Case Report

Severe Thrombocytopenia with Acute Cerebral Infarction: A Case Report and Literature Review

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Abstract

Common causes of thrombocytopenia include pseudo-thrombocytopenia, splenomegaly, decreased bone marrow production, and increased platelet destruction or depletion. The main clinical manifestation is bleeding, and thrombosis-related complications are rare. This article reports an 87-year-old woman with severe thrombocytopenia for more than 7 years. On day 6 in the hospital, the patient suddenly fell into a coma, and emergency head computed tomography (CT) displayed acute cerebral infarction of the left cerebellar hemisphere, brainstem, and left thalamus. Although thrombocytopenia is often associated with bleeding, there is still a need for vigilance against ischemic diseases. We analyzed the possible causes of acute cerebral infarction with thrombocytopenia and reviewed the literature. Our case is different from the causes of cerebral infarction reported in previous articles, so the relationship between thrombocytopenia and acute cerebral infarction needs further study. The patient, in this case, was not given anticoagulant or antiplatelet therapy but recovered well. It shows that individualized treatment is effective.

Keywords: *Acute cerebral infarction, case report, thrombocytopenia, thromboembolism, thrombosis*

Introduction

Cerebral infarction can lead to hemiplegia, aphasia, loss of consciousness, and even death. The most common causes include arteriosclerosis, arteritis, cardiogenic and non-cardiogenic emboli. Patients with cerebral infarction characteristically have markedly enhanced platelet adhesion and aggregation. There are also case reports that essential thrombocytosis is a rare cause of ischemic stroke. Such patients have abnormal platelet aggregation and platelet dysfunction, which is the risk of thrombosis.[1] The normal platelet count range is 150–450 × 10^9/L; thrombocytopenia is divided into mild (100–150 × 10^9/L), moderate (50-99 × 10^9/L), and severe (<50 × 109/L) levels. Thrombocytopenia is commonly manifested as hemorrhage, and thrombosis-related complications are rare. This article reports a case of acute cerebral infarction in a patient with long-term thrombocytopenia.

Case Report

An 87-year-old female patient was admitted to the hospital due to fatigue for more than seven years and an aggravated cough for 15 days. She had no fever or chills for the last 15 days. The patient had a 30-year history of rheumatic heart valve disease. The previous electrocardiogram did not reveal any problems other than myocardial ischemia. The physicians found the patient have routine leukopenia, thrombocytopenia and anemia for more than 7 years. The bone marrow aspiration showed that the bone marrow hyperplasia was not active, the granulocyte ratio is reduced, and the erythroid ratio is increased. Combining the patient's medical history and examination results, the doctor considered the possibility of myelodysplastic syndrome. The patient was not given any other medication before admission except Chuanbei Loquat Paste to relieve cough. At the time of admission, the patient's vital signs were normal. Renal function: urea 16.86 mmol/L (2.8–7.6), creatinine 122.54 μmol/L (48-100). Liver function and blood lipids

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Table 1: MDS patients with acute cerebral infarction

Author/year	Age/sex	MDS typing	Concomitant situation	Platelet count	Cerebral infarction site	Follow-up
Yasuhiro Oki *et al.*/2012[4]	69 (52–81)/ unknown	MDS-U	Patient received decitabine 20 mg/m^2, Grade 3 or greater non-hematologic toxicities included cerebral infarction	Unknown	Cerebral infarction	27 months survival
Ishikawa M *et al.*/2014[3]	75/F	t-MDS	The time from first chemotherapy for ovarian cancer to t-MDS onset was 106 months, the recurrent lesions continued to grow	Unknown	Multiple cerebral infarctions	Died
Halil Onder *et al.*/2015[8]	63/F	MDS-U	Endovascular thrombectomy for left middle cerebral artery stroke	10×10^9/L	Left middle cerebral artery stroke	Good after 3 months
Zhang Yang *et al.*/2015[5]	23/F	MDS-RA	13 days postpartum	$<50\times10^9$/L	Cerebral infarction with right temporal lobe hemorrhage	Lost contact
Bae HW *et al.*/2016[2]	72/F	MDS of the refractory anemia with excess blasts-2 subtype	Following induction chemotherapy with azacitidine until the 16th cycle, the patient achieved complete remission; diabetes mellitus	12×10^9/L	acute infarction in the left cerebral deep white matter near primary motor cortex-white matter junction, corona radiata, and angular gyrus	Not followed up
Sato S *et al.*/2018[6]	25/M	MDS with excess blast 1	Invasion of the central nervous system	Unknown	Acute-stage cerebral infarction in the right parietal lobe	Not followed up
Mariana Guedes *et al.*/2019[7]	84/M	MDS-U	type 2 diabetes, chronic kidney disease, benign prostatic hypertrophy and had a prior intracerebral hemorrhage, varicella-zoster virus infection	52×10^9/L	One acute ischemic lesion in the left frontal and two acute ischemic lesions in both cerebellar lobes	Not followed up

