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Successful Rescue of a Postpartum Woman with Paroxysmal Nocturnal Hemoglobinuria Presenting with Multiple Organ Dysfunction and Splenic Rupture: A Case Report

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Summary

Paroxysmal nocturnal hemoglobinuria (PNH) is a chronic, multi-systemic, progressive and life-threatening clonal disease with low morbidity, caused by acquired hematopoietic stem cell PIG-A gene mutation. Its main clinical features are intravascular hemolysis, high risk thrombosis and bone marrow failure [1]. It is well recognized that intravascular hemolysis is frequently induced and aggravated by several factors such as infection, transfusion, surgery, and pregnancy [2].The leading cause of mortality in PNH is thrombosis and large PNH clones (more than 50% PNH granulocytes) are associated with an increased risk of thrombosis. The abdominal veins are the more common site of thrombosis. Compared with thrombotic events, intraperitoneal bleeding, especially from splenic rupture, is quite rare. So far, only three cases of non-traumatic splenic rupture in PNH have been reported, but none reported in pregnant woman [3-5]. Due to the rarity of PNH with non-traumatic splenic rupture and the non-specific clinical symptom, the correct diagnosis is easily be missed, which may lead to potentially grave medical outcome. Hence, it is essential to consider timely diagnosis of PNH with acute or occult abdominal pain for improved patient management and prognosis.

Keywords: Paroxysmal Nocturnal Hemoglobinuria; Non-Traumatic Splenic Rupture; Pregnant Woman; Multiple Organ Dysfunction Syndrome

Introduction

Paroxysmal sleep hemoglobinuria (PNH) is a low incidence clonal disease. Its main clinical features are intravascular hemolysis, high-risk thrombosis, and bone marrow failure. The leading cause of death in PNH is thrombosis. Intraperitoneal hemorrhage, especially splenic rupture, is quite rare compared to thrombotic events. To date, only three cases of non--traumatic splenic rupture have been reported in PNH, but none in pregnant women. Since non-traumatic splenic rupture in PNH is very rare and the clinical symptoms are not specific, it is easy to miss the diagnosis, which may lead to serious medical consequences. Therefore, consideration of timely diagnosis of PNH with acute or insidious abdominal pain is essential to improve patient management and prognosis. In this paper, we report a case of a woman diagnosed with PNH after delivery with abdominal pain as the first symptom, which rapidly worsened with hemodynamic changes, multiple organ dysfunction syndrome (MODS), and ultimately was found to have splenic rupture. This will help in early diagnosis and timely treatment.

Case

A 25-year-old Chinese female noted occasional anemia at age 15 years, but she first sought medical attention at 24 years of age due to pregnancy. The laboratory examination still revealed anemia. So the patient began to take iron supplements erratically. She had multiple episodes of the typical soyurine during pregnancy. One month before this admission, her platelet count was detected to drop slightly, meanwhile the hemoglobin level remained in the range of 70 to 90 g/l without transfusion. She was admitted at 36 weeks +2 days of menopause.

On admission, temperature was 36.5 ℃， the pulse rate was 84/min and the blood pressure 150/98 mm Hg. The preliminary laboratory results were as follows: hemoglobin (Hb)71 g/l, hematocrit (Hct) 22%,mean white blood cell (WBC) count4.66× 10^9/l, platelet count 84 ×10^9/l, lactate dehydrogenase (LDH) 3575 U/l, aspartate transaminase(AST) 337 U/l, alanine transaminase (ALT) 25 U/l, total bilirubin 27.4umol/l. The ultrasound showed no enlargement of the liver and spleen. Ultrasound of the splenic vein and portal vein showed no thrombosis. The diagnosis of HELLP was initially suspected. Then the patient given birth to a boy on the second hospital day via cesarean section. Further laboratory tests were performed. The Acid HAM lysis test was positive. Flow cytometry showed an abnormal PNH clone. 64.4% of RBCs did not express CD59 and 99.7% of neutrophils were FLAER negative. She was diagnosed with paroxysmal nocturnal hemoglobinuria (PNH).

