Case Report

ANNALS OF MEDICINE & SURGERY

OPEN

Secondary thrombocythemia with ST-segment elevation myocardial infarction as the first manifestation: a case report

Ke Su, MSc[a], Ling Hou, MSc[b], Jinbo Zhao, MSc[a], Yuanhong Li, PhD[a,*]

Introduction: Secondary thrombocythemia (ST), also called reactive thrombocytosis, is caused by a disorder that triggers increased production by normal platelet-forming cells and is characterized by the abnormally increased number of platelet and megakaryocytes in the bone marrow. Previous reports have found complications from malignant tumors, chronic inflammation, acute inflammation, acute hemorrhage, splenectomy, etc. to be the common causes of ST. However, reports of secondary thrombocytosis caused by antibiotics are limited and there are no reports of secondary thrombocytosis with acute myocardial infarction as the first presentation. If the patient is at high risk of thrombosis, intensive antithrombotic therapy is required. To raise clinicians' awareness of drug-induced secondary thrombocytosis and to enhance antithrombotic therapy for high-risk patients, this article presented a case of drug-induced secondary thrombocytosis with acute ST-segment elevation myocardial infarction as the primary manifestation.

Case presentation: An 80-year-old woman was admitted with cardiogenic shock due to post-activity chest pain. She was started on aspirin and clopidogrel antiplatelet therapy, then replaced aspirin with indolibuprofen, which has relatively few side effects. There was no significant decrease in platelet counts during treatment.

Clinical discussion: Secondary thrombocythemia, characterized by nonspecific symptoms, is difficult to diagnose. Secondary thrombocytosis with acute myocardial infarction as the first symptom is uncommon, but is very urgent and associated with a poor prognosis. What's more, cause-specific treatment counts for secondary thrombocythemia. Therefore it is important to search for the causal factor of secondary thrombocytosis. Secondary thrombocytosis caused by cephalosporins is rare. There is a need to arouse the attention of clinicians to the ST caused by cephalosporins and to provide a guide of treatment to these patients.

Conclusion: After a thorough analysis of the pertinent literature, we discovered that several retrospective studies demonstrated the effectiveness of cytoreductive therapy in significantly reducing platelet counts. Based on this finding, we prescribed hydroxyurea to our patient, which led to a gradual decrease in platelet count and ultimately resulted in a return to normal levels.

Keywords: case report, secondary thrombocythemia, ST-segment elevation myocardial infarction

Introduction

Essential thrombocythemia is a major cause of thrombogenesis and is defined by a peripheral platelet count greater than the upper limit of normal or greater than $450 \times 109/l$[1]. According to the etiology, thrombocytosis can be defined as primary or essential thrombocytosis caused by a clonal bone marrow defect such as myeloproliferative neoplasm, secondary thrombocytosis (ST), or inherited thrombocytosis.

Secondary thrombocytosis (ST), also known as reactive thrombocytosis, is brought on by a condition that causes normal platelet-forming cells to produce more platelets than usual. Malignant tumors, chronic inflammation, acute inflammation, acute hemorrhage, spleen removal, medications, and other

HIGHLIGHTS

- Drug-induced secondary thrombocytosis has been reported infrequently and often goes unnoticed by clinicians.
- The symptoms of secondary thrombocytosis are not obvious, making it difficult to detect and diagnose early.
- Secondary thrombocytosis with acute myocardial infarction as the initial symptom is rare, and the onset is urgent with a mostly unfavorable prognosis. It is important to diagnose and treat it promptly.
- This article describes a rare case of drug-induced secondary thrombocytosis for high platelet count with acute ST-segment elevation myocardial infarction as the main manifestation.

[a]Cardiovascular Disease Center, Central Hospital of Tujia and Miao Autonomous Prefecture, Hubei University of Medicine, Enshi Prefecture and [b]Department of Central Hospital of Tujia and Miao Autonomous Prefecture, Hubei University of Medicine, Shiyan, Hubei Province, People's Republic of China

Ke Su and Ling Hou contributed equally to this work.