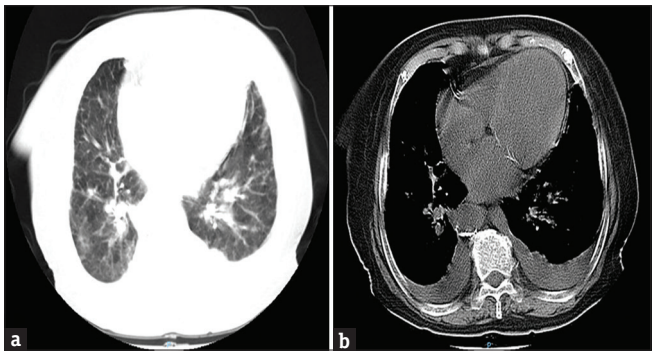

Figure 1: Both lungs are scattered with shadows with unclear borders, as well as enlarged heart shadows. An arc-shaped water-like density shadow can be seen inside the pericardium and behind the side chest cavity. (a) is the lung window, (b) is the mediastinal window at the same level

were normal. The electrocardiogram showed myocardial ischemia. Echocardiography revealed aortic sclerosis, severe mitral, tricuspid, and aortic regurgitation and did not reveal mural thrombus, vegetations and abscesses around the heart valve. The left ventricular ejection fraction was 38%. Color Doppler Ultrasound of the lower extremity vascular and the vessels of the neck and lower extremities showed arteriosclerosis with local lumen stenosis. Lung computed tomography (CT) showed double lung pneumonia, bilateral pleural effusion, and an enlarged heart shadow [Figure 1]. The karyotype analysis of bone marrow chromosomes was normal. The results of the bone marrow aspiration were the same as before. The patient and her family refused to perform a bone marrow biopsy. The patient was treated with infusions of red blood cell suspension (3.5 units in two sessions), anti-infection, correction of heart failure and statin lipid-lowering drugs medication. On day 6 of hospitalization, the patient suddenly fell into coma. The National Institutes of Health Stroke Scale (NIHSS) score was 17 points. The most likely cases of patient coma we analyzed include cerebral hemorrhage and cerebral infarction. Emergency head CT and head magnetic resonance imaging (MRI) on the same day showed acute cerebral infarction in the left cerebellar hemisphere, brain stem, and left thalamus [Figure 2]. A repeat electrocardiogram on the day of cerebral infarction suggested myocardial ischemia and no other abnormalities were seen. The repeat cardiac ultrasound did not show any perivalvular redundancy or attached wall thrombus. The clinical diagnosis was acute cerebral infarction, severe anemia,

