organ system in sarcoidosis. Purely extrapulmonary sarcoidosis is rare. There have been no reports of extrapulmonary sarcoidosis with lesions only in the heart and guts.

## Case summary

A 19-year-old male was admitted for chest symptoms accompanied by remarkably elevated troponin T and creatinine kinase levels. Electrocardiogram (ECG) showed sinus rhythm with a right bundle branch block, broad ST segment elevation, and abnormal Q waves. Endoscopic biopsy revealed granuloma formation in the transverse colon. Based on multimodal imaging, we made a clinical diagnosis of extrapulmonary sarcoidosis involving only the heart and guts. One year of immunosuppressive therapy with prednisolone resolved the inflammation in the guts but not in the heart. He experienced runs of sustained ventricular tachycardia with loss of consciousness and was admitted to our hospital again. The addition of methotrexate markedly reduced cardiac accumulation of fluorodeoxyglucose. No life-threatening ventricular arrhythmias have been recorded afterwards.

## Discussion

This unusual case of cardiac sarcoidosis not only involved rare lesions only in the heart and guts but also presented with ST elevation on ECG. This case suggests that the gastrointestinal tract is a site of effective antigen capture outside of the respiratory tract that can affect the heart.

## Keywords

Cardiac sarcoidosis • Gut • Immunosuppressive therapy • Electrocardiogram • Case report

## ESC Curriculum

6.5 Cardiomyopathy • 2.1 Imaging modalities • 5.6 Ventricular arrhythmia

## Learning points

- The acute phase of cardiac sarcoidosis (CS) can involve ST segment elevation on electrocardiogram.
- CS can coexist with intestinal lesions in purely extrapulmonary sarcoidosis.
- The combination of a corticosteroid and methotrexate is effective when the effect of initial corticosteroid treatment for CS is insufficient.

## Introduction

Sarcoidosis is a systemic inflammatory disease defined histologically by the formation of non-caseating granulomas that can affect any organ.<sup>1</sup> The lung is the most frequently affected organ, in ~90% of patients and 8.3% of patients only have extrapulmonary manifestations.<sup>2</sup> Several diseases resemble sarcoidosis with respect to the formation of granulomas, such as tuberculosis, fungal infections, parasitic diseases, and

inflammatory bowel disease (IBD), especially Crohn's disease.<sup>3</sup> Of note, IBD is rarely complicated by myocarditis, but if it occurs, differentiation from cardiac sarcoidosis (CS) is difficult. Clinically recognizable gastrointestinal involvement in sarcoidosis is uncommon, occurring in 0.1–1.6% of patients.<sup>4</sup> There have been no reports of CS complications with gastrointestinal lesions and no lung, skin, or liver involvement. Here, we report a rare case of extrapulmonary sarcoidosis only involving lesions in the heart and guts, which are uncommon sites.

\* Corresponding author. Tel: +81 6 6771 6051, Email: [takaharu0866@yahoo.co.jp](mailto:takaharu0866@yahoo.co.jp)

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## Timeline

Admission (Day 1)	Left ventricular angiography revealed patchy areas of reduced wall motion. Endomyocardial biopsy showed no abnormal findings.
Day 2	Cardiac enzyme levels peaked: peak creatine kinase, 8110 U/L; peak creatine kinase muscle and brain, 803 U/L.
Day 5	Abdominal computed tomography showed para-aortic lymphadenopathy.
Day 7	Cardiac magnetic resonance imaging with contrast revealed myocardial late gadolinium enhancement.
Day 30	Colonoscopy revealed inflammatory changes in the transverse colon. Endoscopic biopsy revealed epithelioid granulomas.
Day 46	Fluorodeoxyglucose accumulated in the heart and guts.
Day 49	We started prednisone.
6 months after discharge	Follow-up colonoscopy revealed resolution of inflammatory changes in the guts.
12 months after	Fluorodeoxyglucose accumulation in the heart remained strong. The patient experienced sustained ventricular tachycardia. An implantable cardioverter-defibrillator implantation was performed. We added methotrexate.
17 months after	The addition of methotrexate remarkably decreased the accumulation of fluorodeoxyglucose in the heart.
20 months after	There is no episode of shock therapy by the implantable cardioverter-defibrillator.

