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CASE REPORT

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"Y appearance" infarction: caused by essential thrombocythemia

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Abstract

Essential thrombocythemia (ET) is a myeloproliferative malignancy caused by the excessive proliferation of megakaryocytes in the bone marrow, resulting in the overproduction of peripheral platelets. ET can lead to thrombotic events, such as ischemic stroke (IS), though it is a rare cause of IS. Bilateral medial medullary infarction (BMMI), also known as "Y appearance" infarction due to its distinctive imaging morphology, is a rare clinical subtype of IS which typically has a poor prognosis and a high mortality rate. Herein, we report the case of a 43-year-old male with a history of ET. The patient's platelet count was poorly controlled, and he did not receive regular treatment. After developing symptoms such as dizziness, dysphagia, choking on water, slurred speech, blurred vision, and bilateral limb numbness. Head magnetic resonance imaging revealed a "Y appearance" infarction in the bilateral medial medulla. After admission, the patient was administered intravenous antiplatelet therapy with tirofiban. However, when he was switched to oral aspirin after three days, he experienced decreased muscle strength and worsening symptoms. Therefore, tirofiban was continued for 14 days. Upon discharge, the patient experienced residual limb numbness. His National Institutes of Health Stroke Scale score was 1, Modified Rankin Scale score was 0, and platelet count had decreased to the normal range. During the 9-month follow-up period after discharge, the patient still had only mild limb numbness. Our report presents a special case of "Y appearance" infarction due to ET. Owing to fluctuations in the patient's condition, he received long-term high-dose tirofiban, which ultimately led to a significant improvement in his symptoms.

Keywords Essential thrombocythemia , Bilateral medial medullary infarction, "Y appearance" infarction, Tirofiban

Background

Essential thrombocythemia (ET) is a chronic myeloproliferative disorder characterized by the excessive proliferation of megakaryocytes in the bone marrow, resulting in the overproduction of platelets in the peripheral blood [1]. The incidence rate is approximately 1.2–3 cases per 100,000 people [2]. Thrombotic events such as ischemic stroke (IS) are significant complications that threaten the survival of patients with ET [3]. However, ET is a rare cause of IS, with IS resulting from ET accounts for only 0.25–0.54% of all IS cases [4]. Risk factors for thrombosis in patients with ET include age > 60 years, history of thrombosis, cardiovascular risk factors, and the presence of the *JAK2*V617F mutation [5]. According to previous reports, IS caused by ET is more frequently associated

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with lacunar infarction, and is usually less involved in the infratentorial area [6, 7].

Bilateral medial medullary infarction (BMMI) is a form of posterior circulation stroke, commonly referred to as "heart appearance" or "Y appearance" infarction due to its distinctive appearance on head magnetic resonance imaging (MRI). BMMI is exceptionally rarely encountered in clinical practice, accounting for only 0.07–0.21% of all cases of IS [8]. This rarity is attributed to the paired blood supply to the medulla oblongata and the extensive collateral circulation on the medial side [9]. The primary symptoms of BMMI include motor weakness, sensory disturbances, dizziness, nystagmus, dysarthria, and dysphagia, among others [8]. However, there have been no previous reports of "Y appearance" infarction attributed to ET.

Case presentation

A 43-year-old right-handed man presented with sudden onset dizziness and left-sided deafness two weeks prior to admission. Twelve hours before admission, he further experienced difficulty swallowing, coughing upon drinking water, slurred speech, blurred vision, unsteadiness while standing, and numbness in both limbs. The patient had been diagnosed with ET 14 years prior. The bone marrow biopsy revealed a morphology indicative of a myeloproliferative neoplasm, suggesting a diagnosis of ET. Genetic testing identified a *JAK2* mutation, while *BCR/ABL1* fluorescent in situ hybridization testing did not detect the *BCR::ABL1* fusion gene. The patient was prescribed aspirin and hydroxyurea daily; however, his medication adherence was inconsistent. The patient's platelet count typically ranged between 400 and 1500×10^9/L, and he was diagnosed with a splenic infarction, which was accompanied by severe abdominal pain and a splenic abscess 17 years ago. As a result, the patient underwent a splenectomy at that time. Moreover, the patient had hypertension, which was not consistently managed with medication, and he had a 30-year history of smoking. Physical examination revealed poor memory, orientation, and calculation abilities. Vertical coarse nystagmus was observed in all directions of eye movement in both eyes, while bilateral gag reflexes were absent. On admission, the muscle strength of the patient's limbs was normal, but the muscle tone was increased. Hypoesthesia was also observed in the limbs. Hyperreflexia and positive ankle clonus were also observed. The National Institutes of Health Stroke Scale (NIHSS) score was 3 points, and the Modified Rankin Scale (mRS) score before onset was 0 points.

