

World Journal of *Clinical Cases*

World J Clin Cases 2020 March 6; 8(5): 854-1001



**ORIGINAL ARTICLE****Clinical and Translational Research**

- 854** Repair mechanism of astrocytes and non-astrocytes in spinal cord injury
Liu XY, Guo JW, Kou JQ, Sun YL, Zheng XJ

Case Control Study

- 864** Study on the correlation and predictive value of serum pregnancy-associated plasma protein A, triglyceride and serum 25-hydroxyvitamin D levels with gestational diabetes mellitus
Ren Z, Zhe D, Li Z, Sun XP, Yang K, Lin L
- 874** Significance of ^{125}I radioactive seed implantation on growth differentiation factor and programmed death receptor-1 during treatment of oral cancer
Xue G, Feng Y, Li JB

Observational Study

- 887** Computed tomography-based score model/nomogram for predicting technical and midterm outcomes in transjugular intrahepatic portosystemic shunt treatment for symptomatic portal cavernoma
Niu XK, Das SK, Wu HL, Chen Y

META-ANALYSIS

- 900** Efficacy of totally laparoscopic compared with laparoscopic-assisted total gastrectomy for gastric cancer: A meta-analysis
Wang S, Su ML, Liu Y, Huang ZP, Guo N, Chen TJ, Zou ZH

CASE REPORT

- 912** Allograft artery mycotic aneurysm after kidney transplantation: A case report and review of literature
Bindi M, Ferraresso M, De Simeis ML, Raison N, Clementoni L, Delbue S, Perego M, Favi E
- 922** Oxcarbazepine for trigeminal neuralgia may induce lower extremity weakness: A case report
Song HG, Nahm FS
- 928** Acute thrombocytopenia after anticoagulation with rivaroxaban: A case report
He XY, Bai Y
- 932** Surgical resection of a large hypopharyngeal hemangioma in an adult using neodymium-doped yttrium aluminum garnet laser: A case report
Jin M, Wang CY, Da YX, Zhu W, Jiang H

- 939** Combining surgery with ¹²⁵I brachytherapy for recurrent mediastinal dedifferentiated liposarcoma: A case report and review of literature
Chen HG, Zhang K, Wu WB, Wu YH, Zhang J, Gu LJ, Li XJ
- 940** Combining surgery with ¹²⁵I brachytherapy for recurrent mediastinal dedifferentiated liposarcoma: A case report and review of literature
Chen HG, Zhang K, Wu WB, Wu YH, Zhang J, Gu LJ, Li XJ
- 946** Extrapontine myelinolysis caused by rapid correction of pituitrin-induced severe hyponatremia: A case report
Fang LJ, Xu MW, Zhou JY, Pan ZJ
- 947** Extrapontine myelinolysis caused by rapid correction of pituitrin-induced severe hyponatremia: A case report
Fang LJ, Xu MW, Zhou JY, Pan ZJ
- 954** Total endovascular repair of an intraoperative stent-graft deployed in the false lumen of Stanford type A aortic dissection: A case report
Li XR, Tong YH, Li XQ, Liu CJ, Liu C, Liu Z
- 955** Total endovascular repair of an intraoperative stent-graft deployed in the false lumen of Stanford type A aortic dissection: A case report
Li XR, Tong YH, Li XQ, Liu CJ, Liu C, Liu Z
- 963** Muscular involvement of extranodal natural killer/T cell lymphoma misdiagnosed as polymyositis: A case report and review of literature
Liu LH, Huang Q, Liu YH, Yang J, Fu H, Jin L
- 971** Two bone blocks sandwich technique for horizontal reconstruction of severely atrophic alveolar ridge in anterior maxilla: A case report
Xia HB, Zhang YF, Shi B, Wang M
- 980** Anomalous retinal artery associated with branch retinal artery occlusion and neovascular glaucoma: A case report
Yang WJ, Yang YN, Cai MG, Xing YQ
- 986** Misdiagnosis of primary intimal sarcoma of the pulmonary artery as chronic pulmonary embolism: A case report
Lu P, Yin BB
- 995** Late-onset multiple acyl-CoA dehydrogenase deficiency with cardiac syncope: A case report
Pan XQ, Chang XL, Zhang W, Meng HX, Zhang J, Shi JY, Guo JH

