

A case of simultaneous acute cardio-cerebral infarction in a woman with essential thrombocythemia

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Abstract

Essential thrombocythemia (ET) can cause arterial embolism. Patients with arterial thrombosis usually have additional risk factors, such as smoking and hypertension. We report a 70-year-old woman with ET who had no risk factors, except for age. Cranial magnetic resonance imaging showed fresh lacunar infarction in several lobes. Electrocardiography showed ST-segment elevation in leads II, III, and aVF. Coronary angioplasty and stenting were successfully performed. We checked the bone marrow and performed genetic testing. The Janus kinase 2 (JAK2) V617F gene mutation was found. This case was a rare initial presentation of previously undiagnosed ET with embolism of cardiovascular and cerebral vessels. Anti-platelet drugs and hydroxyurea were used to prevent further thrombosis in the coronary and cerebral arteries.

Keywords

Essential thrombocythemia, myocardial infarction, cerebral artery, Janus kinase 2 V617F, arterial thrombosis, embolism

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Introduction

Essential thrombocythemia (ET) is a chronic myeloproliferative neoplasm.¹ ET can result in arterial thrombosis. Approximately 2% patients with ET may develop arterial embolism.² However, multiple arterial embolizations caused by ET at

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the same time are rare. A Janus kinase 2 (JAK2) V617F activating mutation is present in 50% to 60% of ET cases. JAK2-mutated patients with ET are more likely to suffer from a major thrombotic event.³ Hypertension, cigarette smoking, age older than 60 years, and a history of major ischemic events are risk factors for atherothrombotic complications in patients with ET. We report a case of rare initial presentation of previously undiagnosed ET with embolism of cardiovascular and cerebral vessels. The findings in our case suggest that physicians should be aware of an abnormally elevated platelet count, and ET-induced arterial embolism may occur as multiple embolizations.

Case report

A 70-year-old woman was admitted to the hospital with dizziness lasting for 1 day without chest pain. A physical examination showed a blood pressure of 148/62 mmHg, heart rate of 74 beats/minute, and inspiratory rate of 20 beats/minute. A general physical and systemic examination was normal. There were no abnormal heart sounds or murmur. Cranial magnetic resonance imaging (diffusion-weighted imaging sequence)

showed a fresh lacunar infarction in the left parietal lobe and the right frontotemporal lobe (Figure 1). On the second day, routine electrocardiography showed ST-segment elevation in leads II, III, and aVF (Figure 2). A further laboratory examination showed that the troponin I level was significantly elevated, which was consistent with inferior myocardial infarction.

Aspirin, clopidogrel, and unfractionated heparin treatment was started immediately. Coronary angiography showed subtotal occlusion and a thrombus-like filling defect in the right coronary artery (Figure 3a). The left coronary arteries were angiographically normal (Figure 3b). Coronary angioplasty and stenting (3.0 × 29 mm) were successfully performed (Figure 3c). A Thrombolysis In Myocardial Infarction grade 3 flow was obtained.

The patient initially had a slightly elevated platelet count ($466 \times 10^3/\text{mm}^3$). We were concerned about this anomaly and the platelet count ($978 \times 10^3/\text{mm}^3$) had doubled in 3 days. Further bone marrow biopsy showed a markedly high number of megakaryocytes, which were clustered and increased in size. Genetic testing showed

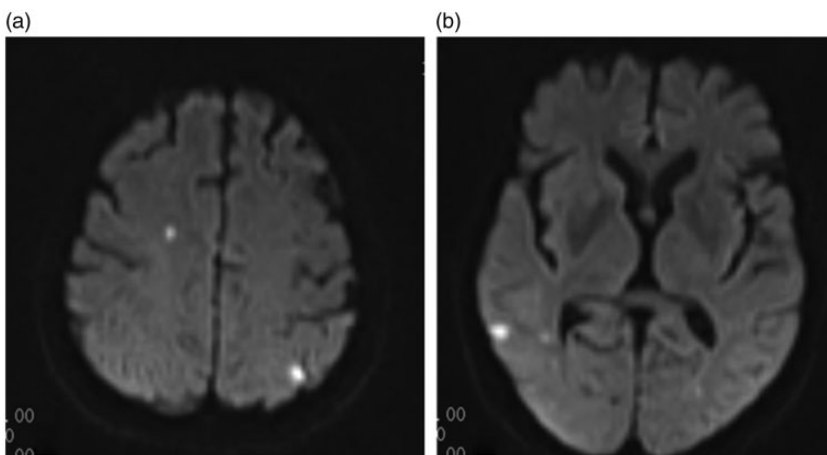


Figure 1. Cranial magnetic resonance images (diffusion-weighted imaging sequence) of the patient. Multiple fresh lacunar infarcts can be seen in the left parietal lobe, right frontal lobe (a) and right frontal lobe (b).



Figure 2. Electrocardiogram of the patient. The electrocardiogram shows that ST segments in leads II, III, and aVF are elevated.