Various examinations revealed a white blood cell count of 23.15×10^9/L, a platelet count of 1576×10^9/L, a low-density lipoprotein cholesterol level of 2.42 mmol/L, and a homocysteine level of 21.3 umol/L. Additionally, bone marrow cytology revealed thrombocytic bone marrow (Fig. 1S). Color doppler ultrasonography of the cervical vessels revealed no atherosclerosis (AS) or plaques. Diffusion-weighted imaging (DWI) of the head revealed bilateral medial medullary cerebral infarction in the medulla oblongata (Fig. 1A). Furthermore, multiple lacunar cerebral infarcts were observed in the left corona radiata, right basal ganglia, and splenium of the corpus callosum (Fig. 2S). T2 fluid-attenuated inversion recovery sequence revealed a medial medullary infarction (Fig. 1B). Magnetic resonance angiography (MRA) indicated a small, thin, left vertebral artery (VA). Chest

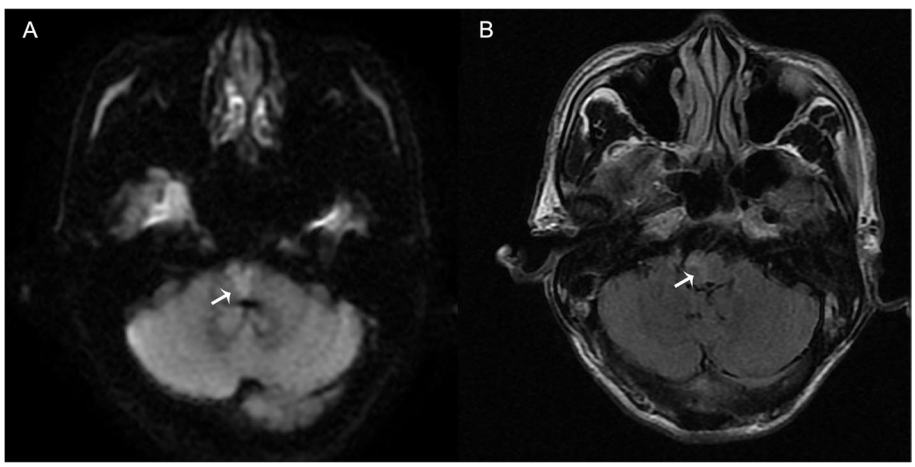

Fig. 1 Results of head magnetic resonance imaging performed in the emergency department. Diffusion-weighted imaging sequence (**A**) showed bilateral medial medullary infarction, and the T2 fluid attenuated inversion recovery sequence (**B**) revealed medial medullary infarction. The arrows indicated the infarction areas

computed tomography (CT) further revealed pneumonia. Given the patient's condition and the risk of progressive stroke, symptomatic treatments, such as tirofiban intravenous antiplatelet therapy, hydroxyurea cytoreductive therapy, and anti-infection therapy, were administered upon admission.

