Clinical Case Report

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Acute myocardial infarction in a Chinese patient with paroxysmal nocturnal hemoglobinuria

A case report

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Abstract

Rationale: Paroxysmal nocturnal hemoglobinuria (PNH) is a clonal hematopoietic stem cell disease. Patients with PNH often experience a high incidence (14%–40%) of thrombotic events, which are mainly venous and rarely arterial thrombotic events. Because it is very rare, delay in diagnosis is common in patients with PNH, imposing a remarkable impact on patient's management and prognosis.

Patient concerns: We presented a 33-year-old female case with no medical history of any systemic illnesses who complained of approximately 1-month progressively worsening constant heartburn, and was also hospitalized twice due to acute myocardial infarction (AMI).

Diagnoses: In our case, AMI occurred twice, whereas there were no cardiovascular risk factors and abnormalities based on the angiography of the coronary artery. Flow cytometry analysis showed that 25% of CD55 and CD59 were lost on the surface of neutrophils, and 30% of CD55 and CD59 were lost on the surface of the blood cells. Thus, our diagnosis of this patient was AMI secondary to PNH.

Interventions and outcomes: For the first myocardial infarction, local hospitals used thrombolytic therapy to alleviate symptoms. After the patient's second myocardial infarction was treated in our hospital, we adopted coronary interventional therapy. Considering the patient's situation, eculizumab was given for treatment. The patient was gradually restored to achieve stability, and the follow-up observation showed that there was no arterial thrombosis.

Lessons: This case report aimed to provide a reliable reference for the rare cause of AMI. In addition, PNH should be highly taken into consideration in young patients who have a rare cause of AMI.

Abbreviations: AMI = acute myocardial infarction, ECG = electrocardiography, LDH = lactate dehydrogenase, PI = phosphatidylinositol, PNH = paroxysmal nocturnal hemoglobinuria, RBCs = red blood cells.

Keywords: acute myocardial infarction, case report, paroxysmal nocturnal hemoglobinuria, thrombotic event

1. Introduction

Paroxysmal nocturnal hemoglobinuria (PNH) is caused by genetic mutation, resulting in deficiency of glycosylphosphatidylinositol anchor for cell membrane proteins, such as complement regulatory proteins CD55 and CD59.[1,2] Therefore, the gold standard test for PNH is flow cytometry of red blood cells (RBCs), demonstrating absent or reduced expression of both CD55 and CD59.[3] In addition, PNH is characterized by thrombotic events, hemolytic anemia, and also varying degrees of cytopenias. The thrombotic events are often venous and rarely arterial.[4] Here, we reported a young female case who complained of approximately 1-month progressively worsening constant heartburn, and experienced hospitalization twice due to acute myocardial infarction (AMI).

2. Case report

A 33-year-old female, who complained of discontinuous chest tightness for 1 month and aggravation for 1 day, was hospitalized in cardiology department of our hospital.

Before 1 month, the patient suffered from chest tightness in the morning, with primordial pain, and hyperhidrosis symptoms aggravated after movement. The patient was examined by electrocardiography (ECG), and the results showed ST-segment elevation in leads II, III, augmented v(unipolar)lead, left leg (AVF), and serum troponin T level (<0.1 ng/mL). The patient was diagnosed with acute inferior myocardial infarction. After treatment with urokinase, the patient's clinical status improved, and then the patient was discharged. Aspirin, clopidogrel, atorvastatin, metoprolol, and perindopril were continuously given after leaving hospital. However, the patient still had

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discontinuous chest tightness that often occurred in the midnight or in the morning.

One day before treatment, the chest tightness re-occurred in the morning, and the patient was again admitted to our hospital for diagnosis. Physical examination results showed that blood pressure (BP) was 109/84 mm Hg, and also ordered cardiac rhythm, low cardiac sounds, no murmur in the aortic valve auscultation location area, and no edema in the legs. The patient once had paroxysmal abdominal pain for within 1 month, without vomiting, fever, chills, black stool, hematochezia, and so on. The proton pump inhibitors were given for preventing acute gastric mucosal lesions as well. Coca Cola-colored urine persisted for 2 months without any treatment. Regarding family history, the patient's mother died at the age of 40 years without any clear causes.

