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INTERMEDIATE

CASE REPORT: CLINICAL CASE

A Clinical Challenge Overcome by His Bundle Pacing

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ABSTRACT

We highlight a diagnostic challenge in a patient with dyspnea on exertion due to radiation therapy–induced severe first-degree atrioventricular block and how permanent His bundle pacing was helpful in overcoming these symptoms. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2020;2:240–4) © 2020 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

HISTORY OF PRESENTATION

A 55-year-old Caucasian woman presented for outpatient cardiovascular evaluation of progressive dyspnea on exertion and associated lightheadedness for 1 month. Previously, she was able to climb several flights of stairs and participate in vigorous aerobic exercise classes with minimal difficulty. However, for the past few months, she had experienced dyspnea when climbing 1 flight of stairs, along with occasional palpitations lasting about 1 to 2 s. She otherwise denied syncope, peripheral edema, claudication, or chest pain. Upon review of the patient's wearable wrist monitor, sudden drops in heart rate were evident during exercise and associated with her symptoms. Her vital signs on examination were as follows: blood pressure 132/62 mm Hg, heart rate 67 beats/min, and weight 72.7 kg. Pertinent findings included a 2/6 crescendo-decrescendo murmur that radiated to the carotid arteries, as well as bilateral surgical scars from previous mastectomy.

LEARNING OBJECTIVES

- AV dyssynchrony should be considered in the differential diagnosis of symptomatic patients with markedly prolonged PR intervals and histories of radiation therapy.
- Permanent HBP may be a superior option to RV pacing in patients with a likely need for a high burden of ventricular pacing.
- HBP is a reasonable and safe option in patients with symptomatic pseudo-pacemaker syndrome due to PR prolongation.

MEDICAL HISTORY

Medical history included non-Hodgkin's lymphoma status post mantle and abdominal radiation therapy and splenectomy; estrogen receptor-positive left breast cancer status post chemotherapy with docetaxel and cyclophosphamide, modified left radical mastectomy, and prophylactic right mastectomy; factor V Leiden mutation; left subclavian artery stenosis and thrombosis; mild to moderate aortic stenosis; and incomplete right bundle branch block (RBBB).

DIFFERENTIAL DIAGNOSIS

The differential diagnosis included complications related to prior chemotherapy and/or radiation

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Informed consent was obtained for this case.

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therapy, including cardiac arrhythmias, coronary ischemia, valvular heart disease, pericardial disease, restrictive lung disease, and cardiomyopathy; other differential diagnoses included pulmonary embolism, pulmonary malignancy, pleural effusion, pneumonia, and asthma.

INVESTIGATIONS

Blood testing did not reveal any abnormalities, and there was no evidence of anemia (hemoglobin 13.5 g/dl), thyroid disorders (thyroid-stimulating hormone 2.4 μIU/ml), or electrolyte disturbances. Baseline electrocardiography (ECG) revealed sinus rhythm with a normal PR interval and an incomplete RBBB pattern (**Figure 1A**), and transthoracic echocardiography revealed an left ventricular ejection fraction of about 55% and mild to moderate aortic stenosis. Coronary angiography, cardiac magnetic resonance imaging, and lung function studies were all unremarkable. Repeat resting ECG was performed given progression of the patient's symptoms, which demonstrated a significant prolongation of the PR interval from 160 to 330 ms with RBBB (**Figure 1B**). Subsequent exercise stress testing with the Bruce protocol revealed a maximum heart rate of 173 beats/min (103% of maximum predicted heart rate) after 10 min of exercise, but with marked PR prolongation (500 ms) associated with dyspnea, similar to her presenting symptoms. A cardiac monitor showed a marked PR prolongation of more than 500 ms associated with reproduction of symptoms (**Figure 1C**).