## Case presentation

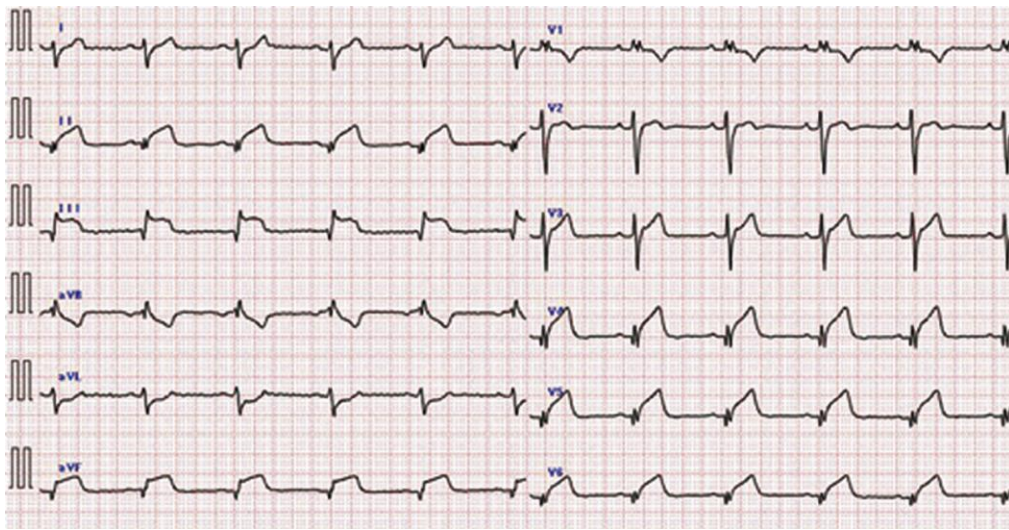
A19-year-old male with sudden chest discomfort was admitted to the hospital. He had no past medical history. He did not have bloody stools

