Is it bradycardia or something else causing symptoms?

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Introduction

Cardiovascular autoregulation is dependent upon a dynamic balance between the sympathetic and parasympathetic branches of the autonomic nervous system.[1] Autonomic failure, often present in patients with Parkinson disease (PD) and other neurodegenerative diseases, results in cardiovascular dysfunction that may be evident early in the progression of PD,[2,3] even before the onset of motor symptoms.[4] Common manifestations of autonomic dysfunction in PD include neurogenic orthostatic hypotension (nOH), supine hypertension, and attenuated heart rate (HR) variability, all of which are associated with increased morbidity and mortality.[5]

nOH, a sustained reduction of systolic blood pressure (BP) of $\geq$ 20 mm Hg or diastolic BP of $\geq$ 10 mm Hg within 3 minutes of standing or head-up tilt to at least 60°, can result from hypoperfusion of the brain upon standing.[6] Supine hypertension, defined as systolic BP $\geq$ 140 mm Hg and/or diastolic BP $\geq$ 90 mm Hg while in the supine position ($\geq$5 minutes of rest), is common in patients with nOH.[7] Patients with autonomic failure often present with both nOH and supine hypertension, as regulatory BP mechanisms are impaired.[8] Normal HR variability and sinoatrial and atrioventricular nodal conduction regulated by both branches of the autonomic nervous system can be disrupted in autonomic dysfunction.[9,10]

Patients with suspected autonomic dysfunction can have associated multisystem autonomic abnormalities. A key abnormality is orthostatic intolerance resulting in nOH; however, many patients also have HR abnormalities, including bradycardia. Because symptoms can be nonspecific and mimic other medical conditions, a comprehensive assessment of underlying conditions to determine the cause of symptoms is necessary before making a recommendation for a specific treatment. In this report, we describe the case of bradycardia in a patient with PD who was referred for a pacemaker.

Case report

An 82-year-old man who was diagnosed with PD 1 year prior and treated with carbidopa-levodopa (1.5 tabs, 25–100 mg 3 times daily) complained of chronic progressive and debilitating lightheadedness, dizziness, and fatigue that worsened with standing. He was referred for a pacemaker because of a slow HR (approximately 50 beats per minute [bpm]) with long-standing, persistent atrial fibrillation, confirmed with 12-lead electrocardiogram (Figure 1). He also had mild left ventricular dysfunction (Figure 1) with New York Heart Association functional class II heart failure symptoms (with normal left ventricular function), hypertension, prior stroke, urinary retention, and seizure disorder. He was treated with warfarin, levetiracetam (1000 mg twice daily), lamotrigine (75 mg in AM and 100 mg in PM), rasagiline (1 mg once daily), oxybutynin (15 mg every 24 hours), and pazopanib (200 mg once daily).

Prior to his referral to the electrophysiology service by a cardiologist, orthostatic vital signs had not been monitored in this patient. A 14-day electrocardiogram assessment (Figure 2) showed 1 pause of 3 seconds' duration and atrial fibrillation burden of 100% with an average HR of 79 bpm. Before consideration of pacemaker implantation, a further history was obtained that suggested symptoms occurred only in the standing position after rising from a seated or lying position. Orthostatic vital signs were obtained and showed that systolic BP decreased from 125 mm Hg to 60 mm Hg within minutes of a positional change from seated to standing, but there was no change in HR associated with this change (HR remained at 75 bpm). Moreover, the patient experienced his typical symptoms upon standing. A diagnosis of nOH was secured, and the pacemaker was not implanted.