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

*Corresponding author. Address: Cardiovascular Disease Center, Central Hospital of Tujia and Miao Autonomous Prefecture, Hubei University of Medicine, Enshi Prefecture 445000, Hubei Province, People's Republic of China. Tel.: +139 868 438 63. E-mail: lyh0101@vip.163.com (Y. Li).

Annals of Medicine & Surgery (2023) 85:4145–4149

Received 28 April 2023; Accepted 1 July 2023

Published online 10 July 2023

http://dx.doi.org/10.1097/MS9.0000000000001067

disorders are known to frequently cause it. Drug-induced ST is less commonly reported, with a total of 198 reported cases of drug-induced ST identified to date. The drugs that may cause ST are summarized as follows: antineoplastic drugs, hematological drugs, antibacterial drugs, skin drugs, antipsychotic drugs, endocrine system, and immune system drugs, etc. Of these, cephalosporins are less commonly reported to cause ST.

Our patient was diagnosed as secondary thrombocytosis due to long-term cephalosporin exposed and had ST-segment elevation myocardial infarction as the first manifestation. The patient's routine blood results suggest persistently elevated platelets and a decreased platelet aggregation response. It is suggested that platelet function should be routinely screened in patients taking long-term antibiotics and antithrombotic therapy should be initiated promptly in high-risk patients.

This case report has been reported in accordance with the SCARE (Surgical CAse REport) criteria[2].

Case presentation

We now report a case of an 80-year-old female who was admitted with post-active chest pain leading to cardiogenic shock. The patient has above 1 year of taking cephalosporins for unknown reasons and no history of hematological tumors, no family history of thrombocytosis, and no previous angina-like attacks.

In terms of physical examination, the patient was in shock on admission, with undetectable blood pressure and a heart rate of 60 beats/min. The patient is apathetic, with a painful face and cold, wet limbs. And no other positive signs were found. Admission ECG was consistent with anterior wall + high lateral wall myocardial infarction changes (Fig. 1).

For the results of laboratory examinations, her initial peripheral blood panel findings were as follows: myoglobin >700 ng/ml, NT-proBNP 284 pg/ml, and CTnT 185 ng/l. The routine blood results on admission suggested an abnormally high platelet count and the dynamic follow-up blood results after admission are shown in Table 1. Other blood biochemistry results including lipids, liver and kidney function are generally normal.

Considering imaging, cardiac ultrasound (Fig. 2) indicates severely reduced left ventricular ejection fraction, consistent with left ventricular infarct changes.

On admission, the patient was in poor general condition and was given a boost and noninvasive ventilator-assisted breathing. Emergency coronary angiography showed (Fig. 3): ~90% stenosis in the middle segment of the left main stem, 80–90% in the middle segment of the proximal anterior descending branch, and a large number of attached thrombi in the vessel. TIMI (thrombolysis in myocardial infarction) grade 2 flow was found in the distal segment of the anterior descending branch. Due to the patient's admission time of more than 72 h and the patient's heavy thrombotic load, direct percutaneous coronary intervention (PCI) is not considered for the time being and elective PCI is proposed in accordance with PCI guidelines[3]. We then gave the patient symptomatic treatment such as pressure raising, fluid replacement and volume expansion, antiplatelet aggregation, and anti-embolism, but the patient's platelet count did not decrease significantly after taking antiplatelet aggregation drugs such as aspirin and indolibuprofen (Table 1).

The patient's platelets were consistently elevated during her hospital stay, all greater than 500, and the patient was diagnosed with thrombocythemia according to the relevant guidelines[4]. We then performed genetic testing on the patient. Negative results for genes associated with essential thrombocythemia including JAK2 V617F, MPL W515L/K, BCR-ABL (P190, P210/P230) fusion gene, and exon 12 of the JAK2 gene. Bone aspiration results (Fig. 4) showed hypoplasia, no megakaryocytes, predominantly neutrophilic cell classification, and scattered aggregates of peripheral platelets were common. Based on the genetic test results and the relevant literature, essential thrombocythemia was ruled out and secondary thrombocytosis was considered, which, together with the patient's medical history, was further considered to be secondary thrombocytosis caused by cephalosporin antibiotics with acute myocardial infarction as the first symptom[5,6].

