World Journal of Clinical Cases

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World J Clin Cases 2020 March 6; 8(5): 928-931

DOI: 10.12998/wjcc.v8.i5.928

ISSN 2307-8960 (online)

CASE REPORT

Acute thrombocytopenia after anticoagulation with rivaroxaban: A case report

Xin-Yi He, Ying Bai

ORCID number: Xin-Yi He (0000-0002-8447-8153); Ying Bai (0000-0002-4178-2403).

Author contributions: He XY collected the clinical data and drafted the manuscript; Bai Y reviewed this manuscript.

Informed consent statement: Written informed consent was obtained from the patient for publication of this report.

Conflict-of-interest statement: The authors declare no conflict of interest for this manuscript.

CARE Checklist (2016) statement: The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

Manuscript source: Unsolicited manuscript

Received: November 24, 2019

Peer-review started: November 24,

Xin-Yi He, Department of Clinical Pharmacy, Xi'an Fourth Hospital, Xi'an 710004, Shaanxi Province, China

Ying Bai, Department of Clinical Pharmacy, Beijing Tongren Hospital of Capital Medical University, Beijing 100730, China

Corresponding author: Ying Bai, MD, Pharmacist, Department of Clinical Pharmacy, Beijing Tongren Hospital of Capital Medical University, No. 1, Dongjiaomin Street, Dongcheng District, Beijing 100730, China. felisha_bai@hotmail.com

Abstract

BACKGROUND

Novel oral anticoagulants (NOACs) are commonly used for the anticoagulation of patients with atrial fibrillation. Reports of thrombocytopenic toxicity of NOACs are limited. In this report, we present a case of thrombocytopenia likely induced by rivaroxaban, which is an extremely rare adverse drug reaction.

CASE SUMMARY

A 70-year-old man presented to the cardiovascular department with a chief complaint of intermittent chest tightness and dyspnea over the last five years. Vital signs were within normal limits at presentation, with a heart rate of 65 beats/min, blood pressure of 138/78 mmHg, respiratory rate of 19 breaths/min, and temperature of 36.1°C. Laboratory tests indicated a platelet count of 163 × 10^9/L on admission. Anticoagulant therapy with rivaroxaban, a NOAC, was started on the second day of hospitalization. The platelet count decreased to 30 × 10^9/L on hospital day 11 and then 10 × 10^9/L on day 12. Rivaroxaban was stopped on day 13 when the platelet count decreased to 5 × 10^9/L. After the cessation of rivaroxaban, the platelet count returned to normal. The patient was diagnosed with thrombocytopenia, which was likely induced by rivaroxaban. The incidence of thrombocytopenic toxicity of NOACs is extremely low.

CONCLUSION

Thrombocytopenia during anticoagulation therapy may be associated with a high risk of life-threatening bleeding. For elderly patients, changes in platelet count should be carefully monitored at the beginning of NOAC treatment, and we should be on the alert for bleeding events as well.

Key words: Thrombocytopenia; Rivaroxaban; Adverse drug reactions; Case report

2019
First decision: December 12, 2019
Revised: January 1, 2020
Accepted: January 8, 2020
Article in press: January 8, 2020
Published online: March 6, 2020

P-Reviewer: Mousa HAL, Vaudo G
S-Editor: Dou Y
L-Editor: MedE- Ma JY
E-Editor: Wu YXJ

Core tip: We report a case of thrombocytopenia which is an extremely rare adverse drug reaction, that is likely induced by rivaroxaban Possible causes of this adverse event were analyzed, and future clinical medication is recommended.

Citation: He XY, Bai Y. Acute thrombocytopenia after anticoagulation with rivaroxaban: A case report. *World J Clin Cases* 2020; 8(5): 928-931
URL: https://www.wjgnet.com/2307-8960/full/v8/i5/928.htm
DOI: https://dx.doi.org/10.12998/wjcc.v8.i5.928

INTRODUCTION

Atrial fibrillation is the most common persistent arrhythmia. Atrial thrombosis is easily formed in patients with atrial fibrillation, which may embolize the systemic circulation[1]. Vitamin K antagonists, such as warfarin, and novel oral anticoagulants (NOACs), such as dabigatran etexilate and rivaroxaban, are commonly used therapeutic drugs in clinical practice. Routine coagulation monitoring along with the international normalized ratio (INR), and long-term patient education are required if the patient takes warfarin, due to its narrow therapeutic index[2]. Rivaroxaban is a selective inhibitor of factor Xa that may offer safe and effective anticoagulation therapy. As NOACs do not require coagulation monitoring, patients have better compliance with the drug therapy. We here present a case of a 70-year-old man diagnosed with thrombocytopenia that was likely induced by rivaroxaban for atrial fibrillation treatment.