MANAGEMENT

The findings of marked first-degree atrioventricular (AV) block, which worsened during exercise stress testing leading to AV dyssynchrony, suggested pseudo-pacemaker syndrome. Given the potential for a high burden of ventricular pacing (given the long PR interval), we decided to pursue dual-chamber pacemaker implantation with His bundle pacing (HBP). After mapping of the His bundle (HB), an area of intra-Hisian delay and disease was identified, and the lead was implanted distal to this region at the HB, resulting in narrowing of the RBBB pattern, suggesting that the delay in the right bundle branch was intra-Hisian (**Figure 2**). The final paced configuration was nonselective HBP (HB plus septal right ventricular [RV] capture) with recruitment and narrowing of the RBBB pattern (Supplemental Figure 1). The pacemaker site healed well, and the patient's symptoms completely resolved. She continues to do well 10 months after device implantation.

DISCUSSION

There are multiple possible causes of dyspnea on exertion in patients with histories of malignancy after radiation therapy, including premature coronary artery disease, valvular heart disease, pericardial disease, cardiomyopathy and heart failure, restrictive lung disease, and cardiac conduction system disease.

Given significant advances in cancer treatment, cancer-related mortality has declined over the years. As a result, there has been increasing recognition of cardiovascular diseases that occur as a consequence of cancer therapy, including damage to the cardiac conduction system. Conduction system injury can be directly related to irradiation or secondary to myocardial inflammation, ischemia, or fibrosis. Up to 75% of patients can have changes on ECG following mediastinal irradiation, but severe conduction abnormalities are not usually evident until years later (1,2). Abnormalities along the entire conduction system in the setting of irradiation have been described, including various degrees of AV block, sick sinus syndrome, prolonged corrected QT interval, supraventricular arrhythmias, and ventricular tachycardia (3,4). RBBB is more common than left bundle branch block because the anteriorly located right bundle is particularly susceptible, which was the case with our patient (3). Nonspecific ST- and T-wave changes are also very common years after radiation (5). The use of routine telemetry or ECG for screening of asymptomatic patients remains uncertain.

"Pseudo-pacemaker syndrome" refers to the occurrence of symptoms in the presence of marked first-degree AV block, when the conducted P wave is too close to the preceding QRS complex, producing the same hemodynamic disturbance as a ventricular paced rhythm with retrograde ventriculoatrial conduction. Pseudo-pacemaker syndrome (as noted in our case) can occur as a result of significantly prolonged PR interval and can result in symptoms due to AV dyssynchrony. After an extensive work-up that included echocardiography and cardiac magnetic resonance imaging (neither of which revealed any abnormalities), as well as chest computed tomography and pulmonary function testing that was unremarkable for any lung disease, our patient was diagnosed with pseudo-pacemaker syndrome, and a decision was made to implant a dual-chamber pacemaker to better achieve AV synchrony.

The choice of type of pacemaker is critical. This patient would require ventricular activation 100% of

ABBREVIATIONS AND ACRONYMS

AV = atrioventricular
ECG = electrocardiography
HB = His bundle
HBP = His bundle pacing
RBBB = right bundle branch block
RV = right ventricular

