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Case Report

Paroxysmal Nocturnal Hemoglobinuria (PNH): So Much for a First Diagnosis: A Case Report

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Abstract: Paroxysmal nocturnal hemoglobinuria (PNH) is a rare acquired disorder of hematopoietic stem cells. Misdiagnosed, patients suffer from true errancy of diagnosis mainly because of the large range of bio-clinical presentations. The following case of a 40-year-old male who went from an unexplored anemia to a falsely diagnosed systemic lupus then an Acute Kidney Injury (AKI) that required some dialysis sessions and later a kidney biopsy which the results threw us off track, highlights that exact problematic and showcases the accuracy and the simplicity of the test once the hypothesis strikes mind: The flow cytometry. Paroxysmal nocturnal hemoglobinuria must be evoked when there is a refractory anemia, a Coombs (-) anemia, thrombosis with hemolysis or cytopenia. The flow cytometry is considered the gold standard diagnostic tool.

Keywords: PNH, Flow cytometry, AKI, hemolytic anemia, Misdiagnosis, Kidney biopsy.

INTRODUCTION

PNH is a rare acquired disorder where hematopoietic stem cells and their cellular progeny lose the ability to anchor certain proteins to the cell surface. Loss of the complement inhibitors, CD55 and CD59, on the surface of red blood cells leads to chronic and/or paroxysmal intravascular hemolysis and a propensity for thrombosis. Flow cytometry is the preferred method for evaluating and diagnosing PNH. First described by Marchiafava and Nazari in 1911 and later by Michelli in 1931, patients suffer from true errancy of diagnosis mainly because of the large range of bio-clinical presentations. The following case highlights that exact problematic. Prompt and accurate diagnosis is particularly important since effective complement inhibitors have become available.

Clinical Features	Immunologic Features
Acute cutaneous lupus (maculopapular lupus rash, malar rash, photosensitive lupus rash, etc.)	High ANA concentration ✓
Chronic cutaneous lupus (discoid rash, mucosal lupus, etc.)	High anti-dsDNA antibody concentration
Oral or nasal ulcers	Presence of anti-Sm
Nonscarring alopecia	Positive APA
✓ Synovitis in ≥2 joints	Low complement (C3, C4, CH50)
✓ Serositis	Direct Coombs test
✓ Renal (urine protein or RBC casts)	Must have a total of 4 features with ≥1 clinical feature and 1 immunologic feature *or* Biopsy-proven LN with anti-dsDNA antibodies or ANA
Neurologic (seizures, psychosis, others)	
✓ Hemolytic anemia	
Leukopenia or lymphopenia (without an identifiable cause)	
Thrombocytopenia (without an identifiable cause)	

ANA: antinuclear antibody; APA: antiphospholipid antibody; dsDNA: double-stranded DNA; LN: lupus nephritis; SLICC: Systemic Lupus International Collaborating Clinics; Sm: Smith.
Source: Reference 1.

Fig n°01: SLICC criteria for systemic lupus, the ones that are checked were found in our patient

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MATERIAL AND METHODS

We report the case of a male subject, aged 40, in his medical history a chronic anemia discovered at the age of 16 but was never explored.

20 years later, he was admitted in internal medicine ward in order to investigate a systemic panel of symptoms made of fatigue, pallor due to a hemolytic anemia, tummy ache, chest pain due to a left pleural effusion, peripheral vascular disease, bilateral and roughly symmetric peripheral arthralgia and brown urine.

After investigation, everything seemed to lead to lupus (Fig n°01), the patient started a steroid based regiment then shortly he developed an AKI that required a couple of hemodialysis sessions plus thrombosis of the left profunda femoris vein, a kidney biopsy showed nothing but some hemosiderin depositions in the renal tubular epithelial cells (Fig n°02).