Medical examinations were conducted as follows: a routine blood test showed that the values of N, RBC, hemoglobin, and platelet were 81.9%, 2.36×10^{12}/L, 97 g/L, and 96×10^{9}/L, respectively; the serum levels of lactate dehydrogenase (LDH), creatine kinase-MB, and troponin T were 1664 IU/L, 75.8 IU/L, and 4.16 ng/mL, respectively. Coombs test, anti-cardiolipin antibodies, and anti-nuclear antibodies were all negative. Flow cytometry analysis showed that 25% of CD55 and CD59 were lost on the surface of neutrophils, and 30% of CD55 and CD59 were lost on the surface of blood cells. Abdominal computed tomography scanning indicated formation of thromboembolic occlusion of the superior mesenteric vein. ECG showed sinus rhythm, and ST-segment elevation in leads II, III, AVF, and pathological Q waves (Fig. 1). Coronary angiography revealed fresh thrombi appeared before the first turning point of the proximal right coronary artery, with thrombolysis in myocardial infarction grade 3 coronary blood flow at the distal segment, decreased movement of inferior walls, and 63.1% of left ventricular ejection fraction (Fig. 2). Thrombus aspiration in coronary artery was used for treatment, and glycoprotein IIb/IIIa receptor antagonists were given after surgery.

Diagnosis of the patient showed PNH, acute inferior myocardial infarction or Killip class I heart failure, and thrombus at the superior mesenteric vein. According to the patients' situation, eculizumab was given for treatment. Eculizumab is a humanized monoclonal antibody, blocking terminal complement by binding to C5, and is the only approved therapeutic method by the US Food and Drug Administration for PNH.[2] Here, the drug (1200 mg) was administered intravenously every 7 days for the first 5 weeks and biweekly thereafter. The patient was gradually restored to stability with a gradual decrease in LDH level. After 2 years of follow-up, no arterial thrombosis occurred in the patient treated with 1200 mg eculizumab every 2 weeks.

This study was approved the ethics committee of our hospital. Informed written consent was obtained from the patient for publication of this case report and accompanying images.

3. Discussion

A case of PNH with repeated AMI was presented here. The diagnosis depended on the results of flow cytometry and medical