Droxidopa, a norepinephrine prodrug approved in the United States for the treatment of orthostatic dizziness,

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KEY TEACHING POINTS

- Autonomic failure associated with Parkinson disease (PD) and other neurodegenerative diseases can result in cardiovascular dysfunction, which can manifest as orthostatic intolerance due to neurogenic orthostatic hypotension (nOH). Patients with autonomic failure may also have other heart rate (HR) abnormalities such as bradycardia. The clinical features of these 2 conditions may overlap (ie, dizziness, syncope, fatigue, weakness, and falls).
- In this case report, an elderly patient with PD and persistent atrial fibrillation, dizziness, and fatigue that worsened upon standing was referred for a pacemaker owing to a slow HR. Symptoms only occurred in the standing position and orthostatic vital signs showed a systolic blood pressure decrease from 125 to 60 mm Hg with no change in HR, leading to a diagnosis of nOH. Droxidopa was prescribed and symptoms resolved completely within the first week and a pacemaker was not implanted.
- When evaluating patients with nonspecific symptoms such as dizziness and fatigue, a comprehensive assessment considering underlying conditions is necessary to aid in accurate diagnosis and appropriate treatment. Collection of pertinent medical history and orthostatic vital signs are key components when screening for nOH.

lightheadedness, or the "feeling that you are about to black out" in adult patients with nOH caused by primary autonomic failure (PD, multiple system atrophy, and pure autonomic failure), dopamine beta-hydroxylase deficiency, and nondiabetic autonomic neuropathy, was prescribed.[11] After titration to 200 mg 3 times daily, the patient's symptoms resolved completely within the first week; symptom resolution has persisted for 3 years. There has been episodic supine hypertension with systolic BP of 180 mm Hg, but no exacerbation of heart failure. No severe hypertension was ever present, and no adjustment of the patient's medications was necessary. Over time, the patient's BP variability normalized; although his HR remained slow, a pacemaker was not considered to be necessary. The patient has been receiving droxidopa for more than 2 years, and as a result of his successful treatment, he has not experienced the symptomatic limitations previously reported and is now able to walk 3 miles per day routinely.

Discussion

The symptoms presented by the patient in this case study are commonly associated with bradycardia and, indeed, he had experienced episodic slow rates in atrial fibrillation. However, when evaluating patients with symptoms potentially due to bradycardia, it is important to consider and evaluate other causes for these symptoms, because a pacemaker may not resolve the problem if the problem is not due to bradycardia. Symptoms of bradycardia may overlap with the clinical manifestations of nOH, which include dizziness, syncope, fatigue, weakness, and falls.[8,12] In this case, the diagnosis of nOH was secured by evaluating orthostatic vital signs, identifying a sustained BP drop upon standing, and confirming that there was no associated change in HR.

The main treatment goals for nOH include reduction of symptom burden, prolongation of standing time, and improvement of physical capabilities.[8] For this patient, treatment of nOH with droxidopa was effective long term despite continued bradycardia. It is important that the presence of nOH be considered among patients with a history of PD. Screening for nOH in these patients by obtaining pertinent medical history and performing an examination that includes collection of orthostatic vital signs can aid in treatment optimization and avoidance of unnecessary surgery. These assessments are especially