After the patient's diagnosis was confirmed and relevant literatures were reviewed[7,8], we treated him with hydroxyurea

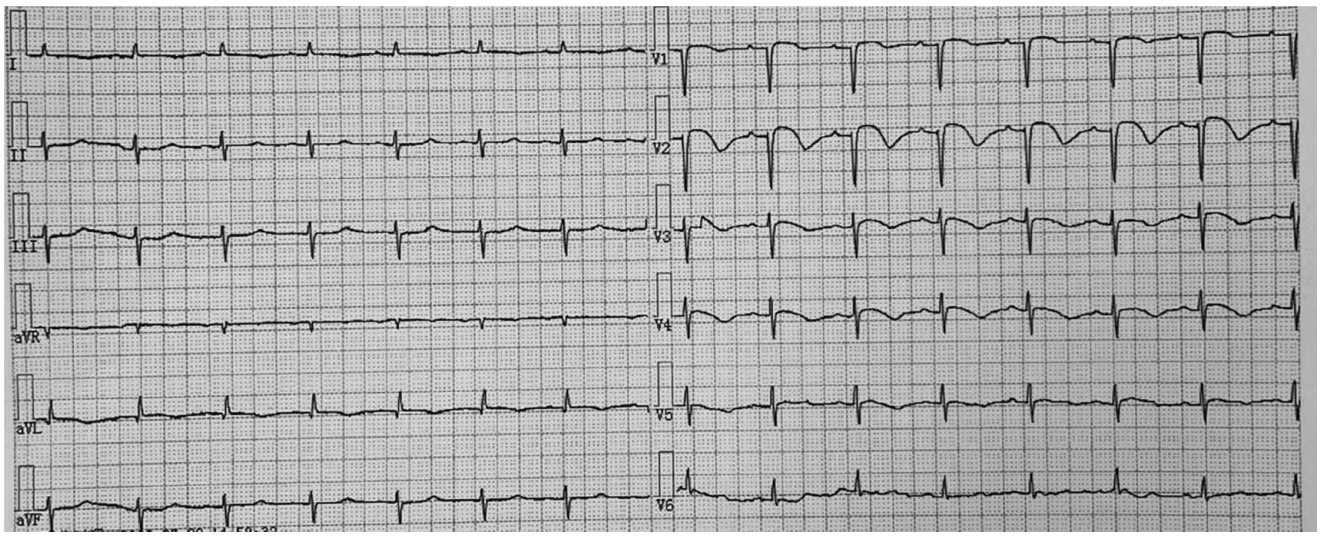

Figure 1. Patient admitted with an emergency ECG consistent with anterior + high lateral wall myocardial infarction.

Table 1

Changes in laboratory index and medication regimens during patient hospital stay

Date	WBC	N%	PLT	RBC	Hb	HCT	MPV	PCT%	Therapeutic regimen	
July7[a]	11.74	89.2	596	3.37	99	0.309	8.3	0.493	Aspirin	Clopidogrel
July14[a]	8.13	73.5	669	3.57	102	0.316	9	0.559		
July18[a]									Aspirin	Ticagrelor
July26[a]									Indobufen	Ticagrelor

[a]The date of the patient's admission to our hospital.

Hb, hemoglobin; MPV, mean platelet volume; N, the count of neutrophils; PCT, procalcitonin; PLT, platelet; RBC, the number of red blood cell; WBC, the count of white blood cell.

and his platelet count started to fall. After the patient's condition stabilized with symptomatic management such as pressure boosting and rehydration, She was treated by a cardiologist with elective PCI and implanted three drug-eluting stents in the anterior descending branch. The patient was discharged from the hospital in good condition and was advised to continue to take hydroxyurea outside the hospital and to review his blood count dynamically. The routine blood test results were normal at 1 week postoperatively.

