

CASE REPORT

A CASE OF THROMBOSIS DUE TO PAROXYSMAL NOCTURNAL HAEMOGLOBINURIA PRESENTING AT AN EARLY AGE

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Paroxysmal Nocturnal Haemoglobinuria (PNH) is an acquired, rare life-threatening disorder characterised by complement mediated hemolytic anemia, thrombosis and impaired bone marrow function. It occasionally presents in childhood or adolescence. This is a case of a 14-year old female presented with complaints of shortness of breath, palpitation and abdominal pain whose laboratory test results were consistent with Coomb's test negative haemolytic anaemia. Contrast enhanced Computed Tomography Scan (CT scan) of abdomen revealed splanchnic circulation thrombosis as well as partially occluding thrombus in the inferior vena cava. Flow cytometry showed loss of CD59 expression on erythrocytes confirming the diagnosis of paroxysmal nocturnal hemoglobinuria. Supportive treatment was given with haematinics, blood transfusions and anticoagulants. After that, hematopoietic stem cell transplantation was conducted successfully as a permanent treatment. PNH can present at an earlier age and therefore should be included in differential diagnosis of haemolytic anaemia.

Keywords: Paroxysmal Nocturnal Hemoglobinuria; Thrombosis; Hematinic

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INTRODUCTION

Paroxysmal Nocturnal Haemoglobinuria (PNH) is a rare acquired hematopoietic stem cell disorder with an estimated prevalence of 1-1.5 persons per million of population and is primarily a disease of younger adults with a median age of diagnosis 30-40 years with occasional cases diagnosed in childhood or adolescence. In PNH haemolysis of red blood cells it occurs because of the mutation in PIG-A gene in stem cells of bone marrow. The bone marrow stem cells produce all the mature blood cells. Hence PIG-A mutation is passed on to all cells derived from mutated bone marrow. Cells showing PIG-A mutation lack special proteins called glycosyl phosphatidylinositol anchor (GPI). These special proteins protect the cells from immune complement system. In the absence of these special anchor proteins uncontrolled activation of complement system occurs.¹ Commonly, patients present with clinical signs and symptoms of anaemia, dyspnoea, abdominal pain, thrombosis, end-organ damage and bone marrow failure with cytopenias. Thromboembolism is one of the most common causes of morbidity and mortality in PNH.² This is a case of a young female who presented with PNH complicated by thrombosis at the age of 14 years.

CASE REPORT

A 14-year-old female patient presented with one-month history of shortness of breath, palpitations and episodic abdominal pain. On examination, there was pallor and a tender non-distended abdomen. No other positive systemic findings were present. Laboratory reports showed haemoglobin

of 6.4 mg/dl, white blood cells $4.81 \times 10^9/L$ Red blood cells $2.5 \times 10^{12}/L$, platelet count of $125 \times 10^9/L$ and a reticulocyte count of 5%. Her lactate dehydrogenase levels were raised with values of 631 IU/L. Bone marrow biopsy was performed and it showed hyperplastic erythropoiesis with megaloblastic changes. Her autoimmune profile, HAM'S test and coomb's test were negative. Ultrasound abdomen and KUB was normal. Contrast enhanced CT scan of chest, abdomen and pelvis with contrast were performed and showed splanchnic circulation thrombosis as well as partially occluding thrombus in the inferior vena cava (Figure-1). There were associated mesenteric inflammatory changes and lymphadenopathy as well as ascites. Analytical flow cytometry revealed loss of expression of FLARE and CD157 antigen on subpopulation of patient leukocytes and loss of CD59 expression on some erythrocytes.

With this, diagnosis of PNH was confirmed. Patient was put on iron and folic acid supplementations, low molecular weight heparin followed by warfarin with close monitoring of INR along with regular blood transfusions. Patient responded to the conservative management and became symptoms free but depended on regular blood transfusions. Anticoagulation was continued till hematopoietic stem cell transplantation was done as it is the only definite cure for PNH. Hematopoietic stem cell transplantation was done in December, 2017 in India. Now the patient is under observation for 6 months for outcome of transplantation.

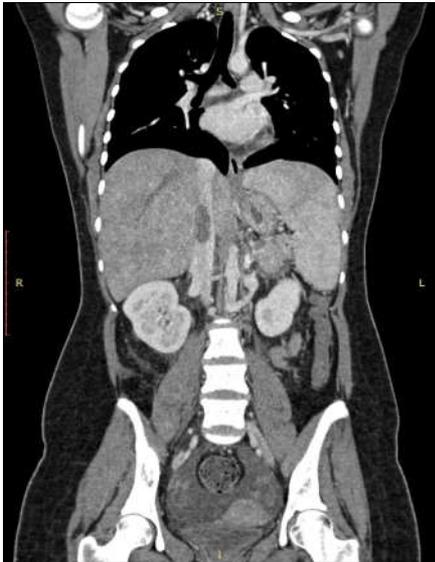


Figure-1: CT scan of chest abdomen and pelvis with contrast showing inferior vena cava thrombosis

DISCUSSION

Hemolytic anemia is a diverse group of intra and extracellular disorders during which breakdown of red blood cells occurs without any defect in erythropoiesis. Paroxysmal Nocturnal Hemoglobinuria is a rare type of intravascular hemolytic disease in which clonal disorder of hematopoietic stem cells related to a somatic mutation in the PIGA gene occurs that involves all blood cells leading to hemolysis, thrombosis and cytopenias.^{3,4} Incidence of PNH is 1–10 cases per million population and is a disease of adults with a median age of onset in thirties to forties.⁵ This case about a 14 year old female diagnosed with PNH contributes to rarity of our case. Paroxysmal Nocturnal Haemoglobinuria is classified into three subtypes. Classical PNH in which there is no underlying bone marrow disease; PNH with the underlying bone marrow disease like aplastic anemia or myelofibrosis; subclinical PNH in which no clinical or laboratory evidence of hemolysis is present but PNH clones are present.⁶ Our case is the one with the classical PNH without any underlying bone disorder. Most common presenting complaints of patients presenting with PNH are related to anemia including: shortness of breath, pallor and palpitations. Other symptoms include

abdominal pain and skin rash. Classical symptom of PNH is red color urine which occurs in 50% of patients but was absent in our patient. Thrombosis is the cause of death in 50% of cases.⁷

In the past, increased severity of PNH RBCs to compliment mediated lysis was demonstrated by HAM test and sucrose hemolysis test. Drawbacks of these tests were that these were nonspecific and difficult to perform. Now-a-days, flow cytometry is the diagnostic test of choice.⁸

Only curative treatment of PNH is hematopoietic stem cell transplantation while all other measures are supportive. Low dose steroids are also useful for the treatment but their role is controversial. Anemia is treated with hematinic and blood transfusions. With the advent of monoclonal antibody Eculizumab, decline in risk of hemolysis and thrombotic events has been seen. Unfortunately, Eculizumab is not available in Pakistan. Long term anticoagulation therapy with warfarin/heparin is being used for prophylaxis in patients with PNH.^{8,9}

CONCLUSION

In a nutshell, PNH is a life-threatening disease which can rarely present at an earlier age and should be included in the differential diagnosis of hemolytic anemia.

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