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CASE REPORT

Intestinal perforation in a patient with paroxysmal nocturnal hemoglobinuria

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Abstract

Paroxysmal nocturnal hemoglobinuria (PNH) is a rare hematologic disorder that manifests with hemolytic anemia, thrombosis, and peripheral blood cytopenias.Acute abdominal pain is one of the PNH clinical manifestations due to venous thrombosis of intra-abdominal sites including hepatic, portal, mesenteric, and splenic veins.Eculizumaband allogeneic bone marrow transplantation (BMT) arethe only widely effective therapies for these patients.

We report a case of PNH disorder which presented with abdominal pain and mild tenderness. Abdominal X ray and sonography revealed intra-peritonealfree fluid and air. At laparotomy, an ischemic segment of jejunum with stricture and perforationwith mesenteric venous thrombosis were found. The patient also had a history of hepatic vein thrombosis two years before.

Key Words: Paroxysmal Nocturnal Hemoglobinuria; Intestinal Perforation; Thrombosis; Abdominal Pain

Introduction

PNH is a clonal hematopoietic stem cell disorder that manifests with hemolytic anemia, thrombosis, andbone marrow failure[1-4].

PNH is of similar frequencies in men and women. On the other hand, it is a rare disease with an estimatedprevalenceof approximately 5 per million [2].

Thrombosis is one of the most immediately life threatening and the most common cause of mortality in PNH patients [1,2]. It occurs in approximately 40% of the patients [5]. Thrombosis in PNH may take place at any site.Nonetheless, venous thrombosis is more frequent than arterial thrombosis. The typical sites consist of intra-abdominal (hepatic, portal, mesenteric, splenic, etc.), hepatic vein thrombosis (Budd-Chiari syndrome), and cerebral (sagital and cavernous sinus)[1].

Microvascular thrombosis with intestinal ischemia and limited infarction can produce gangrenous bowel and intestinal perforation, which are some reasons for acute abdominal pain reported in PNH patients [3, 5, 8-10]

Eculizumab, a first in-class monoclonal antibody, and allogeneic bone marrow transplantation (BMT) are the only widely effective therapies for patients with classical PNH [1].

We report a case of PNH disorder that developed an acute abdominal paindue to intestinal perforation.

Cases

A 45–year–old woman referred with a one-day history of generalized abdominal pain that increased in severity and was associated with

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nausea and vomiting. The patient had an underlying hemolytic disorder, PNH, and a history of hepatic vein thrombosis, hepatomegaly and ascites two years before. She also has a drug history of high dose corticosteroids for two years.

Abdominal examination revealed mild tenderness. Abdominal X ray displayed air under both domes of the diaphragm. Ultrasound revealed significant free fluid within the abdomen. Results of complete blood count analysis were as follows: WBC= 3400cells/mcL, RBC=2.86 million cells/mcL, Hct: 25.8%, Hgb=7.8g/dL, plt=120000/mcL. Her coagulation tests were completely disturbed (PTT>120, PT>60, INR>6).

After correction coagulation tests, a laparotomy was carried out. At laparotomy, she was found with an ischemic jejunal segment forty centimeters after teres ligament with stricture and perforation, and mesenteric venous thromboses were present. This segment was resected, and jejenum was anastomosed.

Discussion

PNH is an acquired chronic hemolytic anemia characterized by persistent intravascular hemolysis, pancytopenia, and venous thrombosis [2].

The absence of two glycosylphosphatidylinositol (GPI) anchored proteins, CD55 and CD59, can lead to uncontrolled complementactivation that accounts for other PNH manifestations [1, 2].

In this case,the patient had a history of hepatic vein thrombosis and its associated complications for two years.

Some patients may present with recurrent attacks of severe abdominal pain defying a specific diagnosis. The pain is eventually found to be related to thrombosis [2].

Abdominal pain has been attributed to intestinal dystonia and spasm andmicrovascular thrombosis with intestinal ischemia and limited intestinal infarction, which are occasionally extensive enough to produce gangrenous bowel[5].

In this case, mesenteric venous thromboses were present in laparotomy, and she was found with the stricture of jejunal segment and perforation due to intestinal ischemia.

In some studies that included a total of 465 patients diagnosed with PNH between 1950 and 2005, 83.45 percent of the patients had abdominal pain in their presentation [11]. However, acute abdominal pain has been reported in some cases with complications of mesenteric thrombosis such as small bowl ischemia and perforation [3,9,10,12].

Based on published cases of intestinal ischemia leading to small bowel perforation, surgery should be considered as the first-line treatment, especially when small bowel lesions are limited[3,12].

Eclizumab is a humanized monoclonal antibody that blocks terminal complement by binding to c5 and is the only US Food and Drug Administration approved therapy for PNH [1]. Long-term glucocorticoids are not indicated because there is no evidence that they have any effect on chronic hemolysis [2, 6]. In patients who are not treated with eculizumab, primary prophylaxis should be considered to reduce the risk of thrombosis if there is no contraindication such as thrombocytopenia or other bleeding risks. However, there is a risk that anticoagulation in these patients may lead to complications and major hemorrhage [7].

In this case,the patient was prescribed methylprednisolone for two years. She was not prescribed eclizumab and anticoagulants.

Conclusions

Because thrombosis is one of the most common causes of mortality and morbidity in PNH patients, it is very important to manage these patients properly and prevent complications. Acute abdominal pain is one of the PNH clinical manifestations due to thrombosis. Thus, it is necessary that physicians consider PNH in their differential diagnosis.

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