Discussion

The annual incidence of essential thrombocythemia is about 1–2.5 per 100 000, mostly in older people (50–60 years old)[9], but the true annual incidence of essential thrombocythemia may be even higher, as many patients may remain asymptomatic for a long time without being diagnosed. 50% of patients with essential thrombocythemia are diagnosed because of abnormal platelet counts on blood counts for other conditions[10].

Essential thrombocythemia is a clonal disorder of hematopoietic stem cells characterized by a persistent increase in platelets, splenomegaly, thrombosis, and hemorrhage. The cause is still unclear and is divided into primary thrombocytosis and secondary thrombocytosis, with thrombotic complications being the main cause of morbidity and mortality, the most frequent sites of thrombotic accumulation being the cerebral vessels and coronary arteries. Secondary thrombocytosis is a thrombocytosis caused by accelerated platelet production, the cause of which is not yet known, and the cause of thrombosis may be related to the massive spontaneous aggregation of platelets in the blood vessels. The cause of thrombosis may be related to the large spontaneous aggregation of platelets in the vessels.

After reviewing the extensive literature[11–18], we found that antibiotics including quinolones, fluconazole, and voriconazole, can also cause secondary thrombocytosis. However, there are few reports of secondary thrombocytosis caused by cephalosporins, and there have been no reports of secondary thrombocytosis caused by cephalosporins with acute myocardial infarction as the first symptom.

The patient has no previous history of cardiovascular disease, a history of above 1 year of cephalosporin use, and the diagnosis of secondary thrombocythemia was made after excluding primary thrombocythemia with the patient's routine blood results and genetic test results. The causes of acute myocardial infarction secondary to thrombocytosis may be thrombocytosis, an increase in the number of platelets and their altered structure and function, increased blood viscosity, and altered platelet surface glycoprotein receptors, which promote platelet adhesion, aggregation, and activation, facilitating thrombosis and the occurrence of coronary embolic events.

According to the recommendations of the guidelines[19], patients have a better prognosis when their platelet count does not exceed 1000×10^9/l, and a single antiplatelet aggregation treatment with aspirin is generally recommended. Before administering warfarin for venous thromboembolism, laboratory

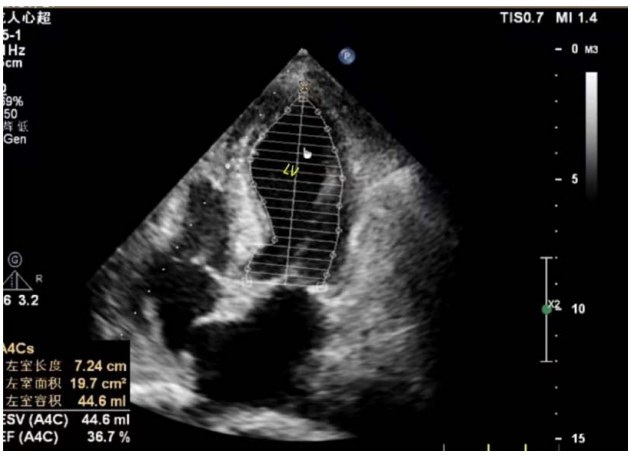

Figure 2. The patient's bedside ultrasound showed a severely reduced left ventricular ejection fraction, consistent with ECG changes.

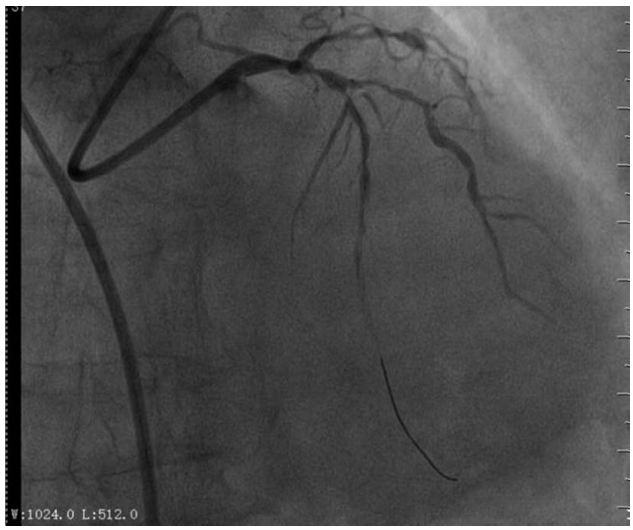

Figure 3. Coronary angiogram showing ~90% stenosis of the mid-left main stem and mid-proximal anterior descending branch stenosis with massive intravascular thrombosis.