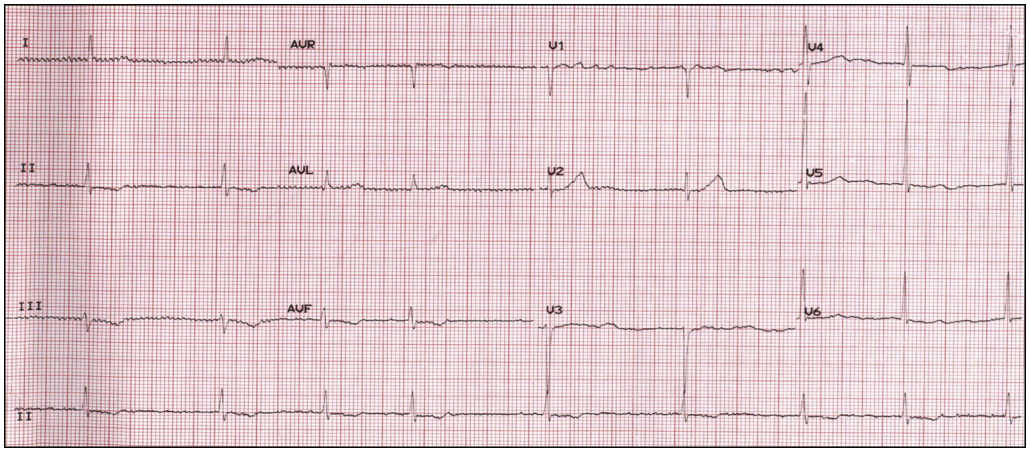

Figure 1 A 12-lead electrocardiogram showing atrial fibrillation and slow ventricular response with nonspecific ST- and T-wave changes.

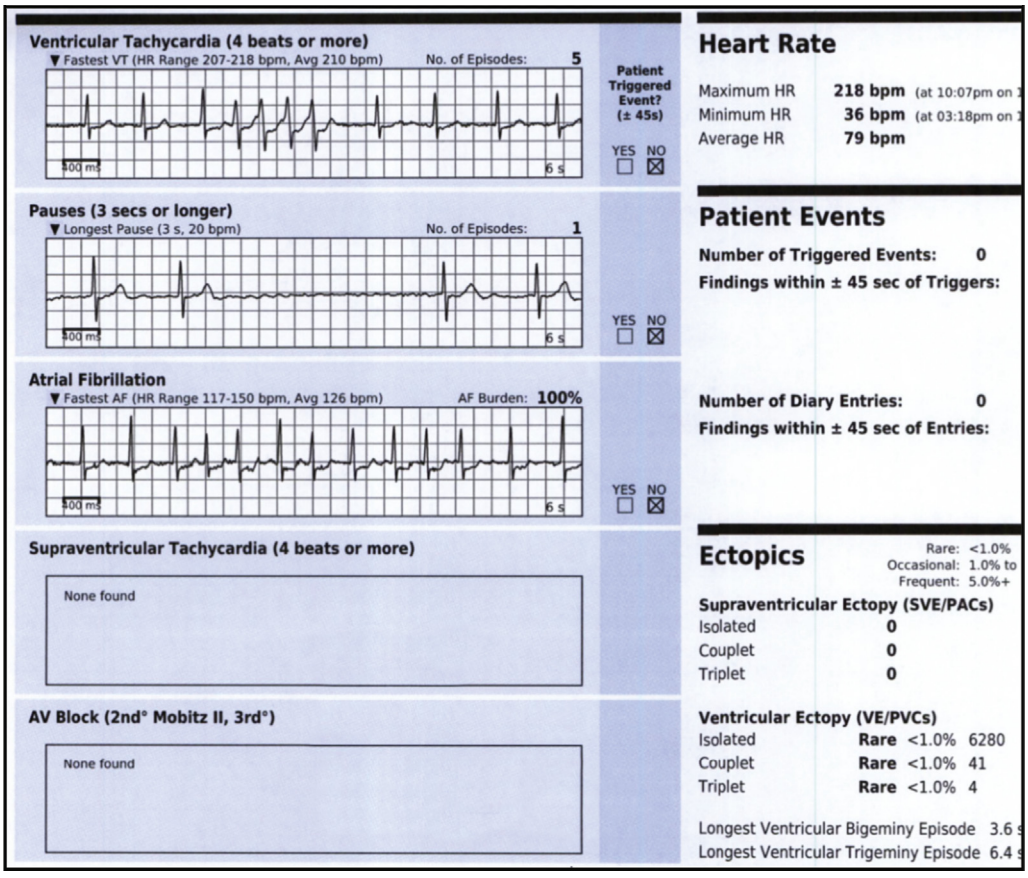

Figure 2 Two week event monitor showing a 4 beat run of nonsustained tachycardia, presumably ventricular, and a long pause in atrial fibrillation.

important because of the high mortality rate and increased risk of cardiovascular comorbidities associated with nOH.[13]

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