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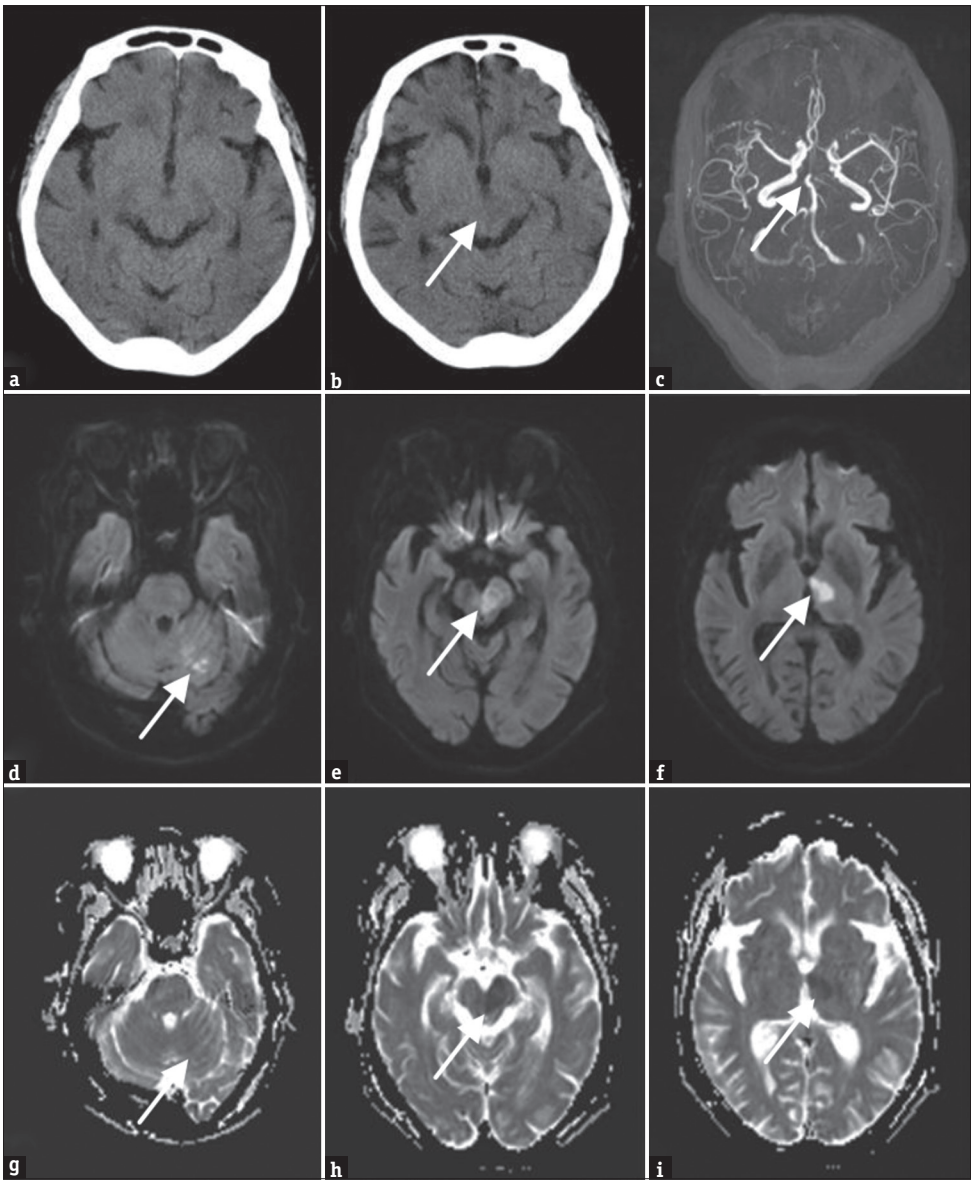

Figure 2: (a) No obvious abnormality was found on head CT before the onset of the disease. (b-i) Brain infarction signals can be observed on head CT, magnetic resonance angiography, and magnetic resonance imaging at the time of stroke onset

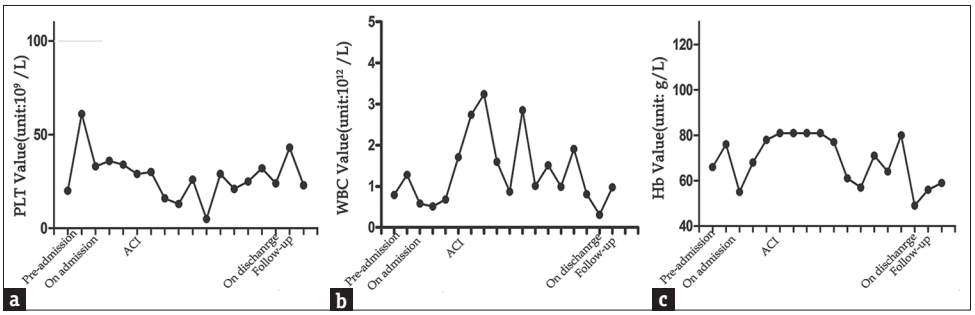

Figure 3: (a) Changes in platelet counts. (b) Changes in white blood cell counts. (c) Changes in hemoglobin. The horizontal line represents the lower limit of the normal range

agranulocytosis, thrombocytopenia, pneumonia, rheumatic heart disease (mitral, tricuspid, and aortic valve with severe regurgitation), class IV cardiac function, hypoproliferative myelodysplastic syndrome, type 2 diabetes mellitus, carotid arteriosclerosis, lower extremity atherosclerosis. The patient was transferred to the Department of Neurology. The patient was given treatment in the neurology department to improve

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circulation, lower cholesterol, anti-infection, and correct heart failure, without anticoagulation or antiplatelet drugs. On day 10 of hospitalization, the patient's platelet count was 13 × 10^9/L, and a platelet transfusion of one unit was given. On day 13 of hospitalization, the patient's platelet count was 5 × 10^9/L, and re-transfusion of 1 unit platelet was given. On the 25th day of hospitalization, the patient›s condition improved significantly, the NIHSS score was 11, and she was discharged. Three months after discharge, the patient could eat with assistance and her NIHSS score was 6. The blood routine of the patient changed significantly before and after admission. The platelet count dropped to the lowest value (5 × 10^9/L) on day 13 of hospitalization. The blood cell fluctuation is shown in Figure 3.

