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CASE REPORT
Arrhythmias/electrophysiology

Intermittent complete atrioventricular block in a 20-year-old woman with cardiac sarcoidosis: a case report

Innu Park [1]*, Elvin Atug[2], Boris A. Hoffmann[1], and Britta U. Goldmann[3]

[1]Department of Cardiology, Asklepios Clinic Hamburg-Harburg, Eissendorfer Pferdeweg 52, 21075 Hamburg, Germany; [2]Department of Pulmonology, Asklepios Clinic Hamburg-Harburg, Eissendorfer Pferdeweg 52, 21075 Hamburg, Germany; and [3]Department of Cardiology, Hospital St. Adolf-Stift, Hamburger Str. 41, 21465 Reinbek, Germany

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Background Atrioventricular conduction disturbance may rarely be caused by cardiac involvement of sarcoidosis.

Case summary A 20-year-old Caucasian female with exertional dyspnoea was admitted to the hospital. Electrocardiogram revealed intermittent complete atrioventricular block with ventricular escape rhythm. Laboratory findings indicated no obvious cause for the complete heart block, and echocardiography showed no abnormalities with normal systolic left ventricular function. However, in gadolinium-enhanced cardiovascular magnetic resonance imaging, a mass at the basal septum with high intensity of T2-weighted signal was found, and 18-fluorodeoxyglucose positron emission tomography revealed severe enhancement in this area and in the mediastinal lymph nodes. The diagnosis of cardiac sarcoidosis was established by the detection of non-caseating epithelioid granulomas in the endobronchial lymph node biopsy. Corticosteroid therapy with oral administration of 30 mg prednisolone was initiated, and complete recovery of atrioventricular block was observed within several weeks, obviating the need for permanent pacemaker implantation.

Discussion Cardiac sarcoidosis can cause complete atrioventricular block and should always be considered, especially in younger patients. Early diagnosis and initiation of corticosteroid therapy may lead to complete recovery of conduction system without the need for permanent pacemaker implantation.

Keywords Complete atrioventricular block • Sarcoidosis • Cardiac pacing • Case report

ESC curriculum 5.7 Bradycardia • 5.9 Pacemakers • 2.3 Cardiac magnetic resonance

Learning points

- Cardiac sarcoidosis is a rare cause of complete atrioventricular block.
- Cardiac imaging (^{67}Ga-citrate scintigraphy or ^{18}F-fluorodeoxyglucose positron emission tomography or gadolinium-enhanced magnetic resonance imaging) plays an important role in diagnosis.
- Early initiation of immunosuppressive therapy may lead to complete recovery of the conduction abnormalities without the need for permanent pacemaker implantation.

* Corresponding author. Tel.: (+49) 40 1818 86 2215, Fax: (+49) 40 1818 86 2431, Email: parkinnu@gmail.com
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Introduction

Complete atrioventricular block can have one of several causes. Cardiac involvement of sarcoidosis may be a rare reason for conduction disorders.[1] In this report, we present a case of clinically isolated cardiac sarcoidosis (CS) with intermittent complete atrioventricular block and intracardiac mass on cardiac magnetic resonance imaging (MRI).

Timeline

Day 1	Presentation in the emergency room with complete atrioventricular block. No obvious cause. Transfer to intermediate care unit. Antibiotic therapy with Ceftriaxone.
Day 4	Changing conduction properties: atrioventricular (AV) block II° to III°.
Day 5	Negative Borrelia titres Immunoglobulin M (IgM)/ Immunoglobulin G (IgG).
Day 7	Intermittent AV block II° to III° in Holter-electrocardiogram (ECG).
Day 11	Cardiac magnetic resonance imaging (MRI) shows a cardiac mass in the basal septum.
Day 16	Positron emission tomography/computed tomography reveals fluorodeoxyglucose accumulation in the basal septum of the heart and two mediastinal lymph nodes.
Day 17	Initiation of corticosteroid therapy (prednisolone 30 mg p.o. once daily).
Day 24	Discharge with AV block I° (PQ interval 240 ms) and right bundle branch block.
Follow-up 3 and 6 months after hospitalization	PQ interval 160 ms. Holter-ECG without relevant AV-conduction disorders. Patient completely asymptomatic.
Follow-up 9 months after hospitalization	Partial remission of pathology in cardiac MRI. Holter-ECG without relevant AV-conduction disorders. Patient completely asymptomatic.

