Heart block in a 60-year-old man with undiagnosed cardiac sarcoidosis

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A 60-year-old man presented to the emergency department after a brief syncopal episode without a prodrome. The patient was alert and oriented after the episode, and witnesses reported no seizure activity. He had no history of syncope, but did have a history of hypertension and left nephrectomy (he was an elective donor). His only medication was amlodipine 5 mg/d orally. He had no allergies and was a half-pack-per-day smoker. He did not use marijuana, alcohol or illicit drugs.

His heart rate was 35–40 beats/min and blood pressure was 190/80 mm Hg. His temperature, oxygen saturation and respiratory rate were normal, as was the remainder of the physical examination. An electrocardiogram (ECG) showed 2:1 atrioventricular (AV) block with left bundle branch block (Figure 1). No previous ECGs were available. Chest radiograph was normal. The patient had a normal complete blood count, electrolytes, renal function, liver enzymes and thyroid-stimulating hormone level, which ruled out electrolyte abnormalities and thyroid disease as a cause of heart block. High-sensitivity troponin-T levels were mildly elevated (23, 60, 84 [reference range 0–14] ng/L). We admitted him for further investigations including C-reactive protein levels, immunoglobulins, vasculitis panel, blood cultures and Lyme serology, and all were negative. Thus, we considered it unlikely that his heart block was caused by infectious or autoimmune diseases (Box 1).

Transthoracic echocardiography (TTE) showed moderately reduced left ventricular systolic function (LVEF 40%) with wall motion abnormalities in a noncoronary distribution and mild left ventricular hypertrophy. Coronary angiography showed normal coronary arteries, which ruled out coronary artery disease. After admission, the patient had multiple episodes of lightheadedness and near syncope with his heart rate dropping into the 20s on telemetry. We inserted an urgent temporary venous pacer.

Unfortunately, the patient continued to have symptoms and episodes of pacer noncapture, so we implanted a magnetic resonance imaging (MRI)–conditional dual-chamber pacemaker on postadmission day 2 before our workup for secondary causes of heart block was complete.

A computed tomography (CT) scan of the patient's chest showed multiple mediastinal and paratracheal lymph nodes larger than 1 cm, scattered pulmonary nodules but no hilar adenopathy, which we felt was suspicious for sarcoidosis. Cardiac MRI showed late gadolinium enhancement in the apical inferior wall and sub-

Key points

- Heart block in patients younger than 65 years is unlikely to be caused by degenerative conduction system disease.
- A complete evaluation for secondary causes of heart block should be undertaken before permanent pacemaker insertion.
- Imaging investigations for cardiac sarcoidosis include transthoracic echocardiography, cardiac magnetic resonance imaging, computed tomography of the chest and fluorodeoxyglucose positron emission tomography.
- Treatment for cardiac sarcoidosis includes immunosuppression with prednisone and sometimes methotrexate.

epicardial enhancement in the basal anterior wall and midseptum, suggesting a nonischemic cardiomyopathy (Figure 2). We did not perform a right ventricular endomyocardial biopsy as the patient's cardiac MRI results showed no late gadolinium enhancement in the region usually targeted for biopsy. Instead, we arranged a transbronchial lung biopsy, which found noncaseating granulomatous inflammation consistent with sarcoidosis.

We started treatment with prednisone 40 mg/d orally, with a planned taper of 5 mg per week. We also started guideline-directed medical therapy for heart failure with reduced EF (angiotensin-converting enzyme inhibitor, β-blocker and mineralocorticoid receptor antagonist), given the patient's reduced LV function.[1,2]

A fluorodeoxyglucose positron emission tomography (PET) scan was ordered but unfortunately not completed until 10 months after admission. It showed intense uptake in the entire anterolateral wall, and moderate uptake throughout the inferior wall, anteroseptum and apex (Figure 3A). Given these results, we increased the patient's prednisone dose from 10 mg to 40 mg and added methotrexate. We changed his pacemaker to a cardiac resynchronization device and implantable cardioverter-defibrillator (CRT-D), as he had persistent LV dysfunction and some high ventricular rate episodes on pacemaker interrogation.[2]