Discussion

When the platelet count is below 10 × 10^9/L, there is a risk of spontaneous bleeding. However, thrombosis-related complications are rare in patients with thrombocytopenia. Our patient was not treated for thrombocytopenia or MDS before the onset of acute cerebral infarction. Her platelet count was 29 × 10^9/L on the day of the onset of cerebral infarction and dropped to 5 × 10^9/L 13 days after onset (without anticoagulation therapy). Further decline in platelets after acute cerebral infarction in this patient may be associated with spontaneous platelet agglutination. The etiology of cerebral infarction, in this case, may be related to the following conditions.

Thrombocytopenia-related diseases

Different types of thrombocytopenia have different mechanisms of action. In our case, we should first consider blood system diseases such as myelodysplastic syndrome (MDS), which is distinct from the usual blood disease that causes cerebral infarction. We reviewed previous reports on MDS complicated with acute cerebral infarction and analyzed seven articles [Table 1]; three cases included chemotherapy drug use,[2-4] one case may have been related to postpartum complications,[5] one case was related to MDS central nervous system invasion,[6] one case was related to varicella-zoster virus infection causing cerebrovascular disease,[7] and one case was related to endovascular thrombectomy for left middle cerebral artery stroke.[8] The age of onset was 23-84 years. However, none of the case reports mention an association between cerebral infarction and thrombocytopenia. It has been reported that there may be a correlation between MDS and large-vessel vasculitis.[9] Vasculitis can lead to arterial stenosis, occlusion, and nonvascular inflammatory embolism. Studies have speculated that MDS patients with trisomy 8 induces abnormal inflammatory processes and activation of immune gene expression, which ultimately leads to or even aggravates blood vessel damage and thrombosis.[10] It is clinically difficult to distinguish between MDS and myeloproliferative neoplasms. The plasminogen activator inhibitor-1 gene 4G4G and infection in patients with essential thrombocytopenia with the Janus kinase 2 V617F mutation were shown to be high-risk factors of thrombotic events.[11] The cause of thrombocytopenia, leukopenia, and anemia in our case was considered to be hypoproliferative myelodysplastic syndrome, but other blood system or genetic diseases still need to be excluded.

Cardiogenic embolism and arteriosclerosis

Cardioembolic cerebral infarctions account for approximately one-quarter of all cerebral infarctions. The most common conditions associated with a high risk of cardiac embolism are atrial fibrillation, recent myocardial infarction and mitral rheumatic stenosis. Studies have shown that nearly one-fifth of patients with non-cardiogenic stroke have congenital or acquired cardiac structural changes.[12] A Korean study reported a cerebral infarction caused by congestive heart failure.[13] The patient, in this case, report had a 30-year history of rheumatic valve disease and heart failure. Therefore, cerebral infarction caused by cardioembolism could not be ruled out. Arteriosclerosis is a chronic inflammatory process that requires a certain number of platelets to participate in the thrombosis and inflammatory processes.[14] Therefore, the occurrence of cere, in this case, on in this case cannot be explained by arteriosclerosis alone. Studies have analyzed the etiology of clots recovered from ischemic stroke patients from the perspective of their etiology, and found that there is a statistically significant difference between clots originating from cardiogenic embolism and aortic atherosclerosis origin.[15] It provides a new direction for us to study the causes of acute cerebral infarction in the future.

Blood transfusion

There is a dose-dependent relationship between the number of red blood cell transfusion units and thrombosis.[16] The pretransfusion hematocrit in this patient was 0.169. She had received red blood cell transfusions three days before the onset of acute cerebral infarction. The true benefit of preventive blood transfusions in patients with thrombocytopenia is unclear. Our patient received platelet transfusion after the onset of cerebral infarction, which was stopped when the platelet count reached 26 × 10^9/L. The patient's acute cerebral infarction gradually resolved.

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Conclusion

In summary, the cause of acute cerebral infarction in our case may be related to several causes, such as blood system disease (MDS), rheumatic valvular heart disease, heart failure, etc. Acute cerebral infarction is rare in the case of severe thrombocytopenia. For similar cases in the future, we can determine the cause from both the primary disease that may cause the cerebral infarction and the components of the cerebral infarction clot. This case also reminds us that in patients at high risk for thrombosis, even in combination with thrombocytopenia, the risk of bleeding and thrombosis should be fully weighed to decide whether to give individualized antithrombotic therapy.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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