Case Report

Ticagrelor-Induced Complete Heart Block: A Rare Entity

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Abstract

Ticagrelor, a purinergic P2Y12 receptor blocker, is a potent platelet antagonist and an important component in the treatment for acute coronary syndromes identified to have a potential risk to cause bradyarrhythmias. Here, we report the case of a diabetic patient of unstable angina with left bundle branch block who was prescribed ticagrelor post angioplasty. Electrocardiogram (ECG) revealed a complete heart block after about 1 week. Ticagrelor was stopped and replaced by clopidogrel. The patient became asymptomatic and ECG showed baseline rhythm after 1 week of stoppage of ticagrelor.

Keywords: Heart block, purinergic P2Y receptor antagonist, ticagrelor

Introduction

Ticagrelor, an antiplatelet agent, is a noncompetitive adenosine diphosphate P2Y12 receptor blocker. Ticagrelor and its metabolite are biologically active, and as compared to clopidogrel, the onset of action is fast and inhibition of platelets is more rapid and consistent.[1] As per the PLATO trial, patients on ticagrelor have an increased risk of ventricular pauses in comparison to clopidogrel. The bradyarrhythmic potential of ticagrelor is transient and is not clinically significant beyond the acute initiation phase of about a week.[2] In spite of this, there have been few case reports of ticagrelor-associated high-degree heart block, requiring interventions like discontinuation of the drug or even pacemaker insertion.[3] Other adverse effects associated with ticagrelor include respiratory distress, dizziness, nausea, hemorrhages, acute kidney injury, and angioedema. Here, we report a case of ticagrelor-induced heart block from our hospital.

Case Report

A 70-year-old male patient, a known case of noninsulin dependent type 2 diabetes mellitus on treatment with oral antidiabetic drugs metformin and voglibose, presented with complaints of dyspnea on exertion for 2 months to the cardiology outpatient department (OPD). He had no complaints of chest pain, orthopnea, or paroxysmal nocturnal dyspnea. Electrocardiogram (ECG) showed a left bundle branch block (LBBB) with discordant ST depression and troponin *t*-test was negative.

The patient was diagnosed as unstable angina. Echocardiography showed mild left ventricular (LV) systolic and diastolic dysfunction, mild mitral regurgitation, LV dyssynchrony, and sclerotic aortic valve disease. Coronary angiography showed double-vessel disease (proximal left anterior descending [LAD]-mid long tubular 90% stenosis with right circumflex anterior [RCA]-mid RCA tubular 50% stenosis) with branch vessel disease (ramus-proximal tubular 80% stenosis and posterior descending artery-discrete 80% stenosis). Percutaneous transluminal coronary angioplasty with stents (2.75 mm × 28 mm XIENCE XPEDITION) to ramus and (3 mm × 48 mm XIENCE XPEDITION) to LAD was done. The patient was put on aspirin and ticagrelor after giving loading doses of 325 mg and 180 mg, respectively. The maintenance dose was 75 mg and 90 mg. The patient was observed in the Intensive Care Unit for 1 day after the procedure and then observed in the ward. He was symptomatically better and discharged from the hospital after 4 days. On discharge, oral hypoglycemic agents were continued as before.

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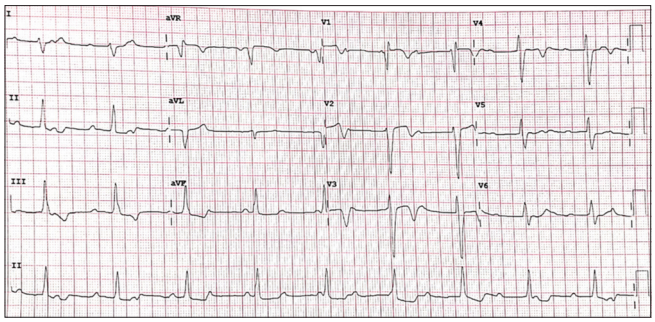

Figure 1: Electrocardiogram showing a complete heart block due to ticagrelor therapy