We repeated the fluorodeoxyglucose PET scan 6 months later. His EF had improved (52%) and there was no substantial inflammation compared with the previous PET scan (Figure 3B). Repeat TTE confirmed normal LV function. The patient is now stable on prednisone 5 mg and methotrexate 15 mg orally.
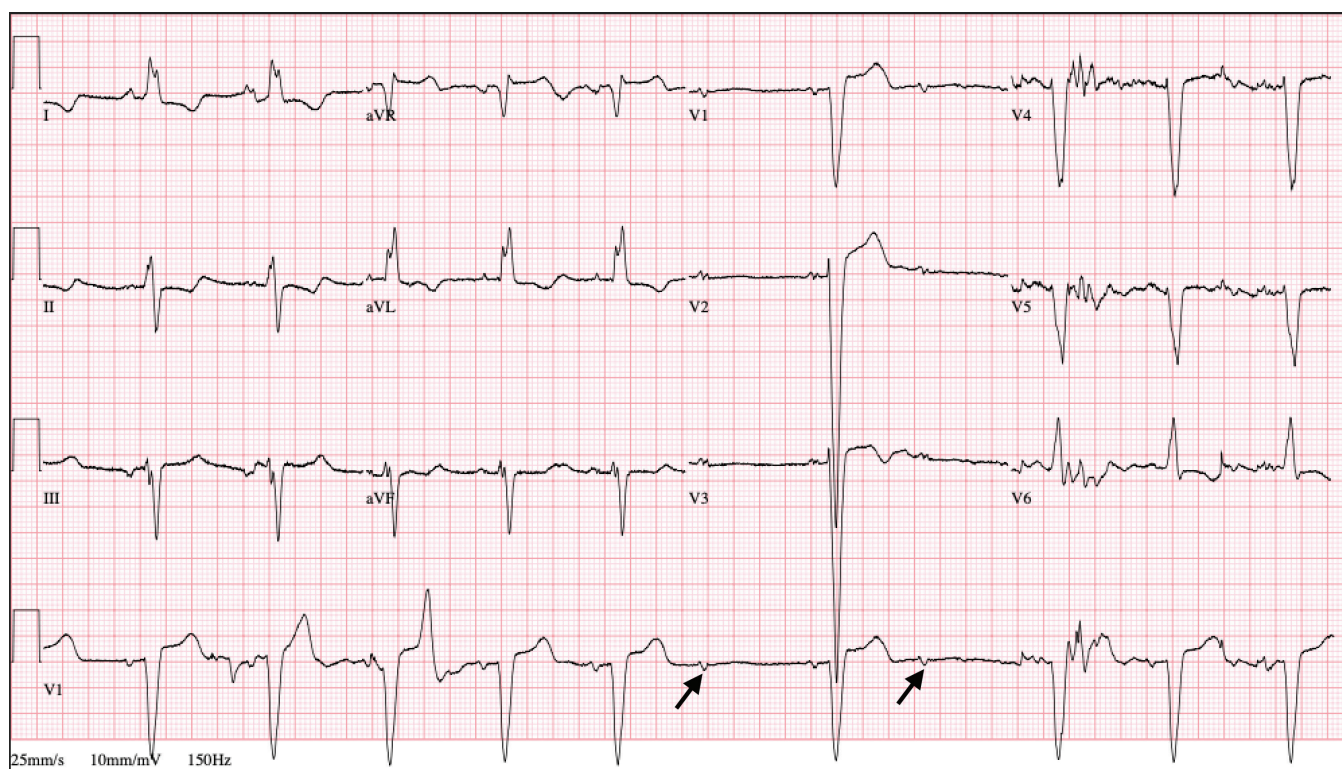
Figure 1: Twelve-lead electrocardiogram of a 60-year-old man, showing atrioventricular block (arrows). Continuous telemetry confirmed high-grade atrioventricular block.