ABOUT COVER

Editorial Board Member of *World Journal of Clinical Cases*, Hitoshi Hirose, MD, PhD, Associate Professor, Department of Cardiothoracic Surgery, Thomas Jefferson University, Philadelphia, PA 19107, United States

AIMS AND SCOPE

The primary aim of *World Journal of Clinical Cases* (WJCC, *World J Clin Cases*) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

INDEXING/ABSTRACTING

The WJCC is now indexed in PubMed, PubMed Central, Science Citation Index Expanded (also known as SciSearch®), and Journal Citation Reports/Science Edition. The 2019 Edition of Journal Citation Reports cites the 2018 impact factor for WJCC as 1.153 (5-year impact factor: N/A), ranking WJCC as 99 among 160 journals in Medicine, General and Internal (quartile in category Q3).

RESPONSIBLE EDITORS FOR THIS ISSUE

Responsible Electronic Editor: *Yan-Xia Xing*

Proofing Production Department Director: *Yun-Xiaojuan Wu*

NAME OF JOURNAL

World Journal of Clinical Cases

ISSN

ISSN 2307-8960 (online)

LAUNCH DATE

April 16, 2013

FREQUENCY

Semimonthly

EDITORS-IN-CHIEF

Dennis A Bloomfield, Bao-Gan Peng, Sandro Vento

EDITORIAL BOARD MEMBERS

<https://www.wjnet.com/2307-8960/editorialboard.htm>

EDITORIAL OFFICE

Jin-Lei Wang, Director

PUBLICATION DATE

March 6, 2020

COPYRIGHT

© 2020 Baishideng Publishing Group Inc

INSTRUCTIONS TO AUTHORS

<https://www.wjnet.com/bpg/gerinfo/204>

GUIDELINES FOR ETHICS DOCUMENTS

<https://www.wjnet.com/bpg/GerInfo/287>

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH

<https://www.wjnet.com/bpg/gerinfo/240>

PUBLICATION MISCONDUCT

<https://www.wjnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

<https://www.wjnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>

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).

Open-Access: This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

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 $163 \times 10^9/L$ on admission. Anticoagulant therapy with rivaroxaban, a NOAC, was started on the second day of hospitalization. The platelet count decreased to $30 \times 10^9/L$ on hospital day 11 and then $10 \times 10^9/L$ on day 12. Rivaroxaban was stopped on day 13 when the platelet count decreased to $5 \times 10^9/L$. 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

©The Author(s) 2020. Published by Baishideng Publishing Group Inc. All rights reserved.

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.wjnet.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 $8.23 \times 10^9/L$, a red blood cell count of $6.64 \times 10^{12}/L$, a hemoglobin level of 135 g/L, a hematocrit level of 0.427, and a platelet count of $163 \times 10^9/L$. 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 $30 \times 10^9/L$ 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 $10 \times 10^9/L$ on hospital day 12, and rivaroxaban was stopped on day 13 when the platelet count decreased to $5 \times 10^9/L$. 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 $36 \times 10^9/L$. On day 15 (the 3rd day after the cessation of rivaroxaban), the platelet count was $60 \times 10^9/L$. 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 $98 \times 10^9/L$ on day 17 (the 5th day after cessation) and then increased to $121 \times 10^9/L$ 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