The patient showed no significant improvement despite the initial treatment regimen. After 72 h of tirofiban administration and a subsequent switch to aspirin, the patient experienced a decline in muscle strength (grade III in the upper limbs and grade II in the lower limbs), along with symptoms of hemoptysis and transient decreases in blood oxygen levels. Additionally, platelet counts remained consistently elevated above 1300×10^9/L. Treatment with tirofiban was continued in response to the worsening IS symptoms. After nearly 14 days of tirofiban, there was a notable improvement in the patient's muscle strength and the symptoms significantly improved. The treatment plan for ET was adjusted to a combination of hydroxyurea tablets, human interaction alfa-2b, and ruxolitinib. Subsequent examinations revealed gradual stabilization of the platelet count to within the normal range. We then discontinued the use of hydroxyurea and human interaction alfa-2b, and gradually reduced the dosage of ruxolitinib. After 23 days of treatment, the patient regained muscle strength without experiencing discomfort, such as dizziness, swallowing difficulties, unclear speech, or blurred vision, and he was discharged with only residual numbness in the limbs. The NIHSS score was 1 point, and the mRS score was 0. Given the patient's classification as high-risk according to the revised International Prognostic Score of thrombosis for ET, and considering the current research evidence [5], we recommended continuing aspirin antiplatelet therapy, hydroxyurea, and other secondary preventive treatments for cerebrovascular diseases upon discharge [10]. Moreover, we advised long-term follow-up treatment in both the neurology and hematology specialties.

To date, the patient's platelet count has been repeatedly rechecked after discharge, with fluctuations ranging from 300 to 600×10^9/L; currently, only mild limb numbness symptoms remain.

Discussion

ET, a rare etiology of IS, is thought to arise via two distinct pathways [11]. First, when ET coincides with cerebrovascular disease risk factors, such as AS, these factors can exacerbate vascular stenosis and occlusion, thereby increasing the risk of IS. Secondly, ET can trigger increased platelet activation and aggregation, thus promoting thrombotic events. ET-induced thrombosis often manifests as multiple infarcts that concurrently affect various vascular regions. Our patient presented with a combination of AS risk factors including hypertension, smoking, and hyperhomocysteinemia. Despite this, the patient's platelet count on admission exceeded 1500×10^9/L and DWI sequencing revealed multiple cerebral infarctions. Hence, we hypothesized that IS in this patient was primarily attributable to ET-induced thrombosis. What was even more interesting was that the patient underwent splenectomy which was due to a splenic infarction combined with a splenic abscess, and the reason for the splenic infarction was believed to be caused by ET which was confirmed in subsequent treatment. Therefore, the thrombocytosis in this patient was considered to be co-caused by ET and splenectomy after splenic infarction due to ET, which further resulted in cerebral infarction. Moreover, the literature has indicated that IS resulting from ET predominantly manifests as watershed and lacunar infarctions [7], predominantly affecting the anterior circulation [12], whereas occurrences in the infratentorial area are exceedingly rare [6, 7]. Our patient had a BMMI with an incidence rate of approximately 0.1% [8, 13].

BMMI is often referred to as "heart appearance" or "Y appearance" infarction. Currently, it is understood that "Y appearance" infarction is commonly associated with lesions in the perforating arteries, and typically results from three primary vascular pathological mechanisms: Thrombus originating from the distal unilateral VA and traversing to the contralateral side through the junction of the vertebrobasilar artery, and blood supply from the narrow or occluded paramedian branches originating from the unilateral VA or bilateral anterior spinal arteries (ASA) originating from the unilateral VA to the bilateral medial medulla due to anatomical variations [8, 14]. Normally, the blood supply to the superior one-third of the anterior-medial territory of medulla oblongata comes from the VA and the inferior two-thirds comes from the ASA [15]. The infarction site in this patient was located in the rostral medulla, so occlusion of the ASA was not considered the cause. The patient's MRA revealed that the left VA was small, indicating left vertebral artery hypoplasia (VAH). Although the blood flow in the VAH is significantly reduced, there is no sign of ischemia due to the compensatory effect of the contralateral VA [16]. Moreover, research suggests that VAH may be associated with variations in the posterior cerebral arterial structure [17]. Though MRA cannot demonstrate the presence of posterior circulation perforating arteries, we believe it is more likely that this patient's blood supply to the bilateral medial medulla was from the narrow or occluded paramedian branches originating from the unilateral VA due to anatomical variations. Furthermore, based on the anatomical arrangement of the medulla oblongata, the medial