Box 1: Causes of heart block in adults

- Increased vagal tone
- Degenerative conduction system disease
- Ischemic (ischemic heart disease, acute myocardial infarction)
- Infectious (Lyme carditis, endocarditis with aortic root abscess, rheumatic fever, viral myocarditis)
- Metabolic (hyperkalemia, hypothyroidism, hyperthyroidism)
- Infiltrative (sarcoidosis, amyloidosis, hemochromatosis)
- Drugs (β-blockers, calcium channel blockers, anti-arrhythmics, digoxin)
- Iatrogenic (cardiac surgery, transcatheter aortic valve replacement, catheter ablation of certain arrhythmias, alcohol septal ablation)

Discussion

The many causes of pathologic AV block include congenital and acquired forms (Box 1). Degenerative causes are by far the most common and are associated with age-related degeneration and fibrosis of the conduction system, diabetes and hypertension.[3] In 1 retrospective analysis, 0.6% of controls and as many as 1.1% of patients in hospital (age 65.8 ± 11.3 yr) with diabetes had complete AV block.[4]

If patients are clinically stable, common and potentially reversible causes of AV block (which are common in patients younger than 65 years) should be considered and treated before a permanent pacemaker is inserted. Reversible causes include medications, ischemia, hyperkalemia, thyroid dysfunction and infections such as Lyme carditis. Lyme disease is a vector-borne infectious illness with dramatically increasing incidence in parts of Canada (144 cases in 2009; 2025 cases in 2017).[5] Atrioventricular block is present in 90% of patients with Lyme carditis and resolves with antibiotics in most cases.[5]

Sarcoidosis is a multisystem granulomatous disease of unknown cause; its hallmark is noncaseating granulomas on biopsy. It primarily affects people in their third to fourth decade of life.[6] Sarcoidosis more commonly affects women, nonsmokers, individuals of African descent and residents in northern latitudes.[6] In 1 Ontario cohort study, the prevalence of sarcoidosis increased between 1996 and 2015, from 66 to 143 cases per 100 000;[7] increasing prevalence is seen worldwide. Sarcoidosis is a great mimicker of other diseases, making diagnosis challenging.

The lungs and hilar lymph nodes are involved in about 90% of patients with sarcoidosis. However, sarcoidosis can also affect other organs, including the heart, liver, skin and eyes. Cardiac sarcoidosis (CS) can be the first clinical manifestation and is associated with a poorer prognosis owing to heart failure or sudden cardiac death.[8] In 1 study, only 19% of patients with EF below 30% were alive after 10 years.[9] Cardiac involvement in sarcoidosis has been reported in as many as 27% of autopsy studies in some North American cohorts, but many cases may be undiagnosed.[10]