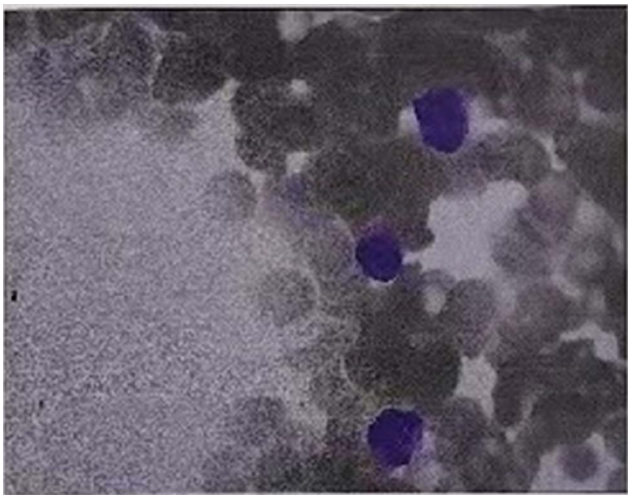

Figure 4. Bone marrow aspiration shows hypoplasia, no megakaryocytes, and predominantly neutrophilic cell classification.

and imaging tests were conducted to rule out other secondary causes of thrombocytosis. However, during our actual consultation, the use of aspirin as part of the patient's treatment did not yield any significant change in their platelet count. After reviewing the data[20], we decided to treat the patient with hydroxyurea chemotherapy, and with the use of hydroxyurea, the patient's platelet count began to gradually decrease and his symptoms were improving. While platelets are now significantly lower in patients treated with hydroxyurea, there is still a risk of in-stent thrombosis after PCI. Therefore, it is still necessary to review the platelets regularly and adjust the dose of hydroxyurea accordingly to keep the platelets within normal limits and reduce the incidence of thrombotic events. Our focus in this article is, therefore, also to add to the knowledge of secondary platelet therapy and to suggest that the combination of chemotherapeutic agents should be considered in high-risk patients at risk of embolism after the ineffective use of combination antiplatelet aggregation agents.

In this article, we describe a case of cephalosporin-induced secondary thrombocytosis with acute myocardial infarction as the first symptom to raise awareness of secondary thrombocytosis for clinicians and to highlight the importance of using hydroxyurea in such patients. Meanwhile, this article adds to the existing literature on secondary thrombocytosis caused by antibiotics, specifically cephalosporins. While antibiotics have been previously identified as a potential cause of secondary thrombocytosis, there are few reported cases of cephalosporin-induced thrombocytosis. This case report adds to the body of literature on this topic and raises awareness among clinicians of the potential for this rare side effect.

Ethical approval

As the case report contains information on the retrospective period, we obtained an exemption for ethical approval from the Institutional Ethical Committee.

Consent

Written informed consent was obtained from the patient for the publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Sources of funding

This work was supported by Enshi Tujia and Miao Autonomous Prefecture Bureau of Science and Technology (Grant Number E20180002).

Author contribution

K.S. and L.H.: led the initial writing of the manuscript, conducted the literature review, revised the manuscript, and was involved in the care of the patient; J.Z.: contributed to the writing of the manuscript, revised the manuscript, and was involved in the care of the patient; Y.L.: led the writing of the final manuscript, revised the manuscript, and was involved in the care of the patient. All the authors approved the final manuscript as submitted.

Conflicts of interest disclosure

There are no conflicts of interest.

Research registration unique identifying number (UIN)

1. Name of the registry: not applicable.
2. Unique identifying number or registration ID: not applicable.
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): not applicable.

Guarantor

The guarantor of this study is Yuanhong Li.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Data availability statement

All supporting documents are submitted along with the case report.

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