Case Report

Paroxysmal Nocturnal Haemoglobinuria (classic category)

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Abstract:

Paroxysmal nocturnal haemoglobinuria (PNH) is a rare disease. The prevalence of clinically significant PNH (i.e. classic PNH) plus patients with relatively large clones that arises in the setting of another marrow failure syndrome is likely in the order of less than 1 case per 200,000 population. Here we present a case of classic PNH who presented with acute kidney injury (AKI) requiring haemodialysis secondary to intravascular haemolysis and haemoglobin of 3.6 gm %. Her diagnosis was suggested by positive HAMS test and confirmed by Flow Cytometry. Patient recovered from AKI after starting danazol and her haemolysis was reduced but not controlled fully. Patient is awaiting treatment with either eculizumab or allogenic bone marrow transplantation.

Key words: Paroxysmal Nocturnal Haemoglobinuria , haemolysis, oliuguria, flow cytometry, eculizumab

Introduction

PNH is an acquired clonal stem cell disorder that results in abnormal sensitivity of the red blood cell membrane to lysis by complement. The underlying cause is a defect in the gene for phosphatidylinositol class A (PIG-A), which results in a deficiency of the glycosylphosphatidylinositol (GPI) anchor for cellular membrane proteins. In particular, the complement-regulating proteins CD55 and CD59 are deficient. Deficiency of GPI-anchored complementary regulatory proteins CD55 and CD59 accounts for the intravascular haemolysis that is the primary clinical manifestation of disease.[2] Based on presenting feature, clinical manifestations, and natural history PNH is classified into three categories. (i) Classic PNH (ii) PNH in the setting of another specified bone marrow disorder (iii) PNH-sc (subclinical).[3] Here we present a case of classic PNH.

Case report

Ms. Regmi, 24, from Bhairahawa (Nepal), presented to TU Teaching Hospital with fever and vomiting for 2 days. Fever was unrecorded and was associated with chills and rigor. The vomiting occurred around 10 times a day, about 50 to 100 ml in each episode. She also complained of headache.

She did not give history of joint pain, photosensitivity, bluish patches, excessive menstrual bleeding, pain abdomen, loose stool, bloody diarrhoea, cough, shortness of breath or altered sensorium. There was no significant drug or allergy history.

She said everybody thought she looked pale for the last few years. She also said one and a half years back a doctor told her haemoglobin was low when she visited a hospital for acute diarrhea and vomiting but the cause for low haemoglobin was not worked up.

She visited a nearby medical centre on 2nd day of her illness where she was given antiemetic, antipyretics and intravenous fluids. At the same medical centre she also received 2 units of whole blood transfusion on account of her haemoglobin level of 3.6 gm/dl. On the 3rd day she developed oliguria and cola colored urine which progressed to anuria within a few hours.On the 4th day her whole body was swollen and she was referred to tertiary care centre.

On examination she was pale and edematous. Blood pressure was 90/60 mm Hg. Rest of the vital signs and examinations were normal.

At presentation her haemoglobin level was 7 gm/dl. She had serum creatinine of 686 µmol/L.

Course during hospital stay

For 10 days she had anuria passing only around 10 ml urine per day and was supported with haemo-dialysis. During hospital stay she developed pneumonia along with para-pneumonic effusion and needed to be in medical ICU for one week. She was treated with supportive medication of antibiotics, packed RBC transfusion (2 units in our centre) along with steroids from the beginning of the treatment course. In view of direct coombs test (DCT) negative hemolytic anemia and cola colored urine, HAMS test was advised which came positive. Then, she was investigated with PNH flow cytometry and FLAER. After 4 sessions of dialysis (Danazol) we added Androgens 400mg BD. Her urine output then started to increase gradually from 10 ml per day to 80 ml per day and then 200 ml per day. She received one more session of dialysis (total 5 sessions) during the recovery phase. Her urine output increased to over 2 L it per day in a few days, followed by normalization ofthe creatinine and the cessation of hemodialysis.

PNH flow cytometry/FLAER test revealed PNH clone within granulocytes (77.6%), monocytes (72.4%) and RBCs (8.6%).She developed pain abdomen which was severe and episodic. In the background of high d-dimer we added UFH considering mesenteric thrombosis. CECT abdomen could not be done due to renal impairment. Her investigations were as follows:

	2016/6/7	6/8	6/9	6/13	6/28	6/31	7/10	7/14
Hb (gm/dl)	3.6		7.6		9.2		10.0	10.4
TC (X109 /L)	4.4		4.5		10.8		6.9	4.4
DC (%)	N-75	N-75			N-87		N-72	N-74
	L-27	L-9			L-13		L-25	L-19
Plt (X109 /L)	180		145		133		158	110
Retic (%)	5.6		5		2			
Cr (µmol/L)	397	609	857			82	57	
Urea (mmol/L)	32	31	17.8			6.7	2.9	
Na (mEq/L)	130	130	138				136	131
K (mEq/L)	3.06	3.4	4.6				4.4	4.7
LDH (U/L)			1925			1200	2428	2773
CPK (U/L)			89					
BILI T/D (µmol/L)	55/10		8/2		8/2			
ALT (U/L)	73	23	10		12			
AST (U/L)	158.9	66			15			
d-Dimer (mg/L)				1.2				0.1
ALP (U/L)	148							
PT (C 11S)	12							
APTT (C 28 S)	38							
Albumin (gm/L)	3.5							
RBS (mmol/L)	5							

Peripheral blood smear- anisocytosis, poikilocytosis, normocytes, microcytes, polychromasia, pencil cells, tear drop cells, acanthocytes, macrocytes, target cells
ANA- Negative
Urine analysis: alb ++, RBC plenty, WBC 2-3.
Direct coombs test- negative
Indirect coombs test- negative
Hemoglobin electrophoresis- normal bands
G6PD Qualitative Screening- normal
HAMS test- positive
PNH Flow Cytometry-
RBC: Partial CD59 deficiency 1.1%
Complete CD59 deficiency 7.5%
Granulocytes: FLAER and CD 55 deficiency 77.6%
Monocytes: FLEAR and CD 55 deficiency 72.4%
Findings consistent with diagnosis of PNH.

Discussion

PNH is an acquired chronic haemolytic anaemia (HA) characterized by persistent intravascular haemolysis subject to recurrent exacerbations. In addition to haemolysis, there is often pancytopenia and a distinct tendency to venous thrombosis.[4] One morning, patient may pass blood instead of urine. Although regarded as classical presentation of PNH, more frequently this symptom is not noticed or suppressed. Even in our patient, apart from cola coloured urine in the setting of oliguria and AKI, she never noticed red urine. Our patient didn't respond to glucocorticoid which was given as prednisolone 1 mg/ kg/day. Her AKI resolved with the initiation of danazol. It was difficult to balance her thrombotic event in the background of low platelets. Patient has been given the option of eculizumab and bone marrow transplant, both of which are not available in our country and is very costly.

Conclusion

In this case report, we present a rare case. PNH does not always present in classical way and high index of suspicion is required not to miss its diagnosis which can present in different ways including as a differential in confusing cases of hemolytic anemia or pancytopenia.

Conflict of interest: None declared

Referances

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