

High-Grade Atrioventricular Block Associated With Acute Influenza

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Influenza causes cardiac and pulmonary complications that can lead to death. Its effect on the conduction system, first described a century ago, has long been thought to be fairly benign. We report 2 cases of high-grade atrioventricular block associated with acute influenza infection. Both patients—a 50-year-old woman with no history of cardiac disease or conduction abnormalities and a 20-year-old man with a history of complex congenital heart disease and conduction abnormalities—received a permanent pacemaker. In the first case, pacemaker interrogation at 4 months revealed persistent atrioventricular block. In the second case, pacemaker interrogation at 3 months suggested resolution. Whether such influenza-associated changes are transient or permanent remains unknown. We recommend keeping a careful watch on influenza patients with cardiac rhythm abnormalities and monitoring them closely to see if the problem resolves. (Tex Heart Inst J 2020;47(3):220-3)

Influenza can exacerbate congestive heart failure and ischemic coronary artery disease and contribute to cardiac morbidity and death.^{1,2} The electrophysiologic effects were first described in 1919 by Cockayne,³ who documented 19 cases of partial heart block and another 113 cases of bradycardia by means of polygram tracing during the influenza epidemic of 1918–1919. In 2005, Ison and associates⁴ reported a series of studies involving 236 previously healthy adults who had uncomplicated acute influenza and found that 39 (16.6%) had new abnormal electrocardiographic (ECG) results, most often sinus arrhythmia, high QRS voltage, and sinus bradycardia. However, none of those findings were considered clinically significant.⁴ We reviewed the literature and found only 4 documented cases of complete heart block associated with influenza virus infection.⁵⁻⁸ In 2 of those cases, the changes were transient.^{7,8} We present the cases of 2 patients with influenza who developed high-grade atrioventricular (AV) block; in one patient, the block persisted several months after influenza symptoms had resolved.

Key words: Atrioventricular block; bradycardia; heart block; influenza, human/complications; purpura, thrombocytopenic, idiopathic

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Case Reports

Patient 1

A 50-year-old woman presented at the emergency department with a several-day history of subjective fever, myalgia, malaise, and dizziness. Her medical history included hypothyroidism, depression, and concomitant use of levothyroxine and fluoxetine, but no cardiac disease or abnormalities. An ECG showed AV dissociation consistent with high-grade AV block (Fig. 1A). A test for influenza A antigen was positive. The patient reported having no symptoms of fatigue or dizziness before the onset of flu-like symptoms. She was hemodynamically stable but was admitted to the cardiac intensive care unit for further monitoring. Laboratory evaluations revealed normal cardiac enzyme levels and thyroid function. Cardiac magnetic resonance images showed no myocardial enhancement or myocarditis. A transthoracic echocardiogram revealed a normal left ventricular ejection fraction of 0.60 and no evidence of structural heart disease. She recovered from her acute illness and was discharged from the hospital with a hemodynamically stable junctional rhythm.

At follow-up in our electrophysiology clinic 3 weeks later, the patient reported symptoms of persistent shortness of breath with minimal exertion and occasional dizziness. Found to be in sinus rhythm with 2:1 AV block (Fig. 1B), she underwent an exercise treadmill test that revealed high-grade AV block (Fig. 1C). At rest, the patient's atrial rate

was 88 beats/min, and her ventricular rate was 44 beats/min (Fig. 1B). With exercise, her atrial rate increased to 136 beats/min, without any observed AV conduction; this was associated with a narrow-complex ventricular escape rhythm of 51 beats/min (Fig. 1C). The patient became extremely fatigued and could not exercise for longer than 2.5 minutes.

Because of her persistent symptoms and high-grade AV block, a dual-chamber pacemaker was implanted. Her symptoms resolved, and her exercise tolerance improved. However, at follow-up 4 months later, pacemaker interrogation revealed <1% atrial pacing and 100% ventricular pacing. The underlying rhythm was complete heart block with a ventricular rate of 35 beats/min.

Patient 2

A 20-year-old man with complex congenital heart disease presented at another facility's emergency department with fever (temperature, 38.9 °C), malaise, fatigue, and increased lethargy. His medical history included multiple surgical treatments for heart disease, including mechanical aortic valve and bovine pulmonary valve replace-

ment with warfarin anticoagulation therapy (Table I). Physical examination revealed a blood pressure of 91/41 mmHg and a heart rate of 131 beats/min. Laboratory tests revealed severe sepsis, acute renal dysfunction (blood urea nitrogen, 83 mg/dL; serum creatinine, 1.84 mg/dL), leukocytosis (white blood cell count, $12.3 \times 10^3/\mu\text{L}$ with left shift), a supratherapeutic international normalized ratio of 11.0, and thrombocytopenia (platelet count, $9 \times 10^3/\mu\text{L}$). A test for influenza A antigen was positive. An ECG revealed sinus tachycardia with baseline right bundle branch block and left anterior fascicular block (Fig. 2A).