CASE PRESENTATION

Chief complaints

A 70-year-old man presented with intermittent chest tightness and dyspnea over the last five years. The condition had aggravated in the past two days.

History of present illness

There was chest tightness, dyspnea, or perspiration during sleep, and these symptoms had improved slightly after sitting up starting five years ago. The patient visited the emergency department, and an electrocardiogram showed atrial fibrillation rhythm without elevation of myocardial enzymes. Coronary angiography was performed four years ago, suggesting that the coronary artery was generally normal. Chest tightness and dyspnea symptoms aggravated two days ago before presentation; therefore, the patient visited the cardiovascular department of Beijing Tongren Hospital.

History of past illness

The patient had a past medical history of atrial fibrillation, hypertension, hyperlipidemia, hyperuricemia, renal insufficiency and prostatic hyperplasia and had been taking irbesartan, metoprolol, spironolactone, and warfarin irregularly.

Personal and family history

The patient had a smoking and drinking history for 30 years.

Physical examination upon admission

Vital signs were within normal limits at presentation, with a heart rate of 65 beats/min, blood pressure of 138/78 mmHg, respiratory rate of 19 breaths/min, and temperature of 36.1 °C. His height was 178 cm, and his weight was 89 kg.

Laboratory examinations

Laboratory examination indicated a white blood cell count of 8.23×10^9/L, a red blood cell count of 6.64×10^{12}/L, a hemoglobin level of 135 g/L, a hematocrit level of 0.427, and a platelet count of 163×10^9/L. The lactate dehydrogenase level was 233 U/L, and the creatine phosphokinase level was 75 U/L. The total cholesterol level was 4.57 mmol/L, and the low-density lipoprotein cholesterol level was 3.09 mmol/L. The K level was 4.57 mmol/L, and the Na level was 141.9 mmol/L. The plasma glucose level was 4.05 mmol/L, and the glycosylated hemoglobin level was 6.30%. The INR was 1.09, and the thrombin time was 30.5 s.

Imaging examinations

Echocardiography showed slow blood flow in the left atrium and left atrium. He was diagnosed with left ventricular systolic dysfunction.

FINAL DIAGNOSIS

The patient was diagnosed with arrhythmia, persistent atrial fibrillation, dilated cardiomyopathy, cardiac function grade III (NYHA), grade 2 hypertension, hyperlipidemia, hyperuricemia, renal insufficiency and thrombocytopenia.

TREATMENT

Anticoagulant therapy with rivaroxaban (10 mg) was started on the second day of hospitalization. The platelet count decreased to 30 × 10^9/L on hospital day 11 (the 10th day after the start of rivaroxaban). Radiofrequency ablation was performed on hospital day 10 (the 9th day after the start of rivaroxaban), and 9000 U heparin was used during the operation. The platelet count continued to decrease to 10 × 10^9/L on hospital day 12, and rivaroxaban was stopped on day 13 when the platelet count decreased to 5 × 10^9/L. The coagulation function test indicated a prothrombin time of 12.6 s, an INR of 1.07, an activated partial thrombin time of 31.7 s, a thrombin time of 15.5 s, a fibrinogen level of 6.07, and a fibrin/fibrinogen degradation products level of 5.48. No significant abnormalities were found in the coagulation or fibrinolytic system. Immune-related thrombocytopenia was also taken into consideration at first, but autoimmune group tests showed negative results. Finally, the patient's thrombocytopenia was strongly suspected to be drug induced. On hospital day 13, the drugs metoprolol, spironolactone, benazepril, atorvastatin, pantoprazole, and rivaroxaban were administered. The patient had been taking these drugs before admission with the exception of atorvastatin, pantoprazole, and rivaroxaban. Since thrombocytopenia was not listed as an adverse effect on the package insert of atorvastatin or pantoprazole, we considered the possibility that the thrombocytopenia was caused by rivaroxaban. On hospital day 14 (the 2nd day after the cessation of rivaroxaban), the platelet count increased to 36 × 10^9/L. On day 15 (the 3rd day after the cessation of rivaroxaban), the platelet count was 60 × 10^9/L. As the patient underwent the radiofrequency ablation during hospitalization, subsequent anticoagulation therapy was needed, and warfarin was used instead of rivaroxaban on hospital day 15.