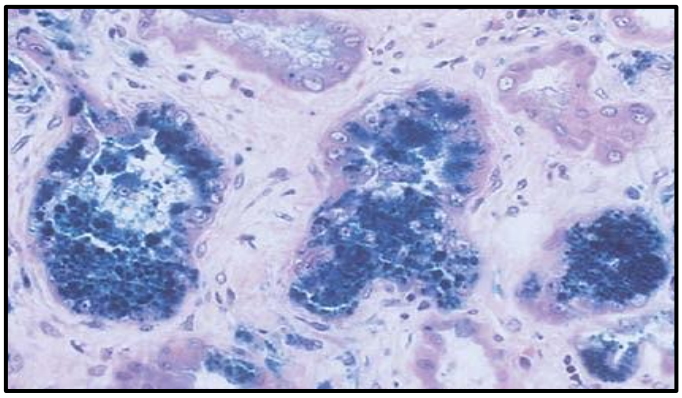

Fig n°02: Hemosiderin depositions in the renal tubular epithelial cells using Pearl's coloring technique

The kidneys recovered their functions fully and the patient received treatment for his thrombosis. 2 years later, the patient came to our nephrology ward in order to investigate the hematuria, he was pale, he complained about sore joints, the rest of the clinical examination was normal. Biologically, there was a hemolytic anemia, Coombs test was negative, the urine stick detected albumin and blood but the latter was absent in the urine sediment exam instead there was hemoglobin which explained the dark color of urine. PNH was diagnosed with flow cytometry (Fig n°03).

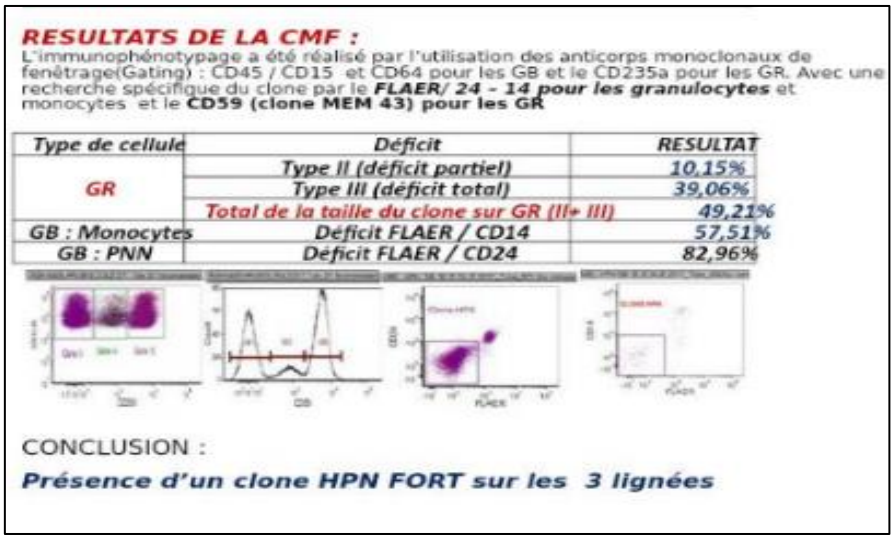

Fig n°03: Results of flow cytometry of the patient showing PHN clones in all lineages

DISCUSSION

Our patient presented at the first place clinical and biological signs leading to a connective tissue disease mainly systemic lupus, but the AKI even if it's found in the latter, showed an important discovery in the biopsy: hemosiderin deposit. The altogether narrows down the hypothesis into incompatible Blood transfusion (ruled out), malaria, autoimmune anemia (Coombs-) and PNH. Once symptomatically treated, the patient recovered every disability and was discharged, which rules out malaria. Later, the patient presented multiple episodes of darkened even brown urine with anemia, the analysis of urine showed hemoglobin and no red blood cells. Flow cytometry showed high percentages of clones in the 03 populations of blood cells.

CONCLUSION

This case shows the ongoing problematic that physicians still encounter these days, even we know now that PNH is known for its polymorphism, the diagnosis doesn't strike physicians' minds, it must be evoked when there is a refractory anemia, a Coombs – anemia, thrombosis wit hemolysis or cytopenia. The flow cytometry is the gold standard diagnostic tool. Prompt and accurate diagnosis is particularly important since effective complement inhibitors have become available.

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