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Case Report

Paroxysmal nocturnal hemoglobinuria presenting as acute renal injury

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ABSTRACT

Paroxysmal nocturnal hemoglobinuria **(**PNH) is an acquired chronic hemolytic anemia characterized by persistent intravascular hemolysiswith occasional or frequent recurrent exacerbations. In addition to hemolysis, there may be, pancytopenia and a distinct tendency to venous thrombosis. This triad makes PNH a truly unique clinical condition; however, not all of these three features manifest on presentation. Not many reports of renal involvement in PNH are available in the literature. We report a case of acute kidney injury (AKI) due to PNH. This case shows AKI as one of the complications of PNH.

Keywords: PNH, Intravascular hemolysis, Hemosiderin, AKI

INTRODUCTION

Paroxysmal nocturnal hemoglobinuria (PNH) is a rare disorder characterized by intravascular hemolysis. It results from an acquired defect in the erythrocyte membrane resulting in a deficiency of complement defense proteins on the RBC surface. This leads to abnormal susceptibility to complement-mediated red blood cell destruction, manifesting as paroxysmal hemolysis.[1] PNH is encountered in all populations throughout the world but it is a rare disease, with an estimated prevalence of ~5 per million (it may be somewhat less rare in Southeast Asia and the far East).[2] We report a case of PNH presenting as AKI.

CASE REPORT

A 19-year-old male had a one-month history of yellowish discoloration of skin, sclera and highly colored urine two years back. It was not associated with fever, pain abdomen, confusion or altered mental status, mucosal bleeding, hematemesis, melena, nausea and vomiting. The patient was evaluated and bone marrow aspiration was done which showed megaloblastic anemia and myelodysplastic syndrome (MDS) with multilineage dysplasia and patient was treated with tablet danazol and tablet cyclosporine for six months. A bone marrow biopsy was done after six months which showed mildly hypercellular bone marrow with erythroid hyperplasia and adequate megakaryocytes. The patient gives a history of blood transfusion (packed red blood cells) one to two units every month and his hemoglobin level were maintained between 5 to 7 gm/dl. The patient was now admitted with a history of fatigue for one month and complaints of three episodes of gross hematuria which was not associated with pain abdomen, and burning micturition. It was associated with nausea and vomiting along with decreased urine output for three days after the onset of the illness. His hemoglobin (Hb) was 4.4 gm/dl, total leucocyte count was 2.56×10^3 /µL, and platelet of 57×10^3/µL. His blood urea was 289 mg/dl and serum creatinine were 7.87 mg/dl. Hemodialysis was initiated in view of uremic symptoms and anuria, and a total of five sessions of hemodialysis were given. Ultrasound revealed normal size liver and echotexture and normal size kidneys. USG renal artery and venous doppler showed no evidence

of thrombosis. The patient was evaluated for pancytopenia and hematuria. A tropical fever workup was done and it was negative for dengue fever, malaria and scrub typhus. His vitamin B12 level and folic acid were in the normal range (477 pg/ml and 5 ng/ml) however serum LDH was raised (1342 U/l). Serum complements levels were normal. Antinuclear antibody (ANA) and antineutrophilic cytoplasmic antibody were normal. The peripheral smear did not show any schistocytes. Urine hemosiderin was positive. The patient was evaluated for intravascular hemolysis. Direct and indirect antiglobulin test was negative. Glucose 6 phosphatase dehydrogenase (G6PD) level was within the normal limit (60 units/gram of hemoglobin). Flow cytometric analysis showed PNH clone with RBCs (21.38%), granulocytes (94.49%), and monocytes (94.75%) suggestive of CD 55 and CD 59 deficiency. The final diagnosis of clinical PNH-hypoplastic MDS (type 3 RBC phenotype). The patient was started on tab danazol and oral steroid and advised for HLA matching and hematopoietic stem cell transfer. During his hospital stay, urine output improved gradually and hemodialysis was stopped. He was discharged with a serum creatinine of 1.19 mg/dl.

DISCUSSION

PNH is a rare acquired clonal disorder, affecting all three blood cell lines. The classical form of PNH affects preferentially young people. They suffer from chronic intravascular hemolytic anemia, due to a continuous state of complement activation, but brisk periods of hemolysis may result from complement activation due to infection, surgery, strenuous activity, drugs and alcohol intake.[3] Since hemolysis is due to abnormal sensitivity of RBC to the lytic action of complement, it manifests when the complement cascade is activated, most often by an infection. Hemoglobinuria after intravascular hemolysis underlies the occurrence of acute renal injury in PNH.

