REVERSIBLE ACUTE KIDNEY INJURY AS THE INITIAL MANIFESTATION OF PAROXYSMAL NOCTURNAL HEMOGLOBINURIA

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ABSTRACT

Paroxysmal nocturnal hemoglobinuria (PNH) is characterized by triad of intravascular hemolysis, pancytopenia, and thromboembolic complications. Renal abnormalities are rare which occur either due to hemolytic crisis or repeated thrombotic episodes involving small venules .We describe a case of a young female presenting with features of oliguric AKI due to hemosiderin tubulotoxicity as the first manifestation of PNH.

KEYWORDS: PNH, AKI.

INTRODUCTION

Paroxysmal nocturnal hemoglobinuria (PNH) is a rare acquired cause of intravascular hemolysis due to defect in hematopoietic stem cells and is often associated with unusual constellation of clinical findings. It is caused by an unusual susceptibility of erythrocytes to the lytic action of the complement due to their membrane abnormalities and is characterized by chronic intravascular hemolysis and thrombotic tendency.[1] Progenies of the affected stem cells are deficient in glycosyl phosphatidylinositol (GPI)-anchored proteins. Shortage of the GPI-anchored complement regulatory proteins such as CD55 and CD59 is responsible for the intravascular hemolysis that is the primary clinical manifestation of the disease.[2]

Although rare, both acute and chronic kidney involvement can occur in PNH.[3,4] Renal failure as the primary presentation leading to subsequent diagnosis of PNH is even rarer.[5,6] Here, we report a case of young female presenting with AKI due to hemosiderin tubulotoxicity as the first manifestation of PNH.

CASE REPORT

24 year old female presented with chief complaints of passage of dark colored urine and reduction in urine output since five days. She also gave history of similar episode 2 years back for which she was not evaluated. She had no previous history of hypertension, diabetes mellitus or any other chronic disease or any chronic drug use. Clinical examination was notable for the presence of jaundice. The laboratory parameters have been summarized below.

Test	Observed value	Reference range
Hematology		
Hemoglobin	4.5	11–16 g/dL
Total leukocyte count	8700	4000-11000 cells/μL
Platelet count	2,20,000	150000-450000cells/μL
Uncorrected reticulocyte count	5.5	0.5%–2.5%
Kidney function tests		
Blood urea	100	10-50 mg/dl
S. Creatinine	2.7	.6-1.1 mg/dl
S. Uric acid	7.1	3.4-7.0 mg/dl
S.Calcium	8.9	8.5-10.4 mg/dl
S.Phosphate	2.5	2.7-4.5 mg/dl
S.Sodium	139	135-155 mEq/l
S. Potassium	3.9	3.5-5.5 mEq/l
Liver Function Tests	Observed value	Reference range
Sr. Bilirubin total	4.9	0.2-0.8 mg/dl
Sr. Bilirubin direct	0.2	0-0.2 mg/dl
Sr. Bilirubin indirect	4.7	0.2-0.7 mg/dl
SGOT	133	Upto 31 U/L
SGPT	15	Upto 34 U/L
ALP	111	39-90 U/L
Sr. Proteins	6.6	6.4-8.3 g/dl
Albumin	4.0	3.8-4.4 g/dl
Urine analysis		
Protein	+++	nil
Blood	Microscopic hematuria	nil
24 hour protein	556.0	28-141 mg/24 hours

Patient was then further worked up for a possible cause of hemolytic anemia and the reports are summarised below.

	Observed value	Reference range
ANA by IFA	Negative	
Hb electrophoresis	Normal	
Folate levels	14.3	(5.4-18) ng/ml
B12 levels	284	200-840 pg/ml
ICT/DCT	Negative	
G6PD	Normal range	

During hospitalisation, renal function worsened and the patient remained oliguric. In view of AKI, microscopic hematuria, and albuminuria renal biopsy was performed Light microscopy of biopsied sample revealed 7 glomeruli which were morphologically unremarkable Tubulointerstitial compartment showed diffuse acute tubular injury (mild degree) as highlighted by cytoplasmic blebbing tubular dilatation with simplification of tubular lining. In addition, significant number of tubules show presence of golden brown pigment in tubular epithelial cells and in tubular casts. There is mild patchy interstitial edema along with minimal interstitial inflammation. No tubular atrophy or interstitial fibrosis identified. Vascular compartment is unremarkable.

Perls stain - Highlight hemosiderin deposition in tubules. Immunofluorescence for IgG, IgA, IgM, C_3, C1q, Kappa and Lambda and congo red stain was negative.