OUTCOME AND FOLLOW-UP

The platelet count was 98 × 10^9/L on day 17 (the 5th day after cessation) and then increased to 121 × 10^9/L within the normal range, on day 19. Subsequent anticoagulation therapy included use of warfarin with careful INR monitoring and dose adjustments. Changes in platelet count during the whole period of hospitalization are shown in Figure 1.

DISCUSSION

Drugs can cause thrombocytopenia, either by the direct toxicity of platelet formation in bone marrow or by increasing platelet destruction through an immune-mediated mechanism[3,4]. The incidence of thrombocytopenic toxicity from NOACs is extremely low[5,6], and only two such cases caused by rivaroxaban had been reported[7,8]. The mechanism of rivaroxaban-induced thrombocytopenia is not yet clear. In the present case, no cell diseases were observed except for thrombocytopenia. In addition, the platelet count improved rapidly once rivaroxaban was discontinued. The package inserts in China for rivaroxaban, updated on April 2017, mentioned thrombocytopenia as a postmarketing adverse reaction. The study on platelet toxicity induced by factor Xa inhibitors is limited. We suspected immune-related thrombocytopenia initially, but the negative autoimmune results excluded this possibility. As heparin was used during the radiofrequency ablation, we also suspected that it was heparin-induced thrombocytopenia (HIT). HIT usually occurs after 5-10 d of continuous heparin therapy. For patients with recent (100 d or less) heparin exposure, HIT may also develop within the first 24 h of heparin exposure[9]. In

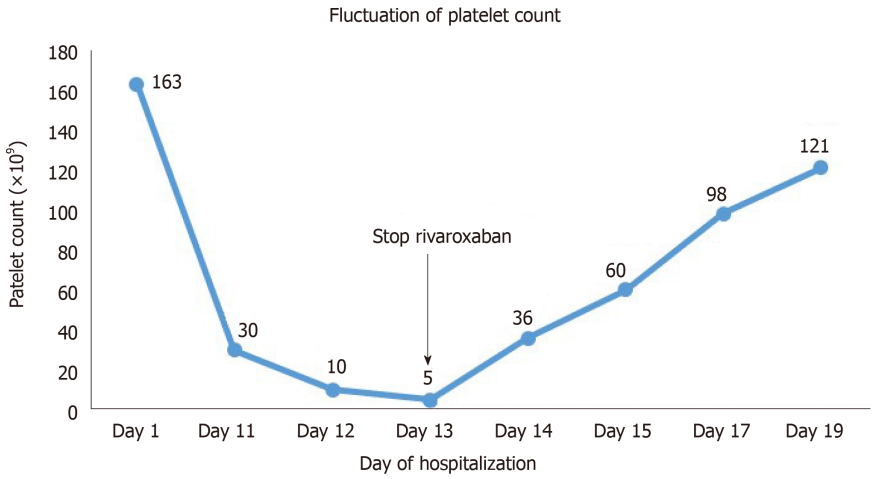

Figure 1 Changes in platelet count during the whole period of hospitalization.

our case, heparin was only used once during the operation and the patient had no history of other heparin exposure. If the platelets had decreased significantly before using heparin, we could have more confidently asserted that the thrombocytopenia was caused by rivaroxaban. Unfortunately, we did not obtain blood test results before using heparin. The Naranjo adverse drug reaction probability scale was used, leading to a calculated score of 4 for rivaroxaban.

CONCLUSION

We describe a case of thrombocytopenia likely induced by rivaroxaban. Thrombocytopenia during anticoagulation therapy may be associated with a high risk of life-threatening bleeding. For elderly patients, changes in platelet count should be carefully monitored at the beginning of NOAC treatment, and we should be on the alert for bleeding events as well. Creatinine clearance and hemoglobin levels should also be measured before a NOAC is used.

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