aspect consists of the pyramidal tract, medial thalamus, medial longitudinal fasciculus, hypoglossal nucleus, and vestibular nucleus in a ventral-to-dorsal sequence [9]. Based on the patient's signs and symptoms, such as decreased muscle strength, increased muscle tone, hyperreflexia of the tendons, and positive ankle clonus, these findings were presumed to be associated with pyramidal tract involvement. This decrease in sensation is attributed to the involvement of the medial thalamus, whereas dizziness and nystagmus are closely associated with the medial longitudinal fasciculus and vestibular nucleus. The patient's symptoms, including dysphagia, coughing upon drinking water, and articulation disorders, suggest that ischemia may extend to the lateral aspect of the medulla oblongata, thereby affecting the nucleus ambiguus and cortical medullary tract. In summary, based on the patient's symptoms, signs, and imaging findings, the diagnosis of "Y appearance" infarction was clear.

According to the *Chinese Experts Consensus on Clinical Application of Tirofiban in Atherosclerotic Cerebrovascular Diseases*, we administered intravenous antiplatelet therapy with tirofiban. Tirofiban, functioning as a glycoprotein IIb/IIIa receptor antagonist, inhibits platelet aggregation by blocking interactions between platelets and fibrinogen [18]. Because of its rapid onset of action during administration and prompt recovery upon cessation, tirofiban typically does not substantially increase the risk of bleeding events, but can effectively prevent thrombosis [19]. This treatment is currently recommended for patients with progressive stroke caused by small artery occlusion, and the duration of administration is at least 24 h. Our patient initially exhibited a decrease in muscle strength after switching to aspirin following 72 h of tirofiban use. Additionally, the patient's platelet count consistently exceeded 1300×10^9/L, which increased the risk of bleeding and thrombus formation in the blood vessels of various organs. Therefore, considering various factors, we continued to use tirofiban for 14 days until the patient's condition stabilized. This approach aims to prevent further deterioration and mitigate the continued activation and aggregation of platelets. In general, the prognosis of patients with BMMI is poor and characterized by limited recovery potential and a high mortality rate [20]. Nevertheless, after long-term tirofiban and other symptomatic supportive treatments, the patient showed remarkable improvement. At the latest follow-up, the patient showed only limb numbness. This is a particular case of "Y appearance" infarction treated with high-dose tirofiban, resulting in a favorable prognosis.

Conclusion

ET and "Y appearance" infarction are rare causes and types of IS, respectively. This case represents a rare reported instance of "Y appearance" infarction attributed to ET. Given the patient's clinical circumstances, a decision was made to administer long-term high-dose tirofiban to effectively address their condition. Ultimately, the patient had a favorable outcome.

Abbreviations

AS	Atherosclerosis
ASA	Anterior spinal artery
BMMI	Bilateral medial medullary infarction
CT	Computed tomography
DWI	Diffusion-weighted imaging
ET	Essential thrombocythemia
IS	Ischemic stroke
MRA	Magnetic resonance angiography
MRI	Magnetic resonance imaging
mRS	Modified rankin scale
NIHSS	National institutes of health stroke scale
VA	Vertebral artery
VAH	Vertebral artery hypoplasia

Supplementary Information

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Supplementary Material 1.

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Authors' contributions

Shuyue Xiao and Yan Ding contributed equally to this work.SY X and YD drafted the manuscript and conducted literature searches, SY X, and ML C edited radiological images and collected clinical data from patients, ML C and AD X revised and finalized the manuscript. All authors have reviewed and approved the final manuscript.

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Availability of data and materials

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

The studies involving humans were approved by the Ethics Committee of the First Affiliated Hospital of Jinan University. All procedures were carried out in compliance with local legislation and institutional guidelines. Prior to their involvement, participants provided written informed consent. Additionally, explicit consent was obtained from individuals for the publication of any potentially identifiable images or data included in this article.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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