Case presentation

A 20-year-old Caucasian female presented to her primary care physician with exertional dyspnoea and recurrent dizziness. In a 12-lead electrocardiogram (ECG), bradycardia due to complete atrioventricular (AV) block was diagnosed, and she was referred to our hospital.

On admission to the emergency department, the patient was asymptomatic at rest. The initial ECG confirmed the diagnosis of third-degree AV block with a ventricular escape rhythm of 34 beats per minute (*Figure 1A*). On physical examination, the patient appeared calm, had a body temperature of 37.3°C, had a blood pressure of 135/80 mmHg, had a respiratory rate of 15 per minute, and had an oxygen saturation of 100%. There was no evidence of erythema nodosum, and in a thorough external examination, no peripheral lymphadenopathy was found. Thoracic and cardiac auscultation was unremarkable as was the abdominal examination. No signs of peripheral oedema or peripheral vascular disease were found. There was no known cardiac disease and no family history of cardiac arrhythmias. Transthoracic echocardiography showed an estimated left ventricular ejection fraction (LVEF) of 60%, mild mitral and tricuspid valve regurgitation, no regional wall motion abnormalities, and no thickening or thinning of the left ventricular wall. Blood counts, cardiac enzymes, and inflammatory markers were all within the normal range, and electrolytes had minor abnormalities with sodium levels of 134 mmol/L (normal range: 135–145 mmol/L) and potassium levels of 4.70 mmol/L (normal range: 3.40–4.50 mmol/L) on admission and were within the normal range on further testing. Renal, liver, and thyroid function tests were within normal ranges. The polymerase chain reaction (PCR) testing for severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) was negative. Although there was no known recent tick bite and no dermal signs of Lyme disease, empiric antibiotic therapy with intravenous ceftriaxone (2 g once daily) was initiated on admission, and the patient was transferred to the intermediate care unit. Serologic results for Lyme disease were negative, as were results for multiple viruses as possible causative agents. Antibiotic therapy with ceftriaxone was therefore discontinued 2 weeks after admission. On further examination, laboratory results detected no abnormalities of serum angiotensin converting enzyme levels (26 U/L, normal range: 20–70 U/L), calcium levels (2.40 mmol/L, normal range: 2.15–2.58 mmol/L), and soluble interleukin-2 receptors (303 kU/L, normal range: 158–623 kU/L). In abdominal sonography, no abnormalities of liver or spleen and no suspicious lymph nodes were found. Duplex ultrasonography of bilateral carotid arteries displayed no signs of vasculitis, intima-media thickness was within normal range, and flow was unremarkable. During further ECG monitoring, there was frequent alternation between first-degree AV block, second-degree AV block (Mobitz I type), second-degree AV block with 2:1 conduction, and complete AV block. After benefit-risk assessment, no temporary (transcutaneous, transvenous) pacing or administration of isoprenaline was required because of haemodynamical stability and asymptomatic patient on resting. After 1 week, there was still no recurrence of ECG findings; a Holter ECG recorded over 24 h demonstrated intermittent complete AV block with asystole pauses of up to 6600 ms during the nighttime.

A cardiac MRI showed late gadolinium enhancement (LGE) in the basal septal wall (*Figure 2A*), but neither MRI nor chest radiograph demonstrated lymphadenopathy. A subsequent ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography (PET) scan exposed strong tracer accumulation at the basal septal wall (*Figure 3A*) with accumulation in a small number of mediastinal lymph nodes (*Figure 3B*). Endobronchial sonography-guided biopsies were obtained from the mediastinal lymph nodes to histologically confirm our suspicion. The results proved single non-caseating epithelioid cell granuloma in the affected lymph nodes. With reference to the criteria for clinical diagnosis of CS of the Japanese Circulation Society,[2] a diagnosis of CS was made.

Immediate corticosteroid therapy with prednisolone 30 mg (0.5 mg/kg body weight) p.o. once daily was initiated. Within a week, there was improvement in AV conduction characteristics. Holter ECG and ECG monitoring did not reveal higher grade AV block. On the day of discharge, the ECG demonstrated an AV block I° (PQ interval 240 ms) and right bundle branch block. Follow-up examinations at 3, 6, and 9 months showed no relevant conduction disturbances on ECG (*Figure 1B*) and Holter ECG. The patient remained completely asymptomatic. A cardiac MRI at 9 months later confirmed a partial reduction of the previously described change in the cardiac septum (*Figure 2B*).