Clinical features of CS include conduction abnormalities such as ventricular tachycardia and atrioventricular blocks, heart failure and sudden cardiac death, and nonspecific symptoms like chest pain, fatigue and presyncope.[8] The degree, location and
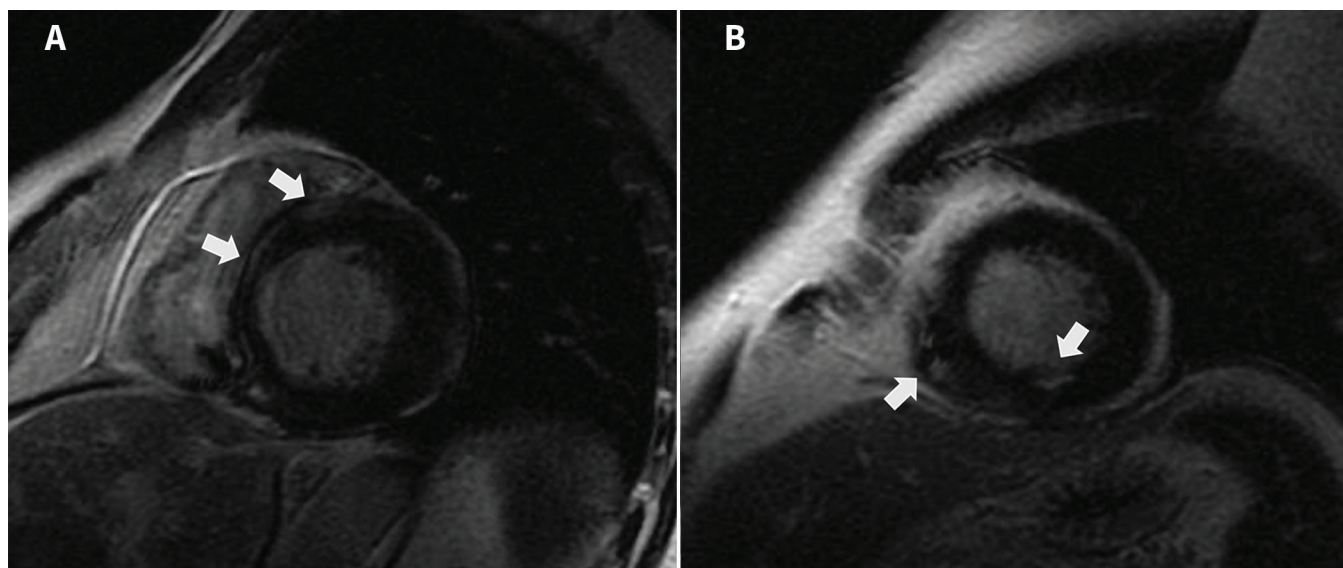
Figure 2: A) Cardiac magnetic resonance imaging (MRI) scan showing subepicardial late gadolinium enhancement (LGE) in basal anterior wall and mid-septum (arrows). B) Cardiac MRI showing LGE in apical inferior wall (subendocardial to midmyocardial) (arrows).
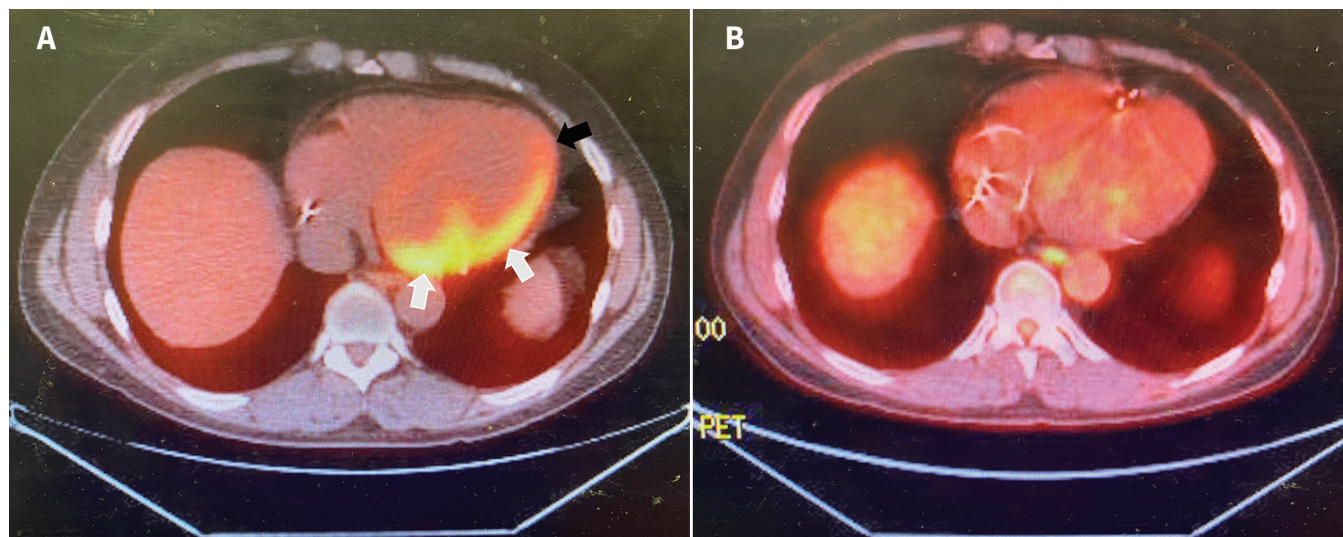

