Severe Symptomatic Bradycardia After Intravenous Immunoglobulin Infusion: A Rare Manifestation

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Abstract

Intravenous immunoglobulins (IVIGs) are immunomodulating agents prepared using pooled plasma from thousands of human donors. These IVIGs have been used to treat a wide range of autoimmune, infectious, and idiopathic diseases. Their use in idiopathic thrombocytopenic purpura (ITP) was first described in 1981 and was found to be an effective alternative to splenectomy. The standard dose of IVIG in patients with ITP is 400 milligrams per kilogram body weight (mg/kg) daily for 5 days however recent data has shown a dose of 1 gram/kilogram/day for 2 days may be more effective. Side-effects during IVIG infusions have been reported in about 5 to 15% of patients. Cardiac related side-effects such as arrhythmias, hypotension, and even myocardial infarction, being rare, have also been documented but are usually seen in patients with underlying cardiac pathologies. This article presents a 61-year-old male with no past cardiac history who developed symptomatic bradycardia after IVIGs infusion.

Keywords: Immunoglobin; Bradycardia; Side effect; Cardiac; Dysrhythmia; Idiopathic thrombocytopenic purpura.

Learning Objectives

1. Increase healthcare providers’ awareness of this serious cardiac side effect of intravenous immunoglobin (IVIG) infusion.
2. Highlight the need for recommendations on the re-administrability of IVIG in patients who develop such side effect.

Introduction

Intravenous Immunoglobulins (IVIGs) are blood products pooled from a large number, usually 1,000 or more, of healthy donors. Their use has recently increased as they showed efficacy in the management of a large variety of autoimmune, infectious, and hematologic diseases. Several cardiac side effects due to IVIGs infusion have been reported including supraventricular tachycardia, hypotension, and bradycardia; however, these are usually rare and associated with an underlying heart disease. We report a patient with no past cardiac history who developed symptomatic bradycardia after IVIGs infusion.

Case Presentation

A 61-year-old male with no medical issues was directed to the emergency department (ED) after his platelet (PLT) count was...
found to be 5000 cell/mm³ during routine blood work. He
denied bruising, epistaxis, or gingival bleeding. Vital signs
on admission were all within normal limits and the patients
recorded weight was 97.9 kg. Physical examination showed
no lymphadenopathy, hepatosplenomegaly, petechiae,
or ecchymoses. Repeat PLT count on admission to the
hospital was 3000 cells/mm³. Other laboratory results
showed WBC 9.1 K/uL, Hgb 13.1 gm/dL, MCV 94.3 fl, RDW
14%, immature platelet fraction 21.9%. Electrocardiogram
(ECG) on admission in the ED showed normal sinus rhythm
with a heart rate in the 90s beats per minute (bpm) (Figure
1). He was admitted with a presumptive diagnosis of
idiopathic thrombocytopenic purpura (ITP). Treatment
was started with two days of prednisone 50 milligrams
(mg) twice daily but had no effect. He was then started
on 3 days of dexamethasone 40 mg intravenously (IV)
with still no improvement, so 1 gm/kg (gram/kilogram)
of intravenous immunoglobulin was infused at an initial
rate of 5.88 gm/hr. Thirty minutes after starting the dose
(Gamunex-C 10%, Grifols Therapeutics Inc, Barcelona)
he developed chest pain and shortness of breath with
heart rate 31 bpm, temperature 98.4 degrees Fahrenheit,
respiratory rate 17 per min, and blood pressure 109/64
mmHg. ECG within 30 minutes after IVIG showed sinus
bradycardia with a heart rate of 30s (Figure 2). Cardiac
troponin levels x² were obtained and were negative (<0.04

![Figure 1](image1.png)

**Figure 1.** EKG on admission prior to IVIG infusion showing normal sinus rhythm with a heart rate of 92 bpm.

![Figure 2](image2.png)

**Figure 2:** Electrocardiogram showing sinus bradycardia after the development of chest pain and shortness of
breath 30 minutes after IVIG infusion.
Emergent transthoracic echocardiogram (TTE) was performed and showed an ejection fraction of 51-54% and no regional or global wall motion abnormalities. IV atropine 0.5 mg corrected his heart rate to 60-70 bpm with resolution of his symptoms. Six hours later he required another dose of atropine for a HR less than 35. The patient required additional atropine 0.5 mg doses 3-4 times a day and eventual dopamine infusion for 1 week. The patient's bradycardia resolved after treatment with atropine and dopamine (Figure 3) and due to adverse reactions, his ITP was ultimately treated with splenectomy rather than IVIG infusions.

Discussion

This case of prolonged symptomatic bradycardia stands in contrast to the majority of reported IVIG-induced dysrhythmia cases as most were in patients with underlying heart disease and/or a history of tachyarrhythmias. Savaşan and co-investigators reported 2 cases of supraventricular tachycardia (SVT) and accelerated ventricular rhythm during IVIG infusion in patients with underlying dysrhythmias before treatment with IVIG⁴. Similarly, Tufekci et al. reported the occurrence of SVT during IVIG infusion in two neonates with history of SVT⁵. This is, to our knowledge, only the 2nd case of IVIG induced symptomatic bradycardia in a person without underlying heart disease. The first case reported was by Raheja and co-investigators who reported in a letter to the editor a similar case of ITP who received IVIG and developed 4 episodes of asymptomatic sinus bradycardia following sequential IVIG infusions⁶. Moreover, the magnitude of the symptomatic bradycardia in the aforementioned case correlated with the dose of the administered IVIG⁶. The mechanism by which IVIG causes cardiovascular side effects remains unclear.

Our patient did not have any underlying cardiac history that might predispose him to bradycardia, and the unremarkable TTE and troponins after the episode excluded any structural heart disease that can explain it. Although our patient received corticosteroids, which have been reported to cause bradycardia⁷-⁹, the temporal association between the IVIG infusion and the development of bradycardia suggest the IVIG as etiology. In addition, the corticosteroids were given for a total of 5 days without any bradycardic episodes or acute side effects prior to receiving his first IVIG infusion.

The risk versus benefit of discontinuation of future IVIG infusion in patients who develop cardiac side effects remain to be determined by larger clinical studies. Due to the prolonged effect in our patient, IVIG was deemed contraindicated, and his ITP was ultimately treated with splenectomy with good outcomes.

Conclusion

Intravenous Immunoglobulin infusion can result in severe bradycardia, even in patients with no previous cardiac history. Albeit rare, it is imperative that physicians recognize, diagnose and treat the rare occurrence of symptomatic bradycardia after IVIG infusion to rapidly and appropriately manage patients and prevent morbidity and mortality from severe bradycardia induced by IVIG infusions.

Conflicts of Interest

The authors have no conflicts of interest to declare

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