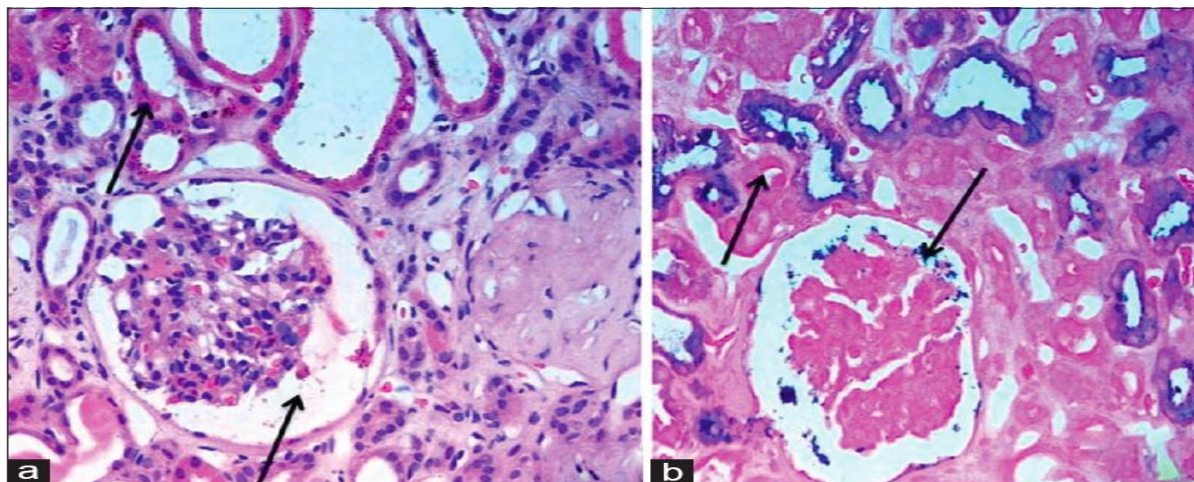The biopsy was suggestive of renal tubule- interstitum damage with hemosiderin deposition.

Fig. 1: (a) Black arrow highlights golden brown hemosiderin pigment both in tubules as well in glomerulus. (b) Prussian blue stain which is strongly positive for hemosiderin in tubules and focally in the glomerulus.

Furthermore, the patient was tested for CD55/CD59 positivity using flow cytometry of peripheral blood granulocytes and it revealed the presence of a PNH clone. The diagnosis of PNH was confirmed She improved with conservative management and Serum creatinine at came down to 1.22 mg/dl.

DISCUSSION

PNH is an acquired clonal disorder of hematopoietic stem cells with a median survival of 10-25 years after diagnosis.[7]

PNH is associated with a wide range of clinical findings .Venous thrombosis is a common problem in patients with PNH and is the leading cause of death in most reports.

Intravascular hemolysis in PNH can lead to acute and chronic renal disease. Only few isolated case reports of acute renal failure complicating PNH have been reported in the literature.[4]

Acute renal failure may occur during severe hemoglobinuric crisis which may be precipitated by blood transfusion, infection, surgical procedure, contrast media, reaction to drugs, sleep and even exercise.[1]

Normally, mild to moderate hemosiderin deposition is only mildly renal toxic. However, in the presence of dehydration and aciduria, it can induce hemoglobinuria-associated acute renal failure. Previous studies demonstrated that hemoglobin induces renal injuries by contraction of renal blood vessels, obstruction because of casts in renal tubular lumens and direct poisonous effects on the kidney.[4] Renal hemosiderosis has been observed in intravascular hemolysis, which can lead apparently to severe tubular atrophy and interstitial fibrosis which causes renal insufficiency.[1] In our case, the presence of hemosiderin on renal biopsy occurred concomitantly with the development of renal insufficiency. A direct nephrotoxic effect of iron by the induction of highly reactive hydroxyl radicals is suggested.[5] Flow cytometric analysis, in which antibodies are directed against complement regulatory proteins CD55 & CD59, is the most informative and sensitive assay available for diagnosis of PNH. The two methods to demonstrate hemosiderosis include renal biopsy and MRI.[1] Because of invasiveness of former method, the imaging findings in MRI are frequently used in assessment of renal cortical hemosiderosis in patients with PNH. For patients with classical PNH, allogeneic hematopoietic cell transplantation (HCT) and complement inhibition with For patients with classical PNH, allogeneic hematopoietic cell transplantation (HCT) and complement inhibition with eculizumab are the only established therapies.

Because, the patient had chronic compensated hemolysis, hemosiderosis was suspected for the etiology of her renal sufficiency. Thus the rarity of renal hemosiderosis as a cause of renal failure in paroxysmal nocturnal hemoglobinuria prompted us to report this case, that also illustrates the importance of early recognition of hemoglobinuric disease in view of definite risk of renal failure and keeping renal hemosiderosis as one of the possibility for the same.

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