On the 6th postpartum day, the patient developed fever accompanied by mild paroxysmal abdominal pain with concurrent distension. Her body temperature was 39℃. The abdominal plain film suggested incomplete intestinal obstruction and then the therapy of anti-infection and antacids was taken. However, the pain was not relieved after treatment. Twelve days later after delivery, the abdominal CT scan (Figure1) demonstrated a markedly enlarged spleen. On the thirteen day after delivery, the patient's abdominal pain worsened. Laboratory tests showed that the patient's hemoglobin sharply dropped from 7–8 g/dl to 4.5 g/dl along with platelets count from 47× 10^9/L to 22×10^9/L within one day. We considered the puerpera developed post-partum hemolytic crises and further transfusions was given. But her condition continued to deteriorate rapidly at the 14th postpartum day.

The patient developed fatigue significantly with dyspnea. She became hemodynamically unstable. The results of laboratory tests suggested metabolic acidosis with decompensated stage of respiratory alkalosis(PH 7.138, BE -21mmol/l), lactic acidosis(17.6mmol/l), hyperkalemia(6.2mmol/l), multiple organ dysfunction syndrome of heart, lung, liver, kidney and blood system. The patient was treated with emergency salvage measures including endotracheal intubation, invasive mechanical ventilation, analgesic and sedation, blood transfusion, continuous renal replacement therapy (CRRT) and so on. The patient's acid-base balance disorder was corrected. However, the patient's abdominal distension was not relieved, and hemoglobin decreased dynamically.

On the 15th postpartum day, a contrast enhanced computerized tomography angiography(CTA) scan of the abdomen(-Figure2) revealed no significant abnormality within the abdominal aorta and its major branches. The lumen of the mesenteric artery and vein were thin but no obvious filling defect was observed. The spleen was larger than before. The density of the liver, spleen and renal cortex was altered. Organ rupture was suspected due to suspicious gas around the spleen. The abdominal CT also suggested new abdominal effu-

sion or hematocele. As her condition remained unstable, urgent exploratory laparotomy was performed. She was found to have multiple rupture and active bleeding on the surface of the spleen(Figure 3). A splenectomy was performed.