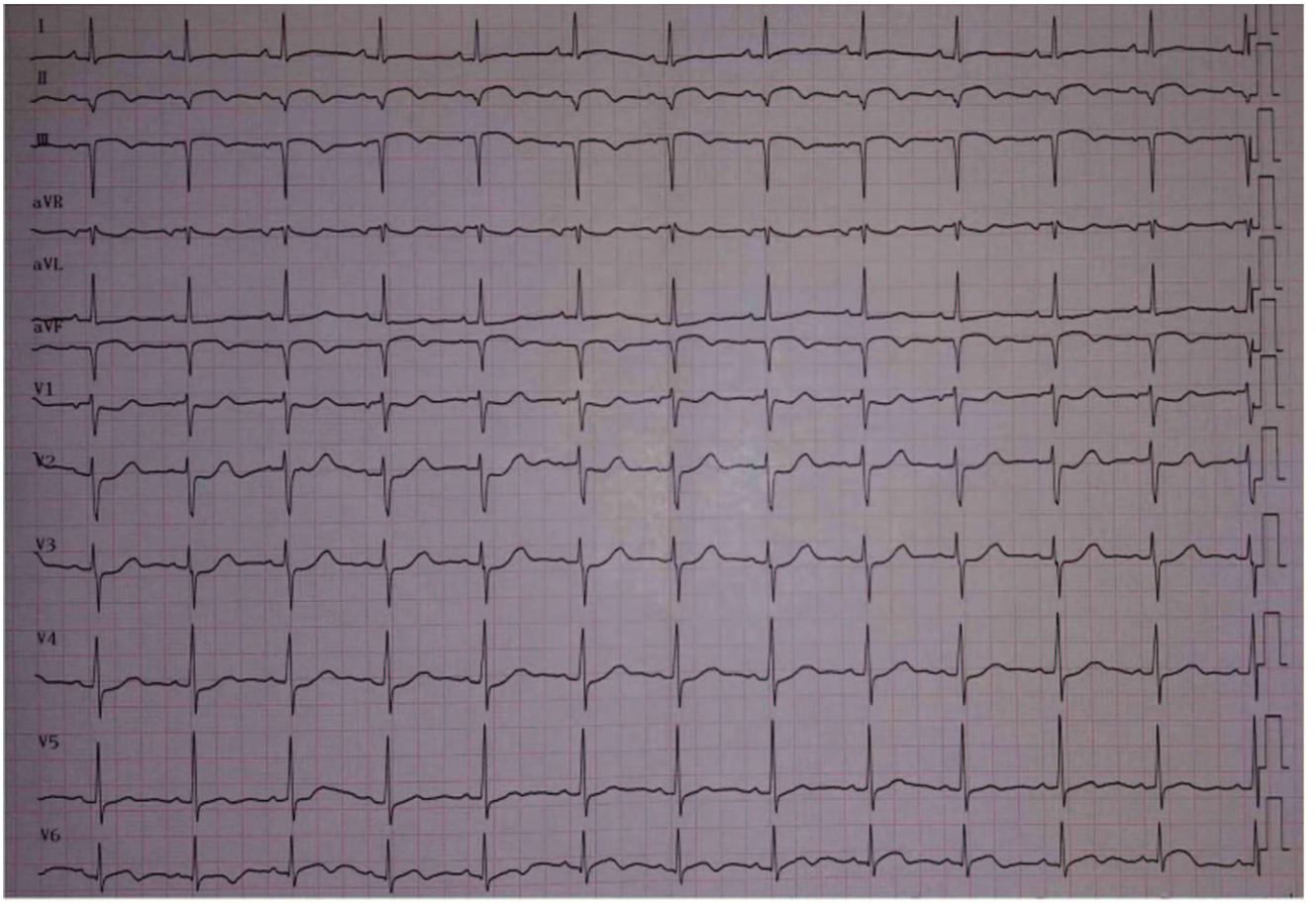

Figure 1. ECG shows sinus rhythm, the II, III, AVF leads of ST-segment elevation, and pathological Q wave form. AVF = augmented v(unipolar)lead, left leg.

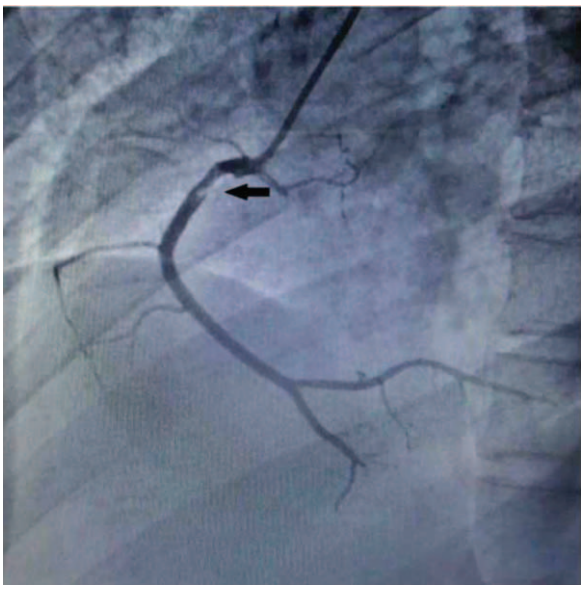

Figure 2. Coronary angiography shows fresh thrombi appeared before the first turning point of the proximal right coronary artery, with TIMI 3 coronary blood flow at the distal segment. TIMI = thrombolysis in myocardial infarction.

images. The gold standard test for PNH was flow cytometry of RBCs, which demonstrated absent or reduced expression of both CD55 and CD59.[3] The case was remarkable, because AMI occurred twice, while there were no cardiovascular risk factors and abnormalities according to the angiography of the coronary artery.

The clinical course of PNH is highly variable, ranging from a mild defect to a lethal process. The main clinical features consist of hemoglobinuria, episodic hemolysis, marrow hypoplasia, and thrombotic disease. At present, PNH can be detected by flow cytometry, which is a highly appropriate diagnostic method for PNH. In PNH, expression of phosphatidylinositol (PI)-anchored proteins is significantly reduced due to mutation of the phosphotidyl inositol glycan complementation group A gene, causing absence of PI-anchored proteins.[5,6] In normal circumstances, these proteins protect against complement-mediated lysis of red cells. Flow cytometry analysis can exactly measure the expression of antigens on each cell membrane and estimate the percentage of deficient cells by using monoclonal antibodies. In our patient, flow cytometry analysis showed that 25% of CD55 and CD59 were lost on the surface of neutrophils, and also 30% of CD55 and CD59 were lost on the surface of the blood cells.