**Table 1** Laboratory findings on admission

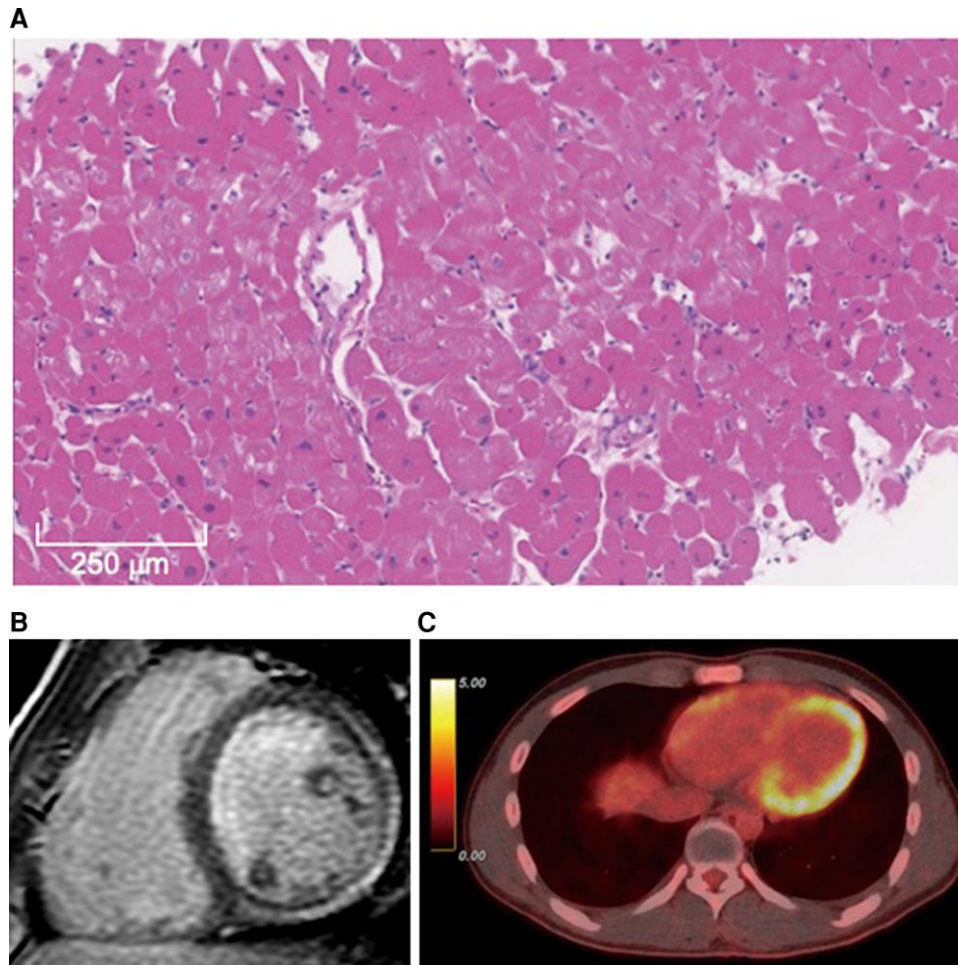
Laboratory data (on admission)		
WBC ( $\mu\text{L}$ )	3500–9800	11 600
RBC ( $10^9/\mu\text{L}$ )	4.3–5.7	4.47
Hb (g/dL)	13.5–17.6	13.1
PLT ( $10^3/\mu\text{L}$ )	131–362	335
Neut (%)	30.0–75.0	83.4
Eo (%)	0–10	0.3
CK (U/L)	30–200	6581
CK-MB (U/L)	25>	717
AST (U/L)	10–33	760
ALT (U/L)	6–35	110
LDH (U/L)	110–225	854
BUN (mg/dL)	8.4–20.4	14.2
Cr (mg/dL)	0.6–1.0	0.99
Ca (mg/dL)	8.8–10.4	9.5
CRP (mg/dL)	0.35>	0.72
Troponin T (ng/mL)	0.1>	>10
sIL2R (U/mL)	157–474	872
Lysozyme ( $\mu\text{g/mL}$ )	5.0–10.2	11.8
ACE (U/L)	7.0–25.0	15.9

First column represented each inspection item, second column were reference ranges and third column were each values.

WBC, white blood cells; RBC, red blood cells; Hb, haemoglobin; Neut, neutrophil; Eo, eosinophil; CK, creatine kinase; CK-MB, creatine kinase muscle and brain; AST, aspartate aminotransferase; ALT, alanine aminotransferase; LDH, lactate dehydrogenase; BUN, blood urea nitrogen; Cr, creatinine; Ca, calcium; CRP, C-reactive protein; sIL2R, soluble interleukin2 receptor; ACE, angiotensin-converting enzyme.



**Figure 1** Unusual electrocardiogram findings for cardiac sarcoidosis. Electrocardiogram on admission showed significant ST elevation in II, III, aVF, V5, and V6 accompanied by right bundle branch block.

