Hemolysis-Induced Acute Renal Failure in Paroxysmal Nocturnal Hemoglobinuria

A.	Aliza	Zeidman ^a
A.	Avry	Chagnac ^b
M.	Meyer	Wisnovitz ^a
M.	Moshe	Mittelman ^a

Departments of ^aMedicine B and ^bNephrology, Hasharon Hospital, Golda Medical Center, Sackler School of Medicine, Tel-Aviv University, Petah-Tikva, Israel

Moshe Mittelman, MD, Department of Medicine B, Hasharon Hospital, Golda Medical Center, PO Box 121, Petah-Tikva 49372 (Israel)

Dear Sir,

Paroxysmal nocturnal hemoglobinuria (PNH) is a rare acquired hematopoietic stem cell disorder characterized by chronic intra-vascular hemolysis and episodes of hemoglobinuria [1-3]. Acute renal failure (ARF) as a complication of PNH is uncommon and usually related to venous thrombosis [2, 3]. ARF due to acute tubular necrosis (ATN) during hemolysis or hemoglobinuria in PNH has been rarely reported [3, 4]. We describe a patient with PNH who developed such a complication and fully recovered on conservative treatment alone, without dialysis.

A 59-year-old woman was admitted for evaluation of fatigue, back pain and 2 episodes of dark urine. Her physical examination was unremarkable. Hemoglobin level was 6.0 g/dl, hematocrit 21%, white blood cell count $3 \times 10^9/l$ (with normal differential count), platelet count $133 \times 10^9/l$, mean corpuscular volume 121 fl and reticulocyte count 3%. Serum bilirubin was 2.5 mg/dl (indirect 1.4 mg/dl) and lactic dehydrogenase (LDH) 2,000 U (normal < 150 U). Serum haptoglobin was 0. Serum urea, creatinine, iron, TIBC (transferrin), vitamin B₁₂, folic acid, erythrocyte glucose-6-phosphate dehydrogenase (G6PD) and hemoglobin electro-phoresis were normal. Coombs' test was negative. Plasma hemoglobin level was 6.3 mg/dl (normal < 1.5 mg/dl). Leukocyte alkaline phosphatase (LAP) score was 4 U (normal 30-100). The bone marrow (BM) was hypo-cellular with erythroid megaloblastosis. A urine sample for myoglobin was negative. Ham and sucrose tests (performed 3 days after admission) were negative.

The patient received 3 U of packed RBC. Three days later, serum urea and creatinine levels rose to 300 and 11 mg/dl, respectively. Serum creatinine phosphokinase (CPK) was normal. Urine flow was 2,000 ml/day with no proteinuria. Urine reacted positively with orthotoluidine and its sediment showed no RBC or casts. Abdominal ultrasound was normal. Kidney biopsy showed focal tubulointerstitial changes, including interstitial edema, tubular cell necrosis and tubular regeneration, as well as acellular tubular (proteinaceous) casts. Glomeruli were normal. These findings suggested pigment-induced ATN. Conservative treatment with intravenous fluids, NaHCO₃ and sodium polystyrene sulfonate was initiated. The following days were characterized by disappearance of the back pain,

stabilization of hematocrit level and a decrease in serum creatinine level to 2.2 mg/ dl a week later.

Pancytopenia, hemolytic anemia, normal serum vitamin B₁₂ and folate levels, hypocellular BM and low LAP score suggest the diagnosis of PNH despite the negative Ham and sucrose tests [1]. ARF complicating PNH is uncommon and is usually due to venous thromboembolism [5] which was excluded here. Ultrasonography ruled out pre- or post-renal azotemia. High serum indirect bilirubin and LDH and the complete absence of serum haptoglobin were consistent with hemolysis. High plasma hemoglobin level and dark urine indicated intravascular hemolysis with hemoglobinuria. Kidney biopsy confirmed the diagnosis of hemoglobin-induced ATN with renal failure.

PNH and ARF due to hemoglobinuria have been rarely reported [2, 3] and are often fatal [6, 7]. The pathogenesis of ARF due to

intravascular hemolysis is not well understood. Possible association of whole blood transfusion, massive hemosiderin deposition, sludging of erythrocytes in the veins and capillaries and a direct tubulotoxic effect of hemoglobin have been suggested [3].

We believe that this rare and severe but potentially reversible complication of hemoglobin-induced ARF should be taken into consideration in patients with PNH.

References

Beutler E: Paroxysmal nocturnal hemoglobinuria; in Williams WJ, Beutler E, Erslev AJ, Lichtman MA (eds): Hematology, ed 4. Maidenhead, McGraw-Hill 1990, pp 188-192.

Mijares RP, Praga M, Izaguirre A: Paroxysmal nocturnal haemoglobinuria presenting as acute renal failure. Nephron 1984;38:69-70.

Clarck DA, Butler SA, Braren V: The kidneys in paroxysmal nocturnal hemoglobinuria. Blood 1981;57:83-89.

Stratta P, Canaves C, Colla L, Vercellone A: Haemolysis, acute renal failure and haemolytic uraemic syndrome. Nephron 1985 ;41:119.

Rubin H: Paroxysmal nocturnal hemoglobinuria with renal failure. JAMA 1971 ;215:433.

Hietzman EJ, Campbell JC, Stephanin M: Paroxysmal nocturnal hemoglobinuria with hemosiderin nephrosis. Am J Clin Pathol 1953; 23: 975-986.

Flamenbaum W, Gehr M, Gross M: Acute renal failure associated with myoglobinuria and hemoglobinuria; in Brenner BM, Lazarus JM (eds): Acute Renal Failure. Philadelphia, Saunders, 1983, pp 269-282.