The patient was prescribed broad-spectrum antibiotics and oseltamivir and was given intravenous (IV) fluids. He was then transferred to our hospital for further care. There, he received a brief infusion of norepinephrine for hypotension and fresh frozen plasma to reduce bleeding risk. His sepsis and acute renal dysfunction improved. He was given platelets for his thrombocytopenia, but the platelet count did not improve proportionally. Suspecting idiopathic thrombocytopenic purpura (ITP), we started the patient on IV methylprednisolone and then administered IV immunoglobulin (IVIG).

During IVIG infusion, the patient had bradycardia with high-grade AV block and worsened left bundle

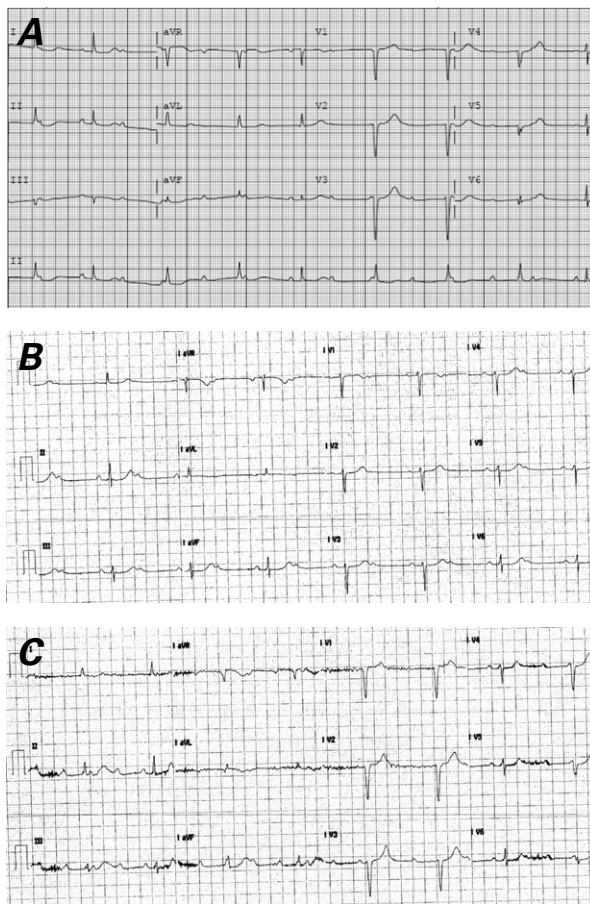


Fig. 1 Patient 1. Electrocardiograms show **A)** complete heart block at presentation, then **B)** sinus rhythm with 2:1 atrioventricular block at rest and **C)** high-grade atrioventricular block during an exercise treadmill test at 3-week follow-up.

TABLE I. Patient 2's Cardiac Surgical History

Age (yr)	Procedures
4	Discrete subaortic stenosis resection
6	Subvalvular aortic stenosis resection Septal myomectomy Ross procedure Pulmonary valve replacement with a 20-mm CryoLife tissue valve
12	Patch aortoplasty to repair supra-avalvular aortic stenosis Subaortic stenosis resection Infundibular resection and pulmonary valve replacement with a 21-mm homograft Infundibular resection and augmentation of right ventricular outflow tract
13	Pulmonary valve replacement with a 23-mm tissue valve Infundibular resection and patch augmentation of right ventricular outflow tract
17*	Aortic valve replacement with a 25-mm Carbomedics Top Hat mechanical valve Pulmonary valve replacement with a 22-mm Medtronic Contegra bovine jugular vein graft

*The patient recovered from the operations he had at 17 years of age, but a pseudoaneurysm with mediastinal hematoma developed postoperatively and had to be evacuated.