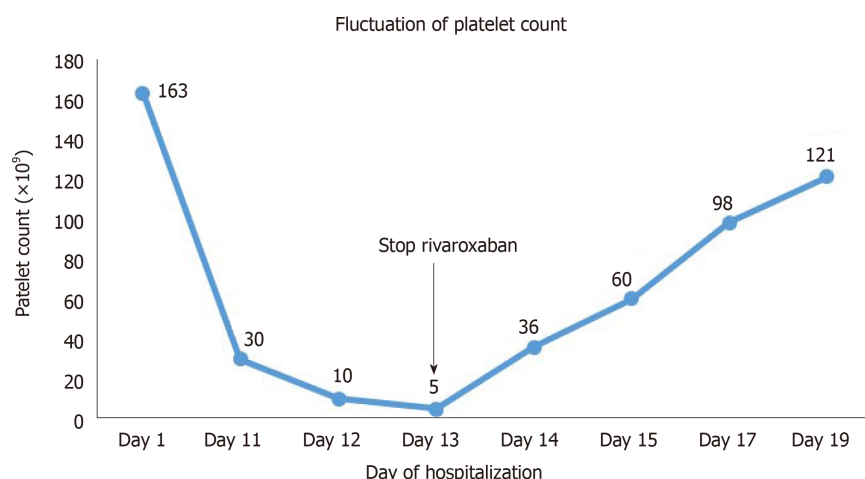


Figure 1 Changes in platelet count during the whole period of hospitalization.

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.

REFERENCES

- 1 **Wolf PA**, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. *Stroke* 1991; **22**: 983-988 [PMID: 1866765 DOI: 10.1161/01.str.22.8.983]
- 2 **Ansell J**, Hirsh J, Hylek E, Jacobson A, Crowther M, Palareti G. Pharmacology and management of the vitamin K antagonists: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). *Chest* 2008; **133**: 160S-198S [PMID: 18574265 DOI: 10.1378/chest.08-0670]
- 3 **van den Bemt PM**, Meyboom RH, Egberts AC. Drug-induced immune thrombocytopenia. *Drug Saf* 2004; **27**: 1243-1252 [PMID: 15588119 DOI: 10.2165/00002018-200427150-00007]
- 4 **Carey PJ**. Drug-induced myelosuppression: diagnosis and management. *Drug Saf* 2003; **26**: 691-706 [PMID: 12862504 DOI: 10.2165/00002018-200326100-00003]
- 5 **Granger CB**, Alexander JH, McMurray JJ, Lopes RD, Hylek EM, Hanna M, Al-Khalidi HR, Ansell J, Atar D, Avezum A, Bahit MC, Diaz R, Easton JD, Ezekowitz JA, Flaker G, Garcia D, Gerasides M, Gersh BJ, Golitsyn S, Goto S, Hermosillo AG, Hohnloser SH, Horowitz J, Mohan P, Jansky P, Lewis BS, Lopez-Sendon JL, Pais P, Parkhomenko A, Verheugt FW, Zhu J, Wallentin L; ARISTOTLE Committees and Investigators. Apixaban versus warfarin in patients with atrial fibrillation. *N Engl J Med* 2011; **365**: 981-992 [PMID: 21870978 DOI: 10.1056/NEJMoal107039]
- 6 **Hori M**, Matsumoto M, Tanahashi N, Momomura S, Uchiyama S, Goto S, Izumi T, Koretsune Y, Kajikawa M, Kato M, Ueda H, Iwamoto K, Tajiri M; J-ROCKET AF study investigators. Rivaroxaban vs. warfarin in Japanese patients with atrial fibrillation – the J-ROCKET AF study –. *Circ J* 2012; **76**: 2104-2111 [PMID: 22664783 DOI: 10.1253/circj.cj-12-0454]
- 7 **Mima Y**, Sangatsuda Y, Yasaka M, Wakugawa Y, Nagata S, Okada Y. Acute thrombocytopenia after initiating anticoagulation with rivaroxaban. *Intern Med* 2014; **53**: 2523-2527 [PMID: 25366015 DOI: 10.2169/internalmedicine.53.2890]
- 8 **Pop MK**, Farokhi F, Iduna L. Drug-induced thrombocytopenia after anticoagulation with rivaroxaban. *Am J Emerg Med* 2018; **36**: 531.e1-531.e2 [PMID: 29306643 DOI: 10.1016/j.ajem.2017.12.052]
- 9 **Warkentin TE**, Kelton JG. Temporal aspects of heparin-induced thrombocytopenia. *N Engl J Med* 2001; **344**: 1286-1292 [PMID: 11320387 DOI: 10.1056/NEJM200104263441704]



Published By Baishideng Publishing Group Inc
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: bpgoffice@wjgnet.com
Help Desk: <https://www.f6publishing.com/helpdesk>
<https://www.wjgnet.com>