Discussion

This report describes the case of a young patient who had complete AV block due to CS. Complete AV block may be caused by e.g. ischaemia, electrolyte disturbances, infection, autoimmune disease, or idiopathic causes (see Supplementary material online, *Figure S1*). Especially in young individuals (<50 years) with structurally normal heart,

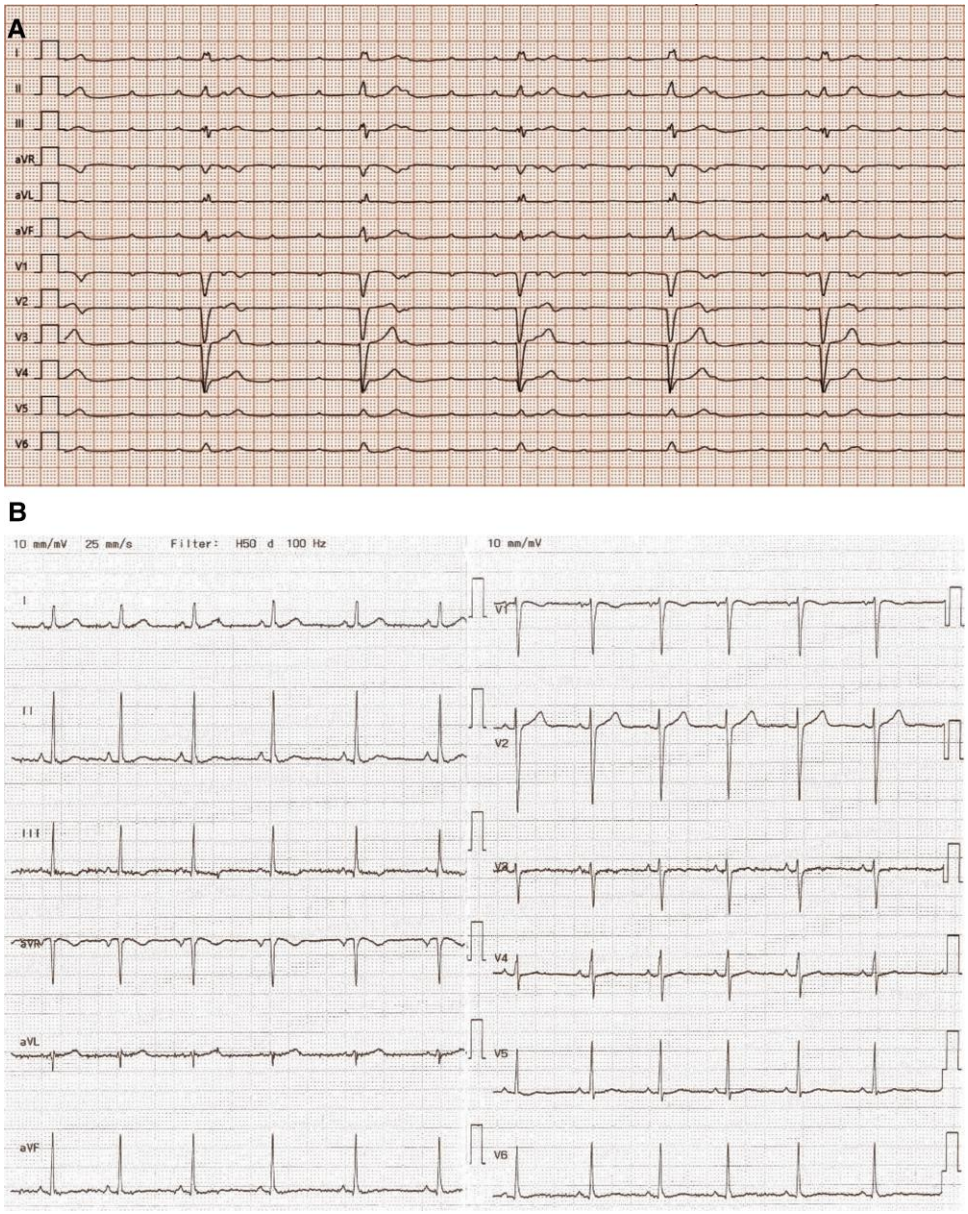

Figure 1 Electrocardiogram (*A* and *B*). Electrocardiogram on admission showed third-degree atrioventricular block with ventricular escape rhythm, 34 bpm (*A*). Resting electrocardiogram at 9-month follow-up without atrioventricular conduction disorder (*B*).

progressive cardiac conduction disease (PCCD) may be diagnosed. Therefore, genetic testing for the common PCCD-associated genes sodium channel protein type 5 subunit alpha (SCN5A), transient receptor potential cation channel subfamily M member 4 (TRPM4) for isolated forms and lamin A/C (LMNA) for PCCD associated with heart failure should be considered.[3]

Nery *et al.*[1] reported that 34% of patients younger than 60 years with complete AV block had previously undiagnosed CS. Therefore, in young adults with unexplained complete AV block, CS should be excluded as a differential diagnosis.