In addition to hemoglobinuria, episodic hemolysis, and marrow hypoplasia, thrombosis is 1 of the most severe complications, which is also the most common cause of death in PNH patients. It often happens in venous system, whereas it rarely occurs in the arterial system. The common sites include intra-abdominal (hepatic, portal, mesenteric, splenic, etc) and cerebral (sagittal and cavernous sinus) veins. In addition, hepatic vein thrombosis is the most common site of thrombosis in PNH, whereas pulmonary embolism and dermal thrombosis are relatively common as well.[6] The possible mechanisms are as follows: endothelial cell damage is an important factor of thrombosis. Release of free hemoglobin activates the endothelium and leads to scavenging of nitric oxide. Reduction of membrane of GPI-anchored urokinase plasminogen activator receptor on granulocytes and platelets of patients with PNH is also associated with thrombophilia.[7] Complement activation also contributes to the prothrombotic tendency of PNH patients.

Regarding the treatment of thrombotic complications of PNH, all PNH patients who experience a thrombotic complication are candidates for indefinite anticoagulation. Anticoagulation prophylaxis against thromboembolic events without prior thrombotic complications has been studied by several scholars, and that is still a hot research topic. In addition, in presence of thrombotic complications, anticoagulants are of great significance to prevent thrombosis in PNH.[5] At present, bone marrow transplantation is a very effective curative therapy for PNH patients, whereas the transplant-related mortality is high.[8]

A number of studies showed that eculizumab can ameliorate the thrombotic tendency of PNH. As eculizumab inhibits the formation of the membrane attack complex and several compensates for the CD59 and CD55 deficiency in PNH patients, thus eculizumab is highly effective in abrogating the intravascular hemolysis, decreasing the risk of thrombosis. The 5-year survival rate of patients with PNH before eculizumab therapy was 67%, which then improved to 96% in patients who received eculizumab.[9] In our case, satisfactory clinical outcomes were achieved with eculizumab. We did not have prophylactic anticoagulation after discharge. However, some studies reported that lifelong anticoagulation may not be necessary for secondary prophylaxis in PNH patients who could be well-treated with eculizumab.[10]

Eventually, it is noteworthy that acute coronary thrombosis, particularly in coronary artery, is 1 of the most serious complications of PNH. Hence, a particular attention should be paid to AMI in patients with PNH.

Author contributions

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References

[1] Le Guyader M, Pineau-Vincent F, Lemaire P. [Paroxysmal nocturnal hemoglobinuria and myelodysplastic syndrome: a case report]. Ann Biol Clin (Paris) 2016;74:106–9.
[2] Devalet B, Mullier F, Chatelain B, et al. Pathophysiology, diagnosis, and treatment of paroxysmal nocturnal hemoglobinuria: a review. Eur J Haematol 2015;95:190–8.
[3] Parker C, Omine M, Richards S, et al. Diagnosis and management of paroxysmal nocturnal hemoglobinuria. Blood 2005;106:3699–709.
[4] Van Bijnen ST, Van Heerde WL, Muus P. Mechanisms and clinical implications of thrombosis in paroxysmal nocturnal hemoglobinuria. J Thromb Haemost 2012;10:1–0.
[5] Brodsky RA. Paroxysmal nocturnal hemoglobinuria. Blood 2014;124: 2804–11.
[6] Doutrelon C, Skopinski S, Boulon C, et al. [Paroxysmal nocturnal hemoglobinuria: an unknown cause of thrombosis?]. J Mal Vasc 2015;40:384–90.
[7] Meletis J, Terpos E. Recent insights into the pathophysiology of paroxysmal nocturnal hemoglobinuria. Med Sci Monit 2003;9:Ra161–72.
[8] Woodard P, Wang W, Pitts N, et al. Successful unrelated donor bone marrow transplantation for paroxysmal nocturnal hemoglobinuria. Bone Marrow Transplant 2001;27:589–92.
[9] Loschi M, Porcher R, Barraco F, et al. Impact of eculizumab treatment on paroxysmal nocturnal hemoglobinuria: a treatment versus no-treatment study. Am J Hematol 2016;91:366–70.
[10] Emadi A, Brodsky RA. Successful discontinuation of anticoagulation following eculizumab administration in paroxysmal nocturnal hemoglobinuria. Am J Hematol 2009;84:699–701.