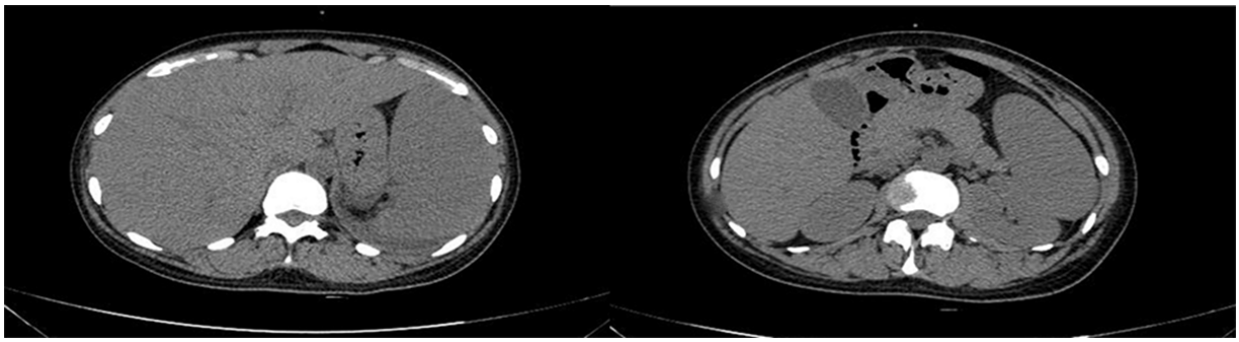

Figure 1: A markedly enlarged spleen

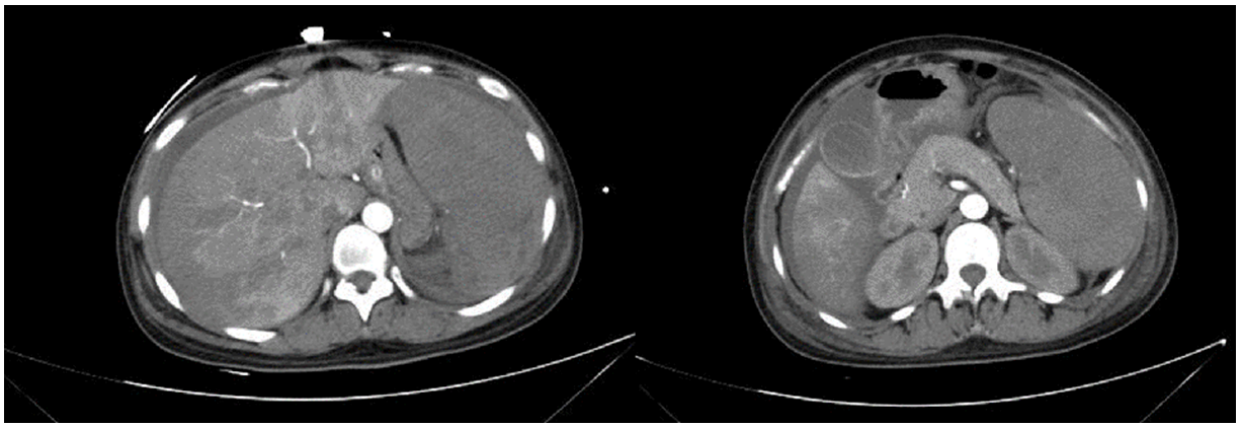

Figure 2: The spleen was larger than before. The density of the liver, spleen and renal cortex was altered

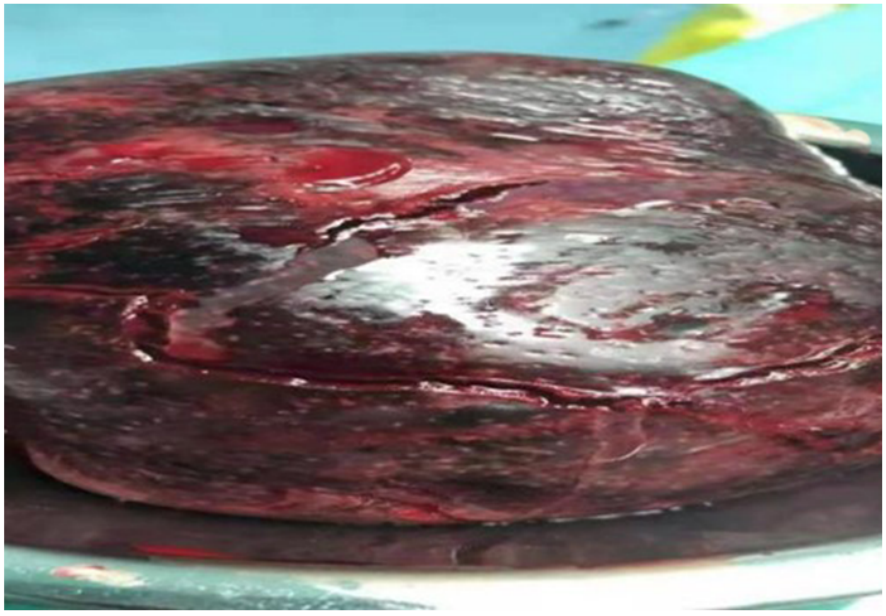

Figure 3: Splenic rupture

Histopathological results showed that splenic lesions were consistent with chronic bruising and splenomegaly, with massive hemorrhage and necrosis. Venules thrombosis were seen in pathological tissue. Unfortunately, histological examination of the liver was not performed.

After splenectomy, the maternal clinical course improved and she was continued to be given40 mg/day methylprednisolone. The HGB gradually stabilized at 80-95g/L, as well as the increase of platelet count. When the platelet count exceeded 70 ×109/L, she was treated with anticoagulation because of worrying about the occurrence of thromboses. She was discharged on the 17th post-splenectomy day.

She recovered well over the last two months of follow-up. Her blood cells gradually returned to normal. The last complete blood cell analysis two months after splenectomy were as follows: hemoglobin 149g/L, platelet count 260*10^9g/ L, WBC count 4.27 $*10^{9}$/l.