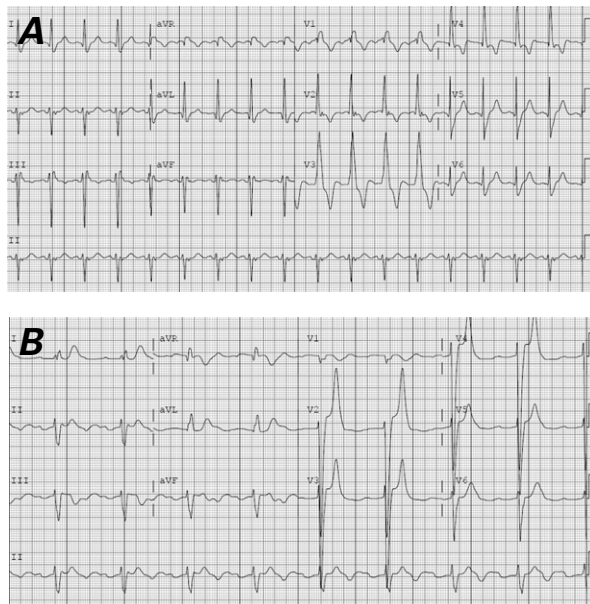


Fig. 2 Patient 2. Electrocardiograms show **A**) sinus tachycardia with right bundle branch block and left anterior fascicular block at presentation and **B**) high-grade atrioventricular block during intravenous immunoglobulin infusion for suspected idiopathic thrombocytopenic purpura.

branch block (Fig. 2B), necessitating placement of a temporary transvenous pacemaker. Laboratory tests revealed normal potassium and cardiac enzyme levels and normal thyroid function. A transesophageal echocardiogram showed no endocarditis or abscess. Serologic tests for ehrlichiosis, Lyme disease, and Rocky Mountain spotted fever were negative, as were tests for HIV and hepatitis. While the patient was hospitalized, his rhythm returned to sinus bradycardia (heart rate, 50–60 beats/min). Because of his apparent right and left bundle conduction disease and intermittent high-grade AV block, a permanent pacemaker was implanted before his discharge from the hospital. Three months later, pacemaker interrogation revealed sinus rhythm with 2% atrial pacing and <1% ventricular pacing.

Discussion

Influenza can worsen cardiac and pulmonary function, thereby increasing mortality rates. A century ago, bradycardia and varying degrees of heart block were noted in patients during the influenza pandemic of 1918–1919.³ A case of influenza-associated complete AV block was first documented in 1968,⁵ and a case of fetal heart block associated with maternal influenza was reported in 1977.⁶ In the latter case,⁶ the complete heart block persisted for more than 7 months. In 2 more cases, one patient had a permanent pacemaker implanted but did not need pacing at follow-up,⁷ and another's heart block resolved spontaneously 10 days into the hospital course.⁸

In our first case, a woman with no cardiac history and normal exercise tolerance developed AV block that was associated with serious flu-like symptoms and necessitated permanent pacemaker implantation. Several months later, she had persistent underlying AV dissociation. Despite previous studies suggesting that ECG changes in patients with influenza are transient, this case indicates that ECG abnormalities may persist.

In our second case, the patient's AV block resolved within days of onset. However, his history of complex congenital heart disease, intermittent high-grade AV block, and conduction disease in both right and left bundles indicated that he also needed a permanent pacemaker. At follow-up, however, device interrogation suggested that his AV block had resolved. Whereas influenza appeared to be the most likely cause of this patient's new-onset conduction abnormalities, his hospital course was complicated, making it more difficult to determine the cause. In addition to complex congenital heart disease associated with baseline conduction disease, there are documented cases of bradycardia associated with oseltamivir use.^{9,10} However, no high-grade AV block has been reported. Our patient was also undergoing IVIG therapy, but we found no reports of this causing AV block. Of note, influenza-associated ITP has been reported.^{11,12} In our patient's case, influenza seems the most likely explanation for his complicated hospital course.

In both patients, high-grade AV block was associated with influenza A virus, the same as that in previous reports. However, the specificity of viral antigen testing is high, so we did not have the virus subtyped by reverse transcriptase polymerase chain reaction in either case. Although ECG changes in patients with influenza have been documented, the mechanism is unknown. Neither of our patients and none of those whose cases were described previously^{7,8} had evidence of myocarditis on cardiac magnetic resonance or cardiac biomarker evaluation; however, none of them underwent myocardial biopsy. Acute coronary syndrome, which can be precipitated by influenza,¹ was not seen in our patients, suggesting that influenza may play a direct role in altering cardiac conduction.

Our cases did raise an important clinical question: was implanting a permanent pacemaker necessary, or should we have waited to see if the patients' arrhythmias abated as their influenza symptoms resolved, as previously suggested by others?^{3,4,7} Of 6 patients with influenza-associated complete heart block that we have identified (including ours),^{5–8} 3 received permanent pacemakers. Subsequent device interrogations showed ventricular pacing $\leq 1\%$ of the time in 2 and persistent AV block with continued pacing requirements in one. Although rare, these cases—along with previous observations of transient cardiac dysrhythmias associated with influenza—demonstrate that watchful waiting for

a return to normal intrinsic cardiac rhythm is reasonable in hemodynamically stable and asymptomatic patients. We recommend keeping a careful watch on influenza patients with cardiac rhythm abnormalities and monitoring them closely to see if the problem resolves.

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