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Case Report

COVID-19 Infection in a Patient with Paroxysmal Nocturnal Hemoglobinuria

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Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS COV-2) activate and enhances complement mediated cell destruction through membrane attack complex (MAC) formation (Ting Gao, 2020) [6]. In paroxysmal nocturnal hemoglobinuria (PNH) there is deficiency of complement regulatory proteins (CD55 and CD59) which enhances the red blood cells (RBC) to lysis by MAC (Rother, 2005) [3]. SARS COV-2 causes complement activation on the other hand individuals with PNH is vulnerable to complement mediated destruction of RBC. In PNH when massive hemolysis occur hemosiderin become deposited in renal tubule causing acute renal tubular necrosis (ATN). If it is diagnosed and treated early it may be reversible but if remain untreated it may progress to chronic kidney disease (CKD) as occur in this patient (Hussain S, 2013) [1]. Individual with PNH when superadded with COVID-19 infection it should be treated with extreme caution to prevent multiple complications.

Keywords: PNH; COVID-19; CKD; Eculizumab; Hb E Trait

Case

The patient was 51 years old gentleman non diabetic normotensive presented with the complaints of feverish for 2 days which was low grade associated with headache and body ache. He also noticed unusual weakness during daily activities. He also noticed cough for same duration which was dry most of the times but occasionally productive with scanty sputum, which had no diurnal variation or any aggravating or relieving factors. There was no history of sore throat, anosmia, and alteration in test sensation, insomnia, hemoptysis, chest pain, joint pain abdominal pain or weight loss. On quires he denies any history of previous tuberculosis or malaria but he gave history of frequent blood transfusion every month for last 6 years and passage of red urine at morning occasionally. He also denies any history of traveling to abroad or risky sexual exposure and history of any cardiovascular operation but gave history of contact with fever and flu like illness of his colleague. He was a government service holder, non-smoker and non-alcoholic. Though he is a defense personal he denies any history of recent long range patrol. He denies taking dapson. On queries he also mentioned occasional intermittent stoppage of urine during micturition.

Figure a

On examination he was found moderately icteric, his body temperature was 100*F, SPO_2 was 97%. There was no organomegaly or lymphadenopathy. He was severely anemic and no evidence of superficial bleeding on skin. His hydration status was normal, no evidence of pitting edema, pulse 110 bpm, BP-100/70 mmHg, respiratory rate-20/min, GCS-15/15. Abdomen examination remained normal with normal digital rectal examination.

Investigations were revealed: Hb-5.6 gm/dl platelets-75000/mm^3, ESR 65mm in first hour ,WBC-5500/mm^3, on PBF-normochromic normocytic anemia, no atypical cell, reticulocyte-11.9, urine for routine examination- RBC-Nil, pus cell-2-3/HPF, epithelial cell- 3-4/HPF, hemoglobin-+++, comb test negative, osmotic fragility test normal, bone marrow-erythroid hyperplasia, chest X-ray- bilateral pneumonitis, HBsAg negative ,anti HCV- negative, echocardiogram-normal, serum bilirubin-3.8 mg/dl, ALT-31 mg/dl, alkaline phosphatase-210mg/dl, serum calcium-8.0 mg/dl TSH -2.7 blood group-B positive, serum vit-B12 assay normal, stool for OBT -normal, LDH-5200, uric acid-7.9, serum creatinine- 3.0 mg/dl six months before which was 2.1 mg/dl, electrolyte-Na/K/Cl-137/4.0/98 mmol/L, D-Dimer-1.31, blood group and Rh typing-B+ve, , Hb electrophoresis- Hb-E trait, USG KUB- enlarged prostate with reduced cortico-medullary differentiation, throat swab for RT-PCR- positive, Blood for malaria not found, serum PSA-normal, PNH disease panel reviled-reduced expression of CD59 and CD55 on neutrophil and RBC. He was diagnosed as a case of 1. COVID -19 pneumonia, 2. Paroxysmal Nocturnal Hemoglobinuria, 3. Hb-E trait, 4. Chronic Kidney Disease stage 3A, 5. Benign enlargement of prostate. Following treatment was given-Inj remdisivir, Inj enoxaparin followed by rivaroxaban 10 mg daily, 05 unit of packed red cell was transfused, folic acid 5mg once daily and tamsulosin 0.4 mg daily was give. Now he is waiting for eculizumab therapy.

Discussion

Severe acute respiratory syndrome coronavirus 2 (SARS COV-2) is an ongoing pandemic, still a lot to know regarding it. There are several known infections like malaria, HIV, mycoplasma, syphilis, EBV, clostridium perfringens that cause hemolysis but regarding SARS COV-2 is yet to be established. SARS COV-2 binds to MASP-2 the key serine protease of lectin pathway of complement activation. Thus it activate complement system and enhances complement mediated cell destruction through membrane attack complex formation (MAC) (Ting Gao, 2020) [6] in Paroxysmal Nocturnal Hemoglobulinemia (PNH) there is a deficient in glycosylphosphatidylinositol (GPI) anchor proteins on red blood cell membrane. Two of these proteins, CD55 and CD59, are complement regulatory proteins (Staurt H Ralston, 2018, p. 950) [4]. CD55 inhibits C3 convertases and CD59 blocks formation of the membrane attack complex (MAC) by inhibiting incorporation of C9 into the MAC. The loss of complement regulatory proteins (CD55 and CD59) in PNH enhances the red blood cells (RBC) vulnerable to hemolysis (Rother, 2005) [3]. SARS COV-2 causes complement activation on the other hand individuals with PNH is vulnerable to complement mediated lysis of RBC. So it may be a devastating condition when individual with PNH become infected with SARS COV-2.

Figure b

PNH is associated with thrombosis at unusual sites such as liver and abdomen; it is also associated with aplastic Anemia and myelodysplastic syndrome (Staurt H Ralston, 2018, p. 950) [4]. When intra-vascular hemolysis occurs free hemoglobin released into plasma and it binds with α2 Globulin produced in liver (Haptoglobin). It also produces met hemoglobin and haemopexin. After saturating all the protecting mechanism hemoglobin appears in urine which is called hemoglobinuria. Renal tubular cell store free hem as hemosiderin, when it sloughed out and shaded with urine it is called haemosiderinuria which is hall mark of intra vascular hemolysis (Staurt H Ralston, 2018, p. 947) [4].

Structural or functional abnormalities of kidney persistent for more than three months are called chronic kidney disease (CKD). Renal involvement in paroxysmal nocturnal Hemoglobulinemia is not usual but reversible acute kidney injury may occur in PNH. In PNH when massive hemolysis occur hemosiderin become deposited in renal tubule causing acute renal tubular necrosis (ATN). If it is diagnosed and treated early it may be reversible but if re-

main unrecognized for long time it may progress to chronic kidney disease (CKD) (Hussain S, 2013) [1]. As patient is normotensive, non-diabetic and urine examination revealed no RBC or protein so probably paroxysmal nocturnal hemoglobinuria was the underlying cause to develop CKD to this patient.

There is a base substitution at codon 26 of the β-globin gene, GAG-AAG, which results in the substitution of lysine for glutamic acid. This imbalance of globin chain causes reduced synthesis of Hb E which manifests as a mild form of β thalassemia (Orkin SH, 1982) [2]. They are mildly anemic and the overall hematological findings are very similar to those of heterozygous β thalassemia (Suthat Fucharoen, 2012) [5]. As this patient was severely anemic so it may not be due to Hemoglobin E trait rather anemia due to intravascular hemolysis.

As patient complains occasional lower urinary symptom (LUTS), digital rectal examination normal and no RBC on routine urine examination moreover PSA