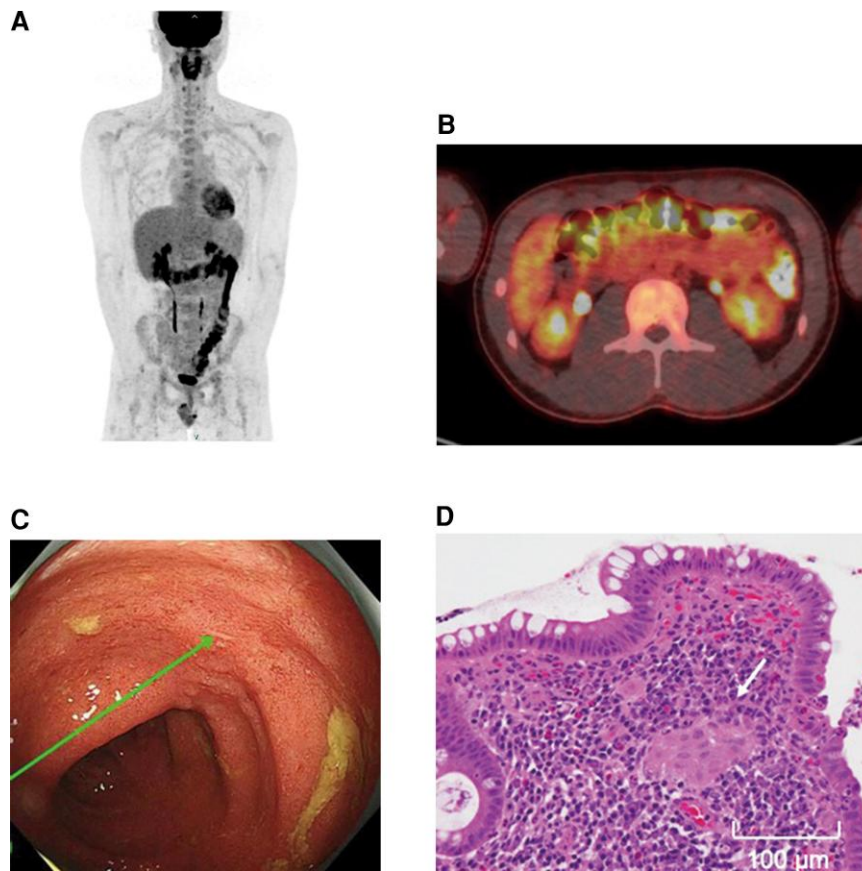


**Figure 2** Cardiac findings compatible with cardiac sarcoidosis. (A) Endomyocardial specimens from the right ventricular septum showed no invasion of lymphocytes and no necrosis. Scale bar represents 250 μm. (B) Cardiac magnetic resonance with contrast showed myocardial late gadolinium enhancement predominantly on the epicardial side of the posterolateral wall. (C) Positron emission tomography revealed focal fluorodeoxyglucose uptake in the posterolateral wall of the left ventricle.

or symptoms of upper respiratory infection before the onset of chest discomfort. He complained of general fatigue and shortness of breath upon exertion. Physiological examination findings were not noteworthy; no skin lesions were noted, blood pressure was 104/54 mmHg, heart rate was 67 beats per minute, and oxygen saturation was 99% on room air. Careful follow-up was performed without inotropic therapy. The initial electrocardiogram (ECG) showed sinus rhythm with a right bundle branch block, ST segment elevation in II, III, aVF, V4, V5, and V6, and abnormal Q waves in the same leads (Figure 1). Peripheral blood tests revealed remarkably elevated troponin T and creatinine kinase levels (Table 1). Echocardiography demonstrated moderate left ventricular hypertrophy accompanied by oedema and left ventricular ejection fraction (LVEF) of 42% with patchy areas of reduced wall motion. Coronary angiography did not reveal significant stenosis (see Supplementary material online, Files S1). Patchy areas of reduced wall motion were demonstrated by LV angiography (see Supplementary material online, Files S2-A and 2-B). Endomyocardial biopsy from the right ventricular septum showed no pathological findings that were consistent with myocarditis (Figure 2A). Subsequent tests reported high levels of soluble interleukin-2 receptor and lysozyme

