CASE REPORT

HAEMOGLOBINURIA AND PORTAL VENOUS THROMBOSIS IN A YOUNG MALE

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Paroxysmal nocturnal haemoglobinuria is a non-malignant stem cell disorder due to acquired somatic mutations in cell surface anchored proteins CD55 and CD59. Both have a compliment inhibitory role and their deficiency leads to intravascular haemolysis. This paper reports a challenging case of a 25 years old male who presented with generalized weakness, exertional dyspnoea and episodic early morning haematuria. Recently, he started developing progressive abdominal distention and dull generalized abdominal pain. Investigations revealed haemoglobin 3.5g/dl with 10% reticulocytes, total bilirubin 54.5 mg/dl, LDH 3155 U/L, negative Coomb's test and erythroid hyperplasia on bone marrow biopsy. Urine complete exam was significant for haemoglobinuria without red blood cells. Doppler scan of abdomen showed portal vein thrombosis. Loss of expression of CD14, CD16, CD55 and CD59 on leukocytes and erythrocytes was seen on PNH analysis, confirming paroxysmal nocturnal haemoglobinuria. He was managed with blood transfusions and was advised folic acid and bone marrow transplant.

Keywords: Paroxysmal nocturnal haemoglobinuria; Portal venous thrombosis; Haemolysis, Haemoglobinuria

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INRODUCTION

Paroxysmal nocturnal haemoglobinuria is a rare and acquired disorder, estimated to affect 1–10 per million people.[1] PNH arises due to non-malignant clonal proliferation of hematopoietic stem cells that have acquired a somatic mutation of phosphatidylinositol glycan class A (PIGA). The progeny of the stem cells affected is deficient in glycosyl phosphatidylinositol–anchored proteins (GPI-APs). Among the GPI-APs are two complement mediated proteins, CD55 and CD59, that have inhibitory roles at different levels of the complement cascade. Their deficiency leads to increased susceptibility to complement mediated intravascular hemolysis.[2]

CASE REPORT

A 25 years old male presented to the outpatient department with complaints of progressive generalized body weakness for 3 years. It was associated with exertional dyspnoea for 2 years but there was no associated orthopnoea, paroxysmal nocturnal dyspnoea, oedema, urinary complaints and weight loss.

He also complained of off and on early morning painless haematuria for 1 year. For the past 2 months, he had dull generalized abdominal pain and progressive abdominal distension which was not associated with jaundice, anorexia, diarrhoea, vomiting, fever and joint pains. Past history was not significant for diabetes, hypertension, smoking or drug abuse.

Examination was unremarkable except for pallor, jaundice, ascities and hepatosplenomegaly. Labs showed haemoglobin 3.5 g/dl with 10% reticulocytes and total bilirubin 54.5 mg/dl. Peripheral smear revealed macrocytosis, hypochromia with spherocytes, eliptocytes and tear drop cells. Rest of the cell lines were normal. Further workup for haemolytic anaemia showed LDH 3155 U/L but direct and indirect Coomb's test were negative.

Bone marrow biopsy was significant for erythroid hyperplasia. Urine complete exam showed haemoglobinuria without red blood cells. Ultrasound abdomen confirmed ascities and hepatosplenomegaly and portal vein thrombosis was found on Doppler ultrasound of abdomen. PNH analysis was then ordered which showed loss of expression of CD14, CD16, CD55 and CD59 on leukocytes and erythrocytes which was consistent with paroxysmal nocturnal haemoglobinuria. He was managed with blood transfusions for anaemia, was discharged on folic acid and advised regular follow-ups.

DISCUSSION

Intravascular haemolysis leads to the characteristic episodic passage of dark urine in paroxysmal nocturnal hemoglobinuria.[1] Presenting features in PNH include symptoms of anaemia, haemoglobinuria, haemorrhagic signs and symptoms, thrombosis or embolism, jaundice, haemolytic and aplastic anaemia. Thrombophilia seen in PNH characteristically manifests as

thrombosis of unusual sites (hepatic, mesenteric, cerebral, dermal veins). PNH may develop in the absence of another bone marrow disorder (BMD), as a condition secondary to BMDs or as subclinical PNH.[2] Thromboembolism is the leading cause of mortality, accounting for 40–67% of deaths with known causes.[3]

Eculizumab, a humanized monoclonal antibody that inhibits terminal complement activation, is approved for the treatment of patients with PNH. It resulted in a 92% reduction in the risk of TE ($p<0.001$)[3] and with a highly significant improvement in patient survival to a level comparable to that of age-matched healthy controls[4]. The only potentially curative therapy for PNH is allogeneic bone marrow transplantation; however, this procedure is associated with substantial morbidity and mortality.[5]

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