Disscusion

Paroxysmal nocturnal hemoglobinuria (PNH) is a rare acquired clonal disorder of hematopoietic stem cells, manifested with intravascular hemolysis, a propensity for thrombosis [6-9], that is due to lack of two complement regulatory proteinsCD55and CD59 on the RBCs surface, especially CD59.In general, the severity of clinical manifestations is considered to related to the size of the PNH clone in untreated patients [1]. Pregnancy can cause more severe complications in patients with PNH, leading to an increased risk of death, and that has been discouraged. The puerperal woman we presented here had a large PNH granulocyte clone of 99%. In addition, she also had never accepted regular treatment before. Soon after delivery, she was in critical condition with multiple organ dysfunction, and her clinical feature was consistent with the above description.

Currently, there are several literatures about pregnant women with PNH that the maternal mortality has been reported to be between 8% and20.8%. Postpartum thromboembolism is considered as the primary cause of death [8,10-12]. Large granulocyte clones are associated with an increased risk of thrombosis. Two previous literatures [13-14] reported the incidence of thrombus at 44% and 54.5% with PNH clone size >50% and 61%, respectively. But reports on non- traumatic splenic rupture with PNH are very rarely [3-5]. Up to now, the patient here is the first puerperal woman that be reported. As we all know, puerperal women are in hypercoagulable state and have the tendency of venous thrombosis. Based on the clinical characteristics of this patient, she was assessed to have a high risk of thrombotic events. When she appeared with acute abdominal pain, we initially considered that she had suffered from abdominal intravascular thrombosis. However, abdominal CTA examination was negative with no thrombosis, and then the diagnosis became more difficult. Due to the rapid deterioration of the patient's condition, an urgent exploratory laparotomy was performed and splenic rupture was found during operation. The final pathological examination revealed small intrasplenic venous thrombosis which could been explained by PNH with large granulocyte clone and hypercoagulable state of perinatal period. But the explanation of nontraumatic splenic rupture is more complicated.

The incidence of non-traumatic splenic rupture is highly infrequent, despite various reports about spontaneous splenic rupture in the literature. In the review of 613 cases [15] that had experienced splenic rupture, only 84 cases were secondary to hematological malignancy, of which acute leukemia and non-Hodgkin lymphoma were the most frequent causes. The other aetiologies of atraumatic splenic ruptures included infectious, medical procedures related, neoplastic disease, medication related, pregnancy-related and others. Spontaneous peripartum splenic rupture has been reported throughout the peripartum period, with fewer cases occurring postpartum [16]. Gokul SR [16] described the case of postpartum hemorrhage due to splenic rupture after emergent cesarean delivery. The mechanism of splenic injury in postpartum was unclear and likely multifactorial.

At present, there are only three cases of PNH with non-traumatic splenic rupture been reported. One patient had suffered widespread thromboses throughout the peripheral and portal veins with occlusion of the splenic and portal veins indicating that the decrease in venous drainage from the spleen contributed to splenomegaly and subsequent splenic rupture [3].The other two patients, similar to the patient reported here, had no evidence of splenic or portal vein thrombosis before splenic infarction and rupture [4,5]. But the histopathological examination of both the case [5] reported by Heather M and the puerperal woman presented here showed small vessel thrombosis. The occurrence of splenic rupture may be related not only to intravascular hemolysis and thrombosis, but

also to extravascular hemolysis. Previous literatures suggested that C3 fragments were not destroyed by the membrane attack complex (MAC) intravascularly could accumulate the GPI-negative red blood cell (lacking CD55) surface and these fragments opsonize the RBCs, causing reticuloendothelial destruction in the liver and spleen [6-9].

This parturient was considered to have both intravascular hemolysis and extravascular hemolysis, which led to splenic congestion and swelling in short time, and eventually resulted in splenic rupture. Unfortunately, the pathological examination of the liver did not been done, whether the existence of hepatic venule thrombosis is unknown.