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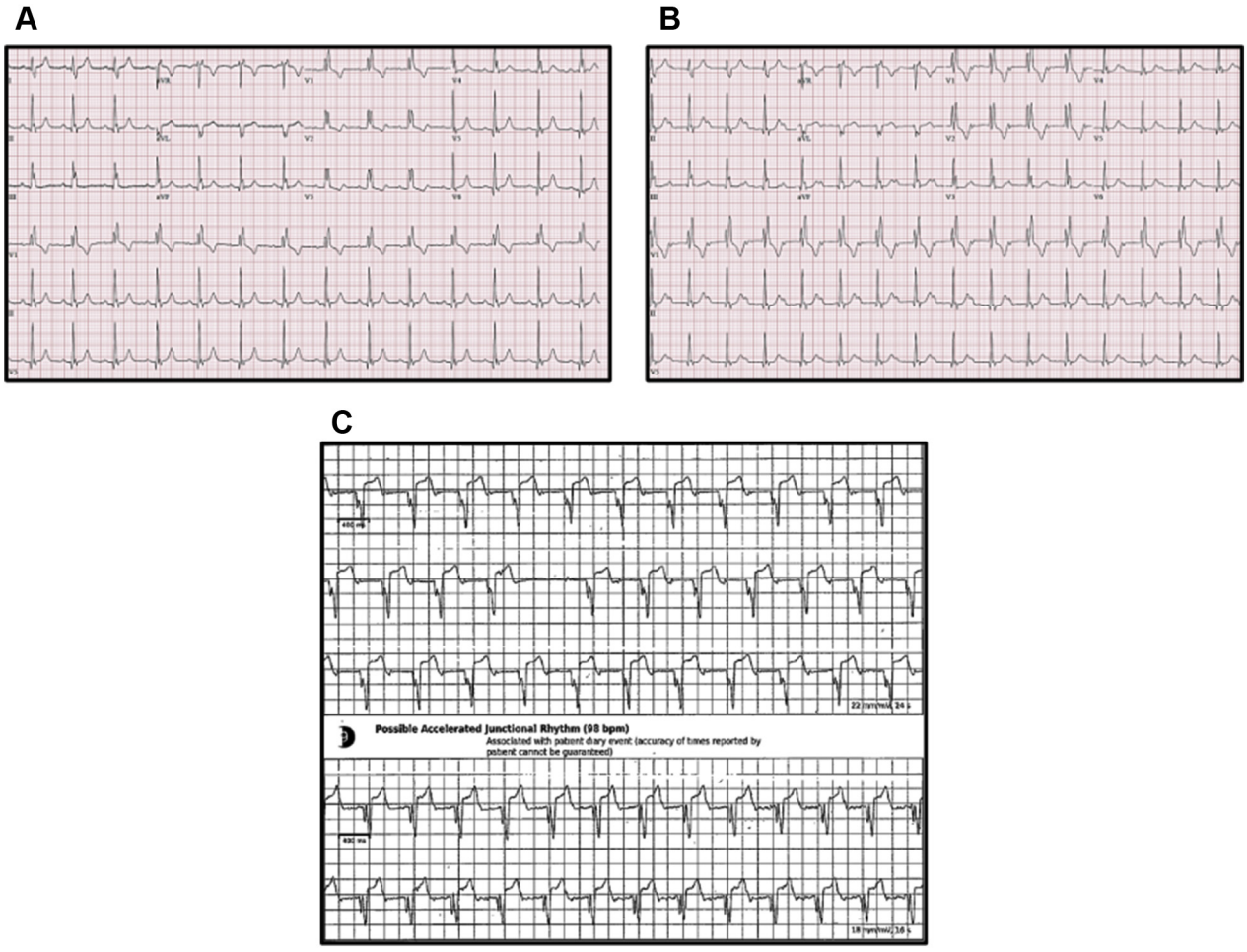
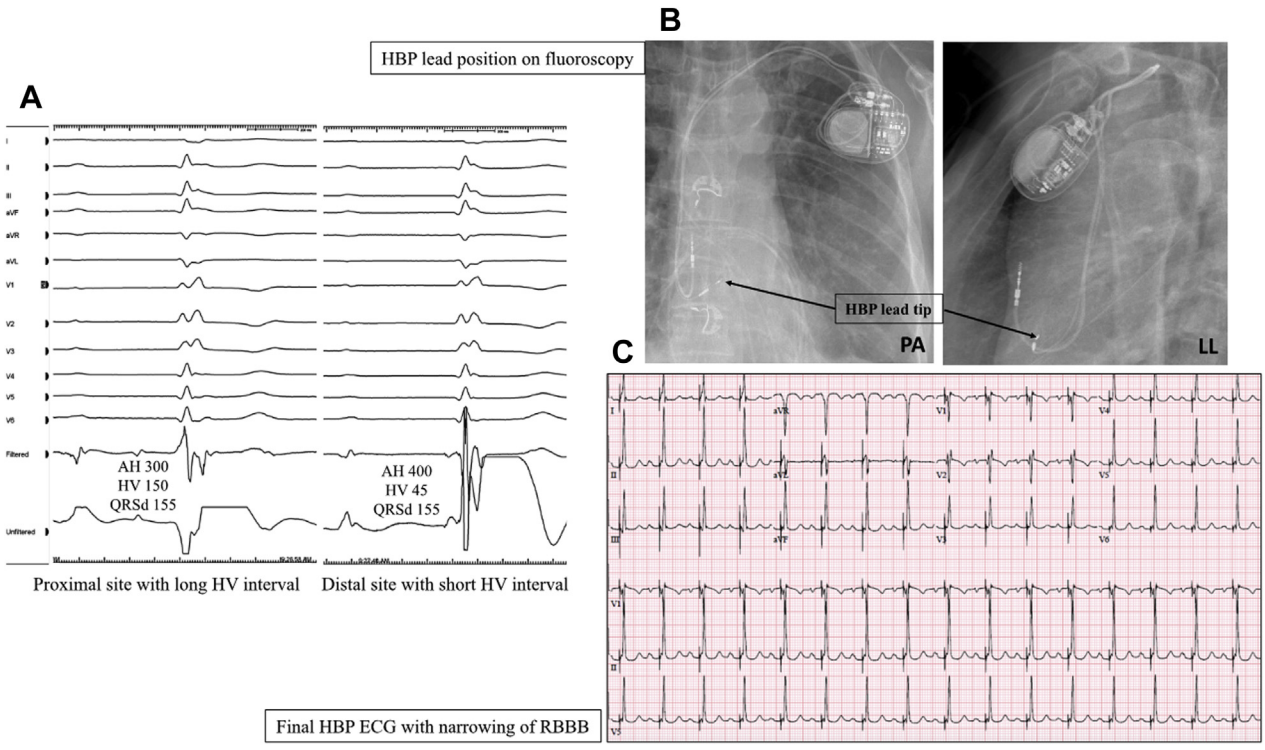
FIGURE 1 **Electrocardiography**