Figure 3: A) Fluorodeoxyglucose positron emission tomography (PET) scan showing intense uptake in the entire anterolateral wall (white arrows), and moderate uptake throughout the inferior wall, basal to mid anteroseptum and apex (black arrow). B) Follow-up PET scan 6 months later, showing no substantial inflammation.

extent of inflammation and fibrosis influence the clinical presentation. For instance, a patient with CS localized to the AV node may present acutely with heart block, but a patient with CS in a patchy distribution may be asymptomatic, despite being at higher risk for heart failure and ventricular arrhythmias.

Diagnosis of CS is histologic, from myocardial tissue, or clinical, based on history and results of invasive and noninvasive investigations.[1] Biomarkers, electrocardiograms and TTE are first-line tests that frequently yield nonspecific findings. For instance, TTE may show regional wall motion abnormalities in a noncoronary distribution with or without LV systolic dysfunction, basal interventricular septum thinning and reduced global longitudinal strain. The gold standard remains endomyocardial biopsy; however, the yield from biopsy is less than 50%.[11] Electroanatomic mapping shows promise

in increasing the yield for endomyocardial biopsy.[12] If tissue diagnosis is not feasible, consensus guidelines from the Heart Rhythm Society and the Japanese Ministry of Health and Welfare criteria can be used.[8] Hybrid cardiac MRI and fluorodeoxyglucose PET imaging detects both inflammation and scar in CS and thus effectively highlights these separate stages of CS in 1 modality.[13] Ideally, this should be completed 3 months after starting or stopping treatment and if there is a change in symptoms.[1,8] Hybrid PET and MRI imaging displays greater sensitivity and specificity in detecting inflammation than PET or MRI alone.[14] This is a novel modality for detection of CS, which exposes the patient to less radiation.

Data on screening for CS in patients with a diagnosis of sarcoidosis are limited; however, the findings of 1 study of diagnostic and prognostic investigations in an outpatient setting

suggested that if a patient has palpitations, syncope or presyncope, an ECG, Holter and TTE should be completed.[15] Abnormal screening tests and ongoing clinical suspicion for CS should trigger further testing with MRI, PET or hybrid imaging.

Management of CS can be challenging and referral to a cardiologist with expertise in CS is recommended.[1] Immunosuppression with prednisone is the mainstay of treatment for CS[1] and should be considered when there is imaging evidence of myocardial inflammation and either atrioventricular blocks, frequent nonsustained or sustained ventricular tachycardia, or LV dysfunction.[8] In addition to glucocorticoids, steroid-sparing agents such as methotrexate, azathioprine and mycophenolate may be considered. Currently, the Cardiac Sarcoidosis Randomized Trial is ongoing, in which patients with CS are randomized to prednisone or prednisone and methotrexate; the trial will provide useful evidence for the treatment of CS.[16] Biologic agents are third-line therapy and their use has been reported in only a small number of cases. Implantable cardioverter-defibrillator therapy should be considered, as patients with sarcoidosis can be susceptible to ventricular arrhythmias.

For patients younger than 65 years who present with heart block, CS should be considered along with other nonischemic causes. Novel imaging techniques such as hybrid PET and MRI have increased the sensitivity and specificity for diagnosis, and ongoing trials will shed further light on management.

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The section Cases presents brief case reports that convey clear, practical lessons. Preference is given to common presentations of important rare conditions, and important unusual presentations of common problems. Articles start with a case presentation (500 words maximum), and a discussion of the underlying condition follows (1000 words maximum). Visual elements (e.g., tables of the differential diagnosis, clinical features or diagnostic approach) are encouraged. Consent from patients for publication of their story is a necessity. See information for authors at www.cmaj.ca.