In conclusion, we first report a case of a critical pregnant woman with PNH who had not been treated before, accompanied by rare complication-spleen rupture. Although the patient's clinical condition have been improved with splenectomy hormone and anticoagulation therapy, clinicians should not only consider the occurrence of thrombosis but also think of the possibility of the unusual complication-spleen rupture, when pregnant women with PNH had suffered from unexplained abdominal pain. The untreated PNH patients tend to have more serious clinical manifestations, just like the pregnant woman reported here that she quickly developed multiple organ dysfunction. Hence, early diagnosis and timely treatment are extremely necessary. In addition, the causes of spontaneous splenic rupture are multifactorial. To avoid serious consequences, all predisposing risk factors for spontaneous splenic rupture should be considered, especially in puerpera with PNH.

Conflict of Interest Statement

The authors have no conflict of interest.

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References

1. Rodolfo D. Cancado, Aderson da Silva Araújob, et al.(2020) Consensus statement for diagnosis and treatment of paroxysmal nocturnal haemoglobinuria. Hematology, Transfusion and Cell Therapy. 1-8.

2. Iwamoto N, Kawaguchi T, Horikawa K, et al. (1994) Haemolysis induced by ascorbic acid in paroxysmal nocturnal haemoglobinuria. Lancet. 343:357.

3. Zimmerman D, Bell W (1980) Venous thrombosis and splenic rupture in paroxysmal nocturnal hemoglobinuria. Am J Med, 68: 275-9.

4. Uzun S, Alpay N, Ozturk GB, et al.Acase of paroxysmal nocturnal hemoglobinuria presenting with intra-abdominal bleeding due to splenic rupture, developing renal infarct. Int J Lab Hematol 2008;30:248–253.

5. Heather M, Mark L. K, et al. (2009) Splenic Infarction and Subsequent Splenic Rupture in a Patient With Paroxysmal Nocturnal Hemoglobinuria and Heparin-Induced Thrombocytopenia. Pediatric Blood Cancer, 53: 472-4.

6. Brodsky R (2014) Paroxysmal nocturnal hemoglobinuria. Blood.124: 2804-11.

7. Rollins SA, Sims PJ (1990) The complement-inhibitory activity ofCD59 resides in its capacity to block incorporation of C9 into membrane C5b-9. J Immunol. 144: 3478-83.

8. Lublin DM, Atkinson JP (1989) Decay-accelerating factor: biochemistry, molecular biology, and function. Annu Rev Immunol. 7: 35-58.

9. Risitano AM, Notaro R, Marando L, Serio B, Ranaldi D, SenecaE, et al. (2009) Complement fraction 3 binding on erythrocytes as additional mechanism of disease in paroxysmal nocturnal hemoglobinuria patients treated by eculizumab. Blood. 113: 4094-100.

10. Ham T (1937) Chronic hemolytic anemia with paroxysmalnocturnal hemoglobinuria. A study of the mechanism of hemolysisin relation to acid base equilibrium. N Engl J Med. 217: 915-7.

11. Rother RP, Rollins SA, Mojcik CF, Brodsky RA, Bell L (2007) Discovery and development of the complement inhibitor eculizumab for the treatment of paroxysmal nocturnal hemoglobinuria. Nat Bio technol. 25: 1256-64.

12. Hill A, Platts PJ, Smith A, Richards SJ, Cullen MJ, Hill QA, et al. (2006) The incidence and prevalence of paroxysmal nocturnal hemoglobinuria (PNH) and survival of patients in Yorkshire. Blood. 108: 985.

13. Hall C, Richards S, Hillmen P (2003) Primary prophylaxis with warfarin prevents thrombosis in paroxysmal nocturnal hemoglobinuria. Blood, 102: 3587-91.

14. Moyo V, Mukhina G, Garrett E, et al. (2004) Natural history of paroxysmal nocturnal hemoglobinuria using modern diagnostic assays. Br J Haematol, 126: 133-8.

15. Aubrey-Bassler FK, Sowers N (2012) 613 cases of splenic rupture without risk factors or previously diagnosed disease : a systematic review. BMC Emerg Med. 12: 11.

16. Gokul SR, Riccio CA. Splenic Rupture and Postpartum Hemorrhage After Emergent Cesarean Delivery: A Case Report. A Pract. 13: 264-6.