(Table 1). Cardiac magnetic resonance (CMR) with contrast revealed myocardial late gadolinium enhancement (LGE) predominantly on the epicardial side of the posterolateral wall (Figure 2B). Fluorine-18-fluorodeoxyglucose ( $^{18}\text{F}$ -FDG) positron emission tomography (PET) revealed fluorodeoxyglucose accumulation in the same regions as LGE detected with CMR (Figure 2C) and in the transverse colon and sigmoid colon (Figures 3A and 3B), but there was no abnormal accumulation in the respiratory tracts. Faecal occult blood was positive, so colonoscopy was performed. Inflammatory changes were observed in the transverse colon (Figure 3C). Epithelioid granulomas were found in a biopsy specimen from the transverse colon (Figure 3D).

Based on these findings, we made a clinical diagnosis of active CS. We administered oral prednisolone (30 mg/day). The dose of prednisolone was decreased by 5 mg each month. At 6-month follow-up, LVEF (57%), and follow-up colonoscopy revealed significant resolution of inflammation. When PET was performed 1 year later, there was still strong accumulation of FDG in the heart (Figures 4A and 4B). After the examination, the patient experienced sudden runs of sustained ventricular tachycardia with loss of consciousness at rest. He was admitted to our hospital again. We performed implantable cardioverter-



**Figure 3** Granulomas in the transverse colon. (A, B) Fluorodeoxyglucose uptake was detected in the transverse to sigmoid colon. (C) Colonoscopy revealed inflammatory changes in the transverse colon. The green arrow shows the area biopsied. (D) Epithelioid granulomas were found in the biopsy tissue from the transverse colon. The white arrow shows a granuloma. Scale bar represents 100  $\mu\text{m}$ .

defibrillator placement. At 4 months after the addition of methotrexate (8 mg/week), there was markedly less cardiac accumulation of FDG (Figures 4A and 4B). Eight months have passed since the addition of methotrexate, there is no episode of heart failure admission nor shock therapy.