The association of PNH and kidney disease was first recognized in the early 1970s. While renal abnormalities in PNH are prevalent, they appeared to be generally mild and may not be brought to medical attention, apart from a few patients presenting with AKI.[4] A lack of two important complement regulatory proteins is observed on the cell surface: 'decay-accelerating factor' (DAF), also called 'CD55' and 'membrane inhibitor of reactive lysis' (MIRL), also called 'CD59'. Thus, red blood cells are more vulnerable to the action of complement.[5] This leads to complement-mediated intravascular hemolysis. As a result, a high concentration of free hemoglobin is found in the plasma, responsible for nitric oxide (NO) scavenging.[6] The role of hemosiderin accumulation in renal tubules as a result of hemolysis and hemoglobinuria, in acute renal toxicity is controversial. It is because intense renal tubular hemosiderosis had been reported in postmortem findings among PNH patients, irrespective of renal function during life and recovery from AKI is not associated with the disappearance of renal hemosiderin. The other possible mechanisms of AKI in PNH are the toxicity of both stromal and free hemoglobin to renal tubules, intrarenal vasoconstriction due to pigments scavenging the vasodilator nitric oxide in renal microcirculation, and intratubular obstruction.[7] NO depletion may also contribute to the development of arterial constriction, leading to reduced blood flow to the kidneys, arterial hypertension and pulmonary hypertension.[8]Hemoglobin filtered from the glomerular during an episode of hemoglobinuria is converted to methemoglobin in the acidic milieu of the distal tubule, which leads to its precipitation and free radical oxidant injury.[9] Flow cytometric analysis of peripheral blood cells (granulocytes or RBCs) using antibodies directed against GPI anchored proteins (GPI-AP) is the most sensitive and informative assay currently available for diagnosis of PNH.[10,11]

Our patient presented with markedly deranged renal functions with very high creatinine, anuria, and hemosiderin in urine with intravascular hemolysis who required hemodialysis, diagnosed as PNH based onflow cytometry.

CONCLUSION

Although renal dysfunction in PNH is rare and as renal dysfunction is a dreadful complication, timely intervention is life-saving for the patient who requires hemodialysis. This case shows that PNH may present with AKI when hemolysis occurs and hemosiderin deposits in the renal tubular epithelial cells. Early diagnosis and treatment are crucial to prevent disease progression.

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REFERENCES

1. Satish S, Rajesh R, Kurian G, Seethalekshmi NV, Unni M, Unni VN. Recurrent acute renal failure. Indian J Nephrol. 2010;20(4):217.
2. Luzzatto L. Hemolytic anemias. In Jameson JL, Kasper DL, Longo DL, Fauci AS, Hauser SL, Loscalzo J, editors. Harrison's Principles of Internal Medicine. 20th ed. New York: Mc Graw Hill. 2018;708-9.
3. Pu JJ, Brodsky RA. Paroxysmal nocturnal hemoglobinuria from bench to bedside. Clin Transl Sci. 2011;4(3):219-24.
4. Chow KM, Lai FM, Wang AY, Chan YL, Tang NL, Li PK. Reversible renal failure in paroxysmal nocturnal hemoglobinuria. Am J Kidney Dis. 2001;37(2):E17.
5. Parker CJ. Management of paroxysmal nocturnal hemoglobinuria in the era of complement inhibitory therapy. Hematology Am Soc Hematol Educ Program. 2011;2011:21-9.
6. Clarkson MR, Friedwald JF, Eustace JA, Rabb H. Acute Kidney injury in Brenner and Rector's The

Kidney. 8th ed. Brenner BM, editor. Philadelphia: Saunders. 2008;943-86.
7. Ram R, Adiraju KP, Gudithi S, Dakshinamurty KV. Renal manifestations in paroxysmal nocturnal hemoglobinuria. Indian J Nephrol. 2017;27(4):289-93.
8. Weitz IC. Thrombosis in patients with paroxysmal nocturnal hemoglobinuria. Semin Thromb Hemost. 2011;37(3):315-21.
9. Nair RK, Khaira A, Sharma A, Mahajan S, Dhinda A. Spectrum of renal involvement in Paroxysmal nocturnal hemoglobinuria: report of three cases and a brief review of literature. Int Urol Nephrol. 2008;40(2):471-5.
10. Parker C, Omine M, Richards S, Nishimura J, Bessler M, Ware R, et al. Diagnosis and management of Paroxysmal nocturnal hemoglobinuria. Blood. 2005;106(12):3699-709.
11. Devalet B, Mullier F, Chatelain B, Dogné JM, Chatelain C. Pathophysiology, diagnosis, and treatment of paroxysmal nocturnal hemoglobinuria: a review. Eur J Haematol. 2015;95(3):190-8.

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