Sarcoidosis is a granulomatous disease of unknown aetiology that can affect any organ. However, most patients present with pulmonary involvement with hilar lymphadenopathy. Cardiac involvement appears to occur in 20–25% of sarcoidosis patients,[4] although most patients are asymptomatic and often only autopsies reveal cardiac abnormalities. Cardiac manifestations include congestive heart failure with left ventricular dysfunction, ventricular arrhythmias, and conduction abnormalities. Complete AV block remains the most common conduction abnormality, affecting up to 30% of patients,[5] and is due to granulomas damaging the AV node in the basal septum. Patients with clinically isolated CS present primarily for cardiac symptoms without clinical evidence of sarcoid involvement in other organs.

Endomyocardial biopsy (EMB) is rarely performed because of procedural risk and patchy infiltration areas leading to low sensitivity but may be positive in up to 50% of patients by means of electroanatomic mapping-guided RV biopsy, especially in patients presenting with ventricular tachycardia.[6] At least two-thirds of initial EMBs are negative, and laboratory findings are non-specific and virtually inconclusive.[7]

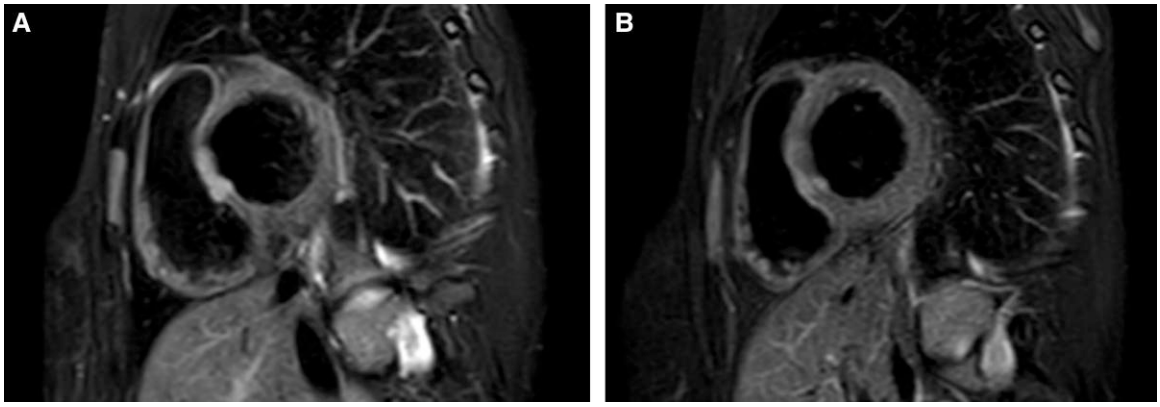

Figure 2 Cardiac magnetic resonance imaging (*A* and *B*). Cardiac magnetic resonance imaging on admission with septal mass in T2-weighted sequences (*A*). At 9-month follow-up regression of septal mass revealed in T2-weighted sequences (*B*).