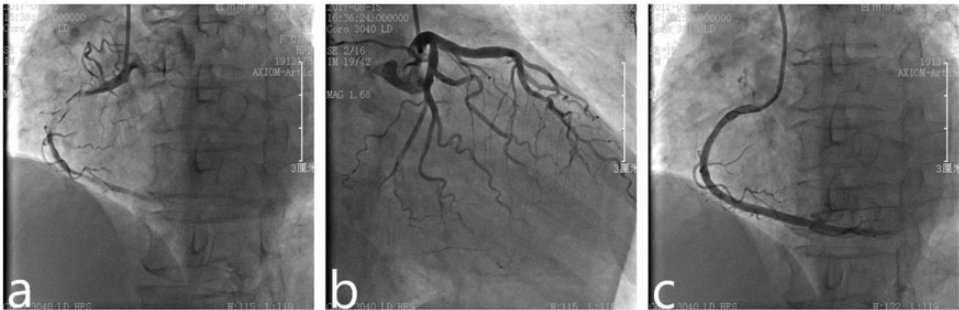


Figure 3. Primary coronary angiography shows subtotal occlusion and a thrombus-like filling defect in the right coronary artery (a). There was no obvious stenosis in the left coronary artery (b). Coronary stenting (3.0×29 mm) was performed (c). Thrombolysis In Myocardial Infarction grade 3 flow was obtained.

30% mutation of the JAK2 V617F gene, while the BCR-ABL gene was negative. The diagnosis of ET was clear according to the 2016 World Health Organization diagnostic criteria for ET.

The patient was non-smoker with no family history of lipidemia, diabetes mellitus, hypertension, or coronary artery disease. Hydroxyurea treatment was added

to the treatment and the patient was discharged.

This report was prepared in compliance with CARE guidelines (<https://www.care-statement.org>). The Ethics Committee of Taizhou First People's Hospital approved the study protocol. Written informed consent was obtained from the patient for publication of this report and accompanying images.

Discussion

ET is a chronic myeloproliferative neoplasm. An increased number of functionally altered thrombocytes leads to thromboembolic complications in the arterial and venous system. In a retrospective, clinical series of 1144 patients with ET, Montanaro et al.⁴ reported an annual rate of thrombotic events of 1.4%, with cerebral and coronary involvement being the first and second in terms of frequency, respectively. With regard to our case, misdiagnosis or a missed diagnosis could have occurred because our patient had combined intracranial and coronary thrombosis at the same time. The patient only had dizziness and no chest pain at the time of onset, although an electrocardiogram indicated elevation of the ST segment in inferior wall leads and marked elevation of myocardial markers.

Because thrombocytosis is occasionally detected, the possibility of reactive thrombocytosis needs to be considered. Reactive thrombocytosis is caused by elevated levels of thrombopoietin and other cytokines, such as interleukin-6, without abnormal changes in bone marrow. The most common causes of reactive thrombocytosis include tissue damage from surgery, infection, malignant tumors, and postoperative status.⁵ Secondary thrombocytosis can lead to severe and even lethal arterial visceral thrombosis.⁶ Our patient did not have these causes and had bone marrow abnormalities. Hypertension and cigarette smoking are risk factors for development of thrombosis in patients with ET.⁷ An age older than 60 years and a history of major ischemic events are also risk factors for atherothrombotic complications in patients with ET.⁸ Apart from age, our patient had no additional risk factor for myocardial infarction, such as hypertension, hyperlipidemia, smoking, and diabetes mellitus.

The JAK2 V617F mutation, which is an acquired gain-of-function mutation in exon

14 of the JAK2 gene, is present in 50% to 60% of patients with ET. Arterial embolism is more likely to occur in patients with positive JAK2 V617F mutations.⁹ Unfortunately, the JAK2 V617F gene mutation was found in our patient.

In our case, platelet counts ($466 \times 10^3/\text{mm}^3$) were not greatly increased at admission, but atherothrombotic complications occurred. Patients with high platelet counts should be evaluated carefully. ET complicated by coronary artery thrombosis has no uniform treatment guidelines worldwide. Therefore, clinical treatment of ET is difficult. Platelet-lowering therapy with hydroxyurea was started in our patient because she was classified as high risk for thrombotic complications. The first-line drug of choice for cytoreductive therapy in ET is hydroxyurea.¹ Patients with ET and the JAK2 V617F mutation are more sensitive to hydroxyurea.¹⁰ Cortelazzo et al.¹¹ showed that patients with ET and platelet counts $< 600 \times 10^3/\text{mm}^3$ have a reduced rate of thrombosis. Carlos et al.¹² showed that there was no direct correlation of platelet counts with thrombotic risk in ET. Therefore, although cytoreductive treatment reduces the rate of vascular complications in high-risk patients, no particular threshold of platelet counts has been shown to be more protective against thrombosis.¹² Patients with ET have a poor response to standardized antiplatelet therapy (e.g., aspirin 100 mg/day and clopidogrel 75 mg/day). A previous study showed that in patients with ET who were carefully managed for their hematological disorder, their responsiveness to aspirin and clopidogrel did not differ from that observed in patients with cardiovascular disease treated with percutaneous intervention.¹³ There is no increased risk of adverse events in patients with ET who are treated with percutaneous intervention, stent implantation, and prolonged dual antiplatelet therapy.¹⁴

Conclusion

ET leading to simultaneous embolism of cardiovascular and cerebral vessels is rare. Caution is advised in patients with acute myocardial infarction who have no chest pain, minimal risk factors, and slightly elevated platelets. Checking the platelet counting is important. Early detection can help doctors identify ET and prevent long-term complications, and these patients can have a normal life span. Implantation of coronary stents is safe for patients with ET and myocardial infarction. Platelet-lowering therapy is also necessary for these patients.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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