Case Report:

Renal failure in Paroxysmal Nocturnal Hemoglobinuria due to Renal Hemosiderosis


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Abstract:
Paroxysmal nocturnal hemoglobinuria (PNH) is a rare and acquired stem cell disease which is characterized with chronic intravascular hemolysis and diffuse venous thrombosis. In PNH, renal failure is rare and, has been commonly reported in association with infection and thrombosis secondary to PNH. We report a case of 19 years old female with PNH presenting with renal failure due to renal hemosiderosis.

Key words: hemosiderosis, hemolysis, Paroxysmal nocturnal hemoglobinuria, renal failure

Introduction

Paroxysmal nocturnal hemoglobinuria (PNH) is a rare acquired clonal disease of hematopoietic stem cells 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.

Mutation of phosphatidylinositol-glycan protein A gene leads to defective biosynthesis of glycosylphosphatidylinositol (GPI) anchored proteins. Renal hemosiderosis is a known complication of chronic intravascular hemolytic states like PNH. In PNH, renal failure is rare and the spectrum of renal involvement in renal hemosiderosis has only been scarcely reported in literature. Here, we report a case of young female of PNH presenting with renal failure due to renal hemosiderosis.

Case report

A 19 years old female with history of chronic anemia and abdominal pain had been referred for evaluation of deteriorating renal function. She had no significant history of hypertension, diabetes mellitus or any other chronic disease. There was also no history of any long term drug usage. The rest of clinical examination was unremarkable. Laboratory analysis showed Hb-6g/dl, TLC-8000/mm3, platelet count-2 lac/mm3, blood urea-50mg/dl, serum creatinine-10mg/dl. Urine examination was unremarkable and ultrasonography showed cortical thinning with smooth contours, the renal cortex appeared hyperechoic with increased corticomedullary differentiation. Clinically, the possibilities of amyloidosis, membranoproliferative glomerulonephritis, IgA nephropathy and PNH were kept. Further investigations were done including flow cytometry analysis of peripheral blood which demonstrated RBCs with
partial CD55 and CD59 expression and hence patient was diagnosed as PNH. Further kidney biopsy was performed to diagnose the cause of renal failure, on histopathology revealed which mild mesangial proliferation, mild fibrosis in interstitium and tubules showed the presence of brown pigment in epithelial cells (fig.1) which on perl’s stain were positive for hemosiderin (fig.2). Vessels are unremarkable. Also congo red stain and immunoflorescence were performed to rule out other differential diagnosis and were found non contributory. So, finally the diagnosis of PNH with renal failure secondary to renal hemosiderosis was made. Further, patient had been managed with dialysis and is on follow up.

Discussion

PNH is an acquired clonal disorder of hematopoietic stem cells with a median survival of 10-25 years after diagnosis. The disease occurs predominantly in adults, and is rare in children and adolescents. The clinical course of any individual patient with PNH cannot be predicted and may vary from severe hemolysis and thrombosis to years of relative quiescence. Venous thrombosis is a common problem in patients with PNH and is the leading cause of death in most reports. Essentially all patients with classic PNH report gross hemoglobinuria at some point during the course of their illness, but this symptom may be absent in patients with PNH/aplastic anemia or PNH/refractory anemia-MDS. A thromboembolic event may be a presenting manifestation in 5% of cases while gastrointestinal complaints (abdominal pain, dysphagia, male impotence) may be the initial manifestation of the disease in approximately 10% of the patients. While renal abnormalities in PNH are prevalent, they appeared to be mild apart from few patients presenting with acute renal failure. Only 7 isolated case reports of acute renal failure complicating PNH has been reported in the literature. 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. Acute renal failure has been reported in literature in association with infection and thrombosis, secondary to PNH which was not evident in our case. Renal function is seldom severely impaired in PNH despite continuing intravascular hemolysis and heavy siderosis of the kidney. Renal hemosiderosis has been observed in intravascular hemolysis, which can lead apparently to severe tubular atrophy and interstitial fibrosis which causes renal insufficiency. Classically it is assumed that renal function is only uncommonly affected by this pathology but recently it has been speculated that hemosiderin deposition in the proximal tubules might be responsible for the proximal renal tubular acidosis in a patient of PNH. In our case, the presence of iron in the kidney as confirmed 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. 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. However, PNH is not a simply binary diagnosis and both flow cytometry on peripheral blood cells and marrow analysis are required for comprehensive disease classification. The two methods to demonstrate hemosiderosis include renal biopsy and MRI. Because of
invasiveness of former method, the imaging findings in MRI stress its importance as a method of choice in assessment of renal cortical hemosiderosis in patients with PNH. Also vascular patency and iron deposition in other parenchymal organs can be evaluated during the same MR study.\(^3\)

For optimum management, the contribution of both hemolysis and marrow failure to the complex anemia of PNH should be determined. Complement inhibition by eculizumab is a promising new approach for the hemolytic anemia. Stem cell transplantation is potentially curative, but the decision on use is best made on case by case basis.

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.

REFERENCES


