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Hidden Hemolysis: A Case of Pancytopenia Revealing Paroxysmal Nocturnal Hemoglobinuria

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Abstract: ***Background: Paroxysmal nocturnal hemoglobinuria (PNH) is a rare acquired clonal hematopoietic stem cell disorder characterized by complement-mediated intravascular hemolysis, cytopenias, and thrombosis. Classical hemoglobinuria may be absent, making diagnosis challenging. Case Presentation: A 42-year-old male presented with persistent fatigue and abdominal pain with a known history of pancytopenia requiring multiple transfusions over one year. Initial evaluation revealed severe pancytopenia with markedly elevated serum lactate dehydrogenase and ferritin levels. Peripheral smear showed normocytic normochromic anemia with leukopenia and thrombocytopenia. Bone marrow biopsy demonstrated normocellular marrow with trilineage hematopoiesis. Flow cytometry for PNH profile revealed significant FLAER/CD24 deficient granulocyte and FLAER/CD14 deficient monocyte populations confirming PNH. Conclusion: PNH should be considered in unexplained pancytopenia even in the absence of overt hemoglobinuria. Early diagnosis with flow cytometry is essential for timely management and improved outcomes.***

Keywords: Paroxysmal nocturnal hemoglobinuria, Pancytopenia, Flow cytometry, Bone marrow biopsy, Intravascular hemolysis

1. Introduction

Paroxysmal nocturnal hemoglobinuria (PNH) is a rare acquired clonal hematopoietic stem cell disorder caused by somatic mutation of the phosphatidylinositol glycan class A (PIGA) gene located on the X chromosome. This results in deficiency of glycosylphosphatidylinositol (GPI)-anchored proteins such as CD55 and CD59, rendering blood cells susceptible to complement-mediated destruction. PNH commonly presents with hemolytic anemia, thrombosis, and bone marrow failure syndromes including aplastic anemia. However, classical nocturnal hemoglobinuria may not always be clinically evident, leading to delayed diagnosis.

2. Case Presentation

A 42-year-old male presented with complaints of persistent fatigue and abdominal pain. He was a known case of pancytopenia for one year and had received multiple blood transfusions previously. There were no associated comorbidities. The patient was an alcoholic and tobacco chewer.

Initial investigations revealed hemoglobin of 7.3 g/dL, total leukocyte count of 3250/cumm, and platelet count of 33,000/cumm. During hospitalization, hemoglobin further dropped to 4.9 g/dL with worsening leukopenia and thrombocytopenia. Peripheral smear demonstrated normocytic normochromic red blood cells without anisopoikilocytosis, leukopenia, and thrombocytopenia. Reticulocyte count was 2.56%. Urinalysis did not reveal gross hemoglobinuria.

Serum lactate dehydrogenase was markedly elevated at 2439 U/L. Ferritin level was elevated to 3146.2 ng/mL. Complement levels were reduced with low C3 and C4 levels. Ultrasonography of abdomen and pelvis showed hepatomegaly.

Bone marrow biopsy showed normocellular marrow with trilineage hematopoiesis. Flow cytometry for PNH profile demonstrated FLAER/CD24 deficient granulocytes (50.5%), FLAER/CD14 deficient monocytes (71.2%), and CD59 deficient red blood cells (4.2%), confirming the diagnosis of PNH.

3. Discussion

This case highlights an uncommon presentation of PNH presenting predominantly as pancytopenia without classical hemoglobinuria. PNH frequently overlaps with aplastic anemia and other bone marrow failure syndromes, which may obscure diagnosis. Persistent cytopenias associated with elevated LDH and ferritin should prompt evaluation for occult hemolysis and PNH.

Flow cytometry using FLAER-based assays remains the gold standard diagnostic modality. Early recognition is essential because timely initiation of targeted therapy such as eculizumab can significantly reduce morbidity and improve survival.

4. Conclusion

PNH should be considered in patients with unexplained persistent pancytopenia even in the absence of overt hemoglobinuria. High clinical suspicion and prompt flow cytometric evaluation are crucial for early diagnosis and initiation of appropriate therapy.

Detailed Investigation Chart

Investigation	Result	Reference / Remark
Hemoglobin	7.3 → 4.9 → 7.8 g/dL	Severe anemia
WBC Count	3250 → 1510 → 4100 /cumm	Leukopenia
Platelet Count	33,000 → 45,000 → 31,000 /cumm	Thrombocytopenia
PCV	22.6 → 13.2 → 22.2	Reduced
CRP	89.41 → 17.49	Inflammatory marker elevated
Procalcitonin	3.89 → 0.07	Initially elevated
Total Bilirubin	0.8 mg/dL	Within normal range
Direct Bilirubin	0.4 mg/dL	Normal
Indirect Bilirubin	0.4 mg/dL	Normal
Albumin/Globulin	3.5 / 2.4	Normal ratio
SGOT/SGPT	46 / 38 U/L	Mild elevation
ALP	91 U/L	Normal
Peripheral Smear	Normocytic normochromic RBCs	No anisopoikilocytosis
Reticulocyte Count	2.56%	Mildly elevated
Vitamin B12	320 pg/mL	Normal
Urine Routine	Trace blood, RBC absent	No gross hemoglobinuria
Serum LDH	2439 U/L	Markedly elevated
Ferritin	3146.2 ng/mL	Markedly elevated
Triglycerides	94 mg/dL	Normal
C3	79 mg/dL	Reduced
C4	7.62 mg/dL	Reduced
USG Abdomen	Hepatomegaly	Suggestive finding
Bone Marrow Biopsy	Normocellular marrow with trilineage hematopoiesis	
PNH Flow Cytometry - Granulocytes	FLAER/CD24 deficiency 50.5%	Positive PNH clone
PNH Flow Cytometry - Monocytes	FLAER/CD14 deficiency 71.2%	Positive PNH clone
PNH Flow Cytometry - RBCs	CD59 deficiency 4.2%	Positive PNH clone

Management
Inj Romiplostim 250mg 1/week s/c
Inj Pegfilgrastim 300mg 1-0-0 sc
T Danazol 200mg 1-1-1-1 p/o
Patient was advised about Eculizumab therapy
Discharged on
T Danazol 200mg 1-1-1-1 po
T Prednisolone 40mg in tapering dose
T Homocheck 1-0-1 po

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