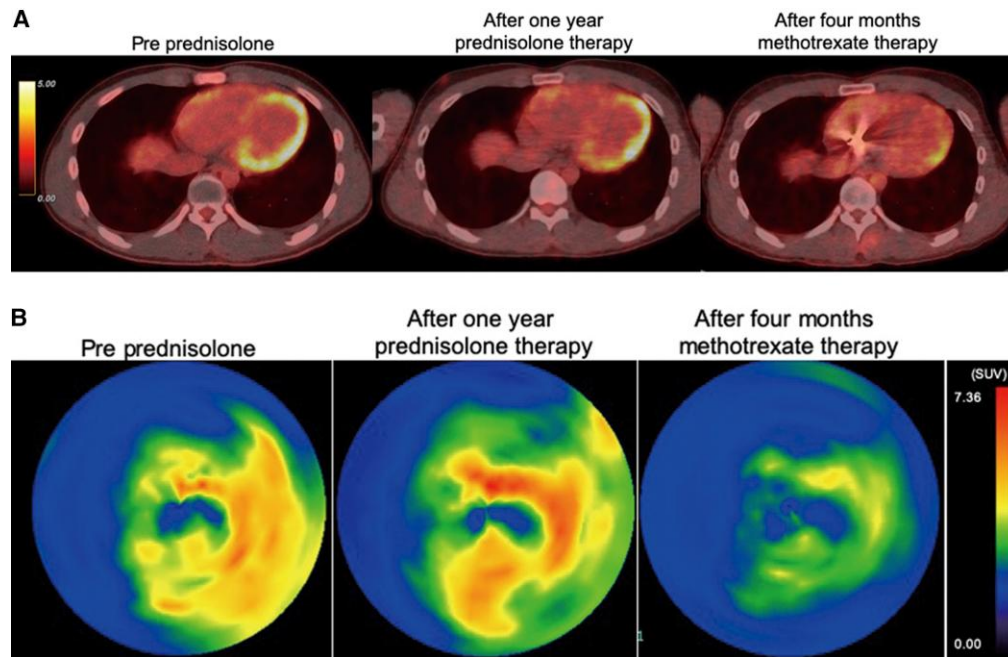
## Discussion

The diagnosis of CS is challenging. We could not detect granulomas with endomyocardial biopsy because we could not biopsy from the affected areas observed with CMR or PET. Based on endoscopic findings and the histological finding of non-caseating epithelioid granulomas in the transverse colon, intestinal lesions were diagnosed as sarcoidosis. ECG findings on admission were interesting in this case because CS is often accompanied by conduction abnormalities and ventricular arrhythmias.<sup>1</sup> Few reports have described ST segment elevation. It might reflect different action potential configurations within the LV wall which were made by inflammation on the epicardial side of the myocardium.<sup>5,6</sup> Although the ECG findings were unusual, LV angiography and laboratory examinations were helpful for making the diagnosis. In addition to the presence of granulomas, the Heart Rhythm Society criteria were met: (i) abnormal uptake on  $^{18}\text{F}$ -FDG and (ii) LGE on CMR. After 1 year of prednisolone, life-threatening

ventricular tachycardia, which is a major criterion, occurred, strengthening the support for the diagnosis of CS.<sup>7</sup> The addition of methotrexate is effective when initial corticosteroid treatment for CS is insufficient.<sup>8</sup>

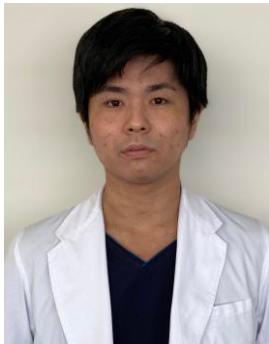
There are several reports of myocarditis associated with Crohn's disease. The onset of myocarditis reportedly occurs during the course of Crohn's disease.<sup>9</sup> Furthermore, endoscopy did not show longitudinal ulcers, a cobblestone appearance, or discontinuous lesions; there were few findings characteristic of Crohn's disease. A life-threatening arrhythmia was observed after 1 year of prednisolone treatment, which is consistent with sarcoidosis.

The clinical course of sarcoidosis is more diverse than previously thought. Although the immunopathogenesis of sarcoidosis is currently unknown, most believe that it is an antigen-driven disease.<sup>10</sup> In extrapulmonary sarcoidosis, the skin is the most common organ involved, found in nearly one-half of patients.<sup>2</sup> The low prevalence of gastrointestinal involvement seems somewhat strange because the gastrointestinal tract is frequently exposed to many antigens.<sup>4</sup> This low prevalence might be due to insufficient scrutiny because of poorly described abdominal symptoms. Although sarcoidosis with gastrointestinal involvement is rare, this case suggests that the gastrointestinal tract can be an effective site of antigen capture outside of the respiratory tract. The details of the relationships between the heart and gastrointestinal tract are not well known, but this case implies an immunological link between them.



**Figure 4** Sustained uptake of fluorodeoxyglucose in the chronic phase, which decreased with methotrexate. (A) Left panel: fusion computed tomography before the start of prednisolone showing strong accumulation of fluorodeoxyglucose in the heart. Centre panel: accumulation of fluorodeoxyglucose 1 year later, with little improvement. Right panel: the addition of methotrexate markedly reduced cardiac accumulation of fluorodeoxyglucose. (B) Comparison of chronic phase uptake during fluorodeoxyglucose based on standard uptake values before treatment (left), prior to (centre) and after (right) the addition of methotrexate.

## Lead author biography



Shun Sasaki is a Medical doctor at Osaka Police Hospital in Japan. Dr. Sasaki graduated from Tohoku University in 2016.

## Supplementary material

Supplementary material is available at *European Heart Journal – Case Reports* online.

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**Slide sets:** A fully edited slide set detailing this case and suitable for local presentation is available online as [Supplementary data](#).

**Consent:** The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

**Conflict of interest:** None declared.

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