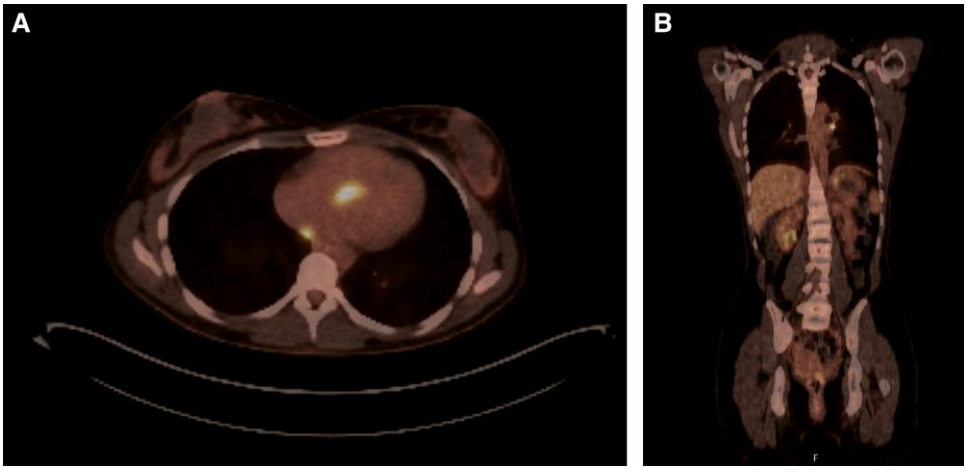

Figure 3 Positron emission tomography/computed tomography with tracer accumulation in the cardiac septal wall (*A*) and in mediastinal lymph nodes (*B*).

Experts from three independent organizations have developed consensus pathways for the diagnosis of CS in the absence of histologic evidence of EMB all of which relate to the clinical presentation of reduced LVEF, conduction disturbances, ventricular arrhythmias, and imaging with positive gallium scan, cardiac MRI, and cardiac ^{18}F-FDG imaging.[2,8,9]

Cardiac MRI and ^{18}F-FDG PET/computed tomography (CT) are used as diagnostic surrogate tests with high sensitivity and specificity. Although focal LGE on cardiac MRI and increased glucose uptake on ^{18}F-FDG PET/CT are non-specific signs of myocardial injury or inflammation, they provide landmark evidence of cardiac involvement of sarcoidosis when extra-CS is histologically proven.[10] Cardiac MRI with T2 weighting allows identification of small myocardial scars and oedema, while ^{18}F-FDG PET/CT identifies areas of active inflammation in active disease.[11]

In sarcoidosis with primary pulmonary involvement, many patients spontaneously enter remission without therapy. However, in CS, steroid therapy has been shown to promote survival and is generally considered the first-line treatment.[12] Early administration of immunosuppressants can halt or reverse cardiac damage.[5] A long-term benefit of steroid therapy in reducing clinical morbidity and mortality has been demonstrated.[13] Steroid therapy has been reported to be effective in AV block,[14] and a meta-analysis of 10 studies found that steroids improved about half of the patients with AV block but not those without AV block.[15] Early initiation of steroid therapy appears to be critical for AV block recovery, which is not seen in patients in whom therapy is initiated later than 1 month after diagnosis.[16] However, there is evidence that steroids are unable to reduce fatal cardiac events in high-grade AV block despite reducing active inflammation in ^{18}F-FDG-PET/CT.[17] The side effects of long-term steroid therapy such as weight gain, hyperglycaemia, increased risk of infections, or osteoporosis have led to an increasing usage of steroid-sparing therapies with synthetic disease-modifying antirheumatic drugs and biological disease-modifying antirheumatic drugs, such as methotrexate or azathioprine. Although data from retrospective studies showed benefit of steroid-sparing agents, to date there are no published randomized

controlled trials regarding the role of steroid-sparing agents in systemic or CS.[18]

Consequently, close follow-up is essential in patients with CS. The patient in this case was therefore scheduled for follow-up with Holter ECG every 3 months and cardiac imaging after 3, 9, and 24 months after initiation of immunosupressive therapy. To reduce the amount of radiation exposure regarding her young age and because of good assessability of the cardiac involvement, cardiac imaging with cardiac MRI instead of serial ^{18}F-FDG PET/CT was intended.

In summary, CS, although rare, may be the cause of complete AV block, especially in young patients. Without clinically obvious extracardiac involvement, it may be difficult to diagnose CS with certainty. Imaging techniques, such as cardiac MRI and ^{18}F-FDG-PET/CT, are crucial in this case. Systemic steroid therapy initiated early can avoid permanent pacemaker implantation. Thorough follow-up is essential.

Lead author biography

Innu Park graduated from Paracelsus Medical University of Salzburg, Austria. After completing his cardiology training in 2019, he is currently working as a senior physician for cardiology at the Department of Cardiology at the Asklepios Clinic Hamburg-Harburg, Germany.

Supplementary material

Supplementary material is available at *European Heart Journal—Case Reports*

Slide sets: A fully edited set of slides detailing this case, suitable for on-site presentation, is available online as supplemental data.

Consent: The authors acknowledge that written informed consent was obtained from the patient for submission and publication of this case report, including images and associated text, in accordance with COPE guidelines.

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Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

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