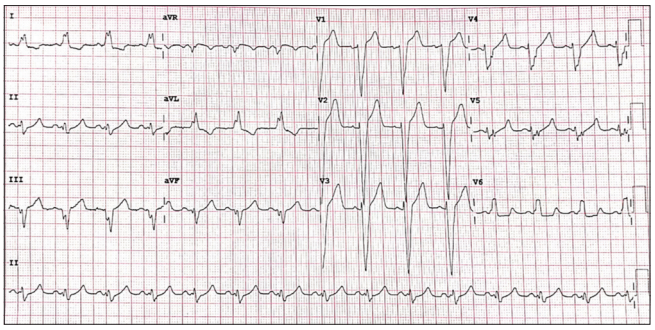

Figure 2: Electrocardiogram showing return to left bundle branch block with normal sinus rhythm post stoppage of ticagrelor therapy

The patient was asked to follow-up after 1 month. However, after 1 week, the patient revisited the OPD with complaints of breathlessness (New York Heart Association CLASS III). No associated chest pain or sweating was present. On investigation, ECG showed a complete heart block, as shown in Figure 1.

Echocardiography showed no new wall hypokinesia. Serum electrolytes and thyroid profiles were normal. The patient was not on any other medication that could cause bradyarrhythmia. Since there was no prior history of atrioventricular (AV) conduction blocks and no new electrolyte abnormality like hyperkalemia or elevation of troponin T, it was suspected to be a drug-induced heart block. Thus, ticagrelor was replaced with clopidogrel 300 mg loading dose, followed by maintenance with 75 mg once a day. Repeat ECG showed LBBB (same as ECG findings prior to this episode) with a return to normal sinus rhythm, as shown in Figure 2.

HOLTER study did not show any bradyarrhythmia episodes. The patient was symptomatically better and discharged with the above changes in prior medications. The patient was advised a follow-up visit to the cardiology OPD after 1 month, wherein the patient was found to be symptomatically stable and no new ECG changes were seen and he returned to sinus rhythm.

Hence, the patient was diagnosed as ticagrelor-induced heart block with objective evidence. An assessment of HV interval (time from initial detection of his bundle [H] potential and onset of ventricular [V] activity) in view of LBBB, should heart block of any degree occur has been planned for him.

Discussion

Dual antiplatelet therapy with aspirin and P2Y12 platelet receptor inhibitor is the backbone for the treatment of acute coronary syndromes.[1] Current European Society of Cardiology guidelines recommend the use of ticagrelor along with aspirin in patients with acute coronary syndrome regardless of an initial treatment strategy.[4] This patient is a known case of diabetes mellitus which increases the propensity for platelet reactivity. As a result, the need for potent antiplatelet therapy is further necessitated. Ticagrelor is known to be a more potent antiplatelet agent compared to clopidogrel and prasugrel.[1] The mechanism of ticagrelor-induced bradyarrhythmia is not clearly understood. Ticagrelor inhibits adenosine reuptake due to structural similarities between the two. Ischemic milieu further augments adenosine release from the myocardium which stimulates adenosine A1 receptors in the conduction tissue. The sinoatrial node is suppressed, affecting its automaticity, and there is a delay in the impulse conduction in AV node.[4] An interference with equilibrative nucleoside transporter-1-mediated adenosine degradation may also be the cause.[4]

Causality assessment of this adverse drug reaction was done using the World Health Organization Scale, and ticagrelor was found to be probably associated with the adverse event.[5]

Conclusion

Our case highlights the risk of ticagrelor-induced bradyarrhythmia events, especially in patients with an already compromised conduction system. In the view of scarcity of such reports, it is imperative to report this case to increase awareness among treating physicians and patients alike, owing to its seriousness. In conclusion, we advise caution with the use of ticagrelor as an antiplatelet agent in treatment of coronary artery disease and it becomes all the more crucial in patients with concomitant diabetes mellitus.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the legal guardian has given his consent for images and other clinical information to be reported in the journal. The guardian understands that names and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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