(A) Baseline electrocardiogram (before symptom onset): heart rate (HR) 84 beats/min, PR interval 160 ms, incomplete right bundle branch block (IRBBB) 118 ms. **(B)** Baseline electrocardiogram (after developing symptoms): HR 94 beats/min, PR interval 320 ms, right bundle branch block 130 ms. **(C)** Long-term (14-day) cardiac monitor with markedly prolonged PR interval (>500 ms) and a blocked premature atrial contraction. This strip was associated with a patient diary event when she was experiencing symptoms.

the time given the very long PR interval, as it is not possible to program such long AV delays. It has been well established that long-term RV apical pacing is associated with adverse clinical outcomes. RV pacing-induced cardiomyopathy is a well-known cause of left ventricular dysfunction. RV pacing results in dyssynchronous contraction of the ventricles and increases the risk for heart failure hospitalization (6–9). HBP reduces ventricular dyssynchrony by simultaneous activation of the ventricles via an intact distal His-Purkinje system and has been shown to reduce the risk for heart failure hospitalizations compared with RV pacing (10–12). HBP has therefore been shown to be a superior pacing strategy to RV apical pacing, and can be a feasible alternative option to cardiac resynchronization therapy with biventricular pacing in patients with both AV dyssynchrony and left bundle branch block and RBBB (13). We therefore chose to proceed with HBP. As noted in **Figure 2A**, we were able to identify the site of disease within the HB that resulted in PR prolongation and RBBB and

FIGURE 2 **After HBP**



(A) Proximal site with long HV interval on the left and distal site with short HV interval on the right. **(B)** His bundle pacing (HBP) lead position on fluoroscopy. **(C)** Final HBP electrocardiogram ECG with narrowing of right bundle branch block.

successfully implant the pacing lead at the HB distal to disease, resulting in narrowing of the QRS complex in addition.

FOLLOW-UP

The patient has remained symptom-free since HBP implantation and has returned to her baseline level of activity after 10 months of follow-up. During routine follow-up in the cardiac device clinic, R-wave amplitude, pacer threshold, lead impendence, and percentage of ventricular pacing were recorded. The post-procedural course has been uneventful, with no lead-related complications, including lead displacement, significant increase in pacer threshold, or lead dislodgement.

CONCLUSIONS

Cardiac dysfunction from chest radiation can involve the conduction system. AV dyssynchrony should be considered in symptomatic patients with markedly prolonged PR intervals with histories of radiation therapy. HBP provides AV synchrony while maintaining interventricular synchrony and can provide an effective approach to management of pseudo-pacemaker syndrome due to PR prolongation.

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REFERENCES

1. Adams MJ, Lipsitz SR, Colan SD, et al. Cardiovascular status in long-term survivors of Hodgkin's disease treated with chest radiotherapy. J Clin Oncol 2004;22:3139–48.

2. Desai MY, Jellis CL, Kotecha R, Johnston DR, Griffin BP. Radiation-associated cardiac disease: a practical approach to diagnosis and management. J Am Coll Cardiol Img 2018;11:1132–49.

3. Larsen RL, Jakacki RI, Vetter VL, Meadows AT, Silber JH, Barber G. Electrocardiographic changes and arrhythmias after cancer therapy in children and young adults. Am J Cardiol 1992;70:73–7.

4. Heidenreich PA, Kapoor JR. Radiation induced heart disease: systemic disorders in heart disease. Heart 2009;95:252–8.

5. Strender LE, Lindahl J, Larsson LE. Incidence of heart disease and functional significance of changes in the electrocardiogram 10 years after

radiotherapy for breast cancer. Cancer 1986;57:929–34.

6. Sweeney MO, Hellkamp AS, Ellenbogen KA, et al. Adverse effect of ventricular pacing on heart failure and atrial fibrillation among patients with normal baseline QRS duration in a clinical trial of pacemaker therapy for sinus node dysfunction. Circulation 2003;107:2932–7.

7. Khurshid S, Epstein AE, Verdino RJ, et al. Incidence and predictors of right ventricular pacing-induced cardiomyopathy. Heart Rhythm 2014;11:1619–25.

8. Wilkoff BL, Cook JR, Epstein AE, et al. Dual-chamber pacing or ventricular backup pacing in patients with an implantable defibrillator: the Dual Chamber and VVI Implantable Defibrillator (DAVID) trial. JAMA 2002;288:3115–23.

9. Kiehl EL, Makki T, Kumar R, et al. Incidence and predictors of right ventricular pacing-induced cardiomyopathy in patients with complete atrioventricular block and preserved left ventricular systolic function. Heart Rhythm 2016;13:2272–8.

10. Sharma PS, Dandamudi G, Naperkowski A, et al. Permanent His-bundle pacing is feasible, safe, and superior to right ventricular pacing in routine clinical practice. Heart Rhythm 2015;12:305–12.

11. Vijayaraman P, Naperkowski A, Subzposh FA, et al. Permanent His-bundle pacing: Long-term lead performance and clinical outcomes. Heart Rhythm 2018;15:696–702.

12. Abdelrahman M, Subzposh FA, Beer D, et al. Clinical outcomes of His bundle pacing compared to right ventricular pacing. J Am Coll Cardiol 2018;71:2319–30.

13. Sharma PS, Dandamudi G, Herweg B, et al. Permanent His-bundle pacing as an alternative to biventricular pacing for cardiac resynchronization therapy: a multicenter experience. Heart Rhythm 2018;15:413–20.

KEY WORDS cardiac pacemaker, cardiac resynchronization therapy, electroanatomic mapping, electrocardiography, electrophysiology, shortness of breath

APPENDIX For a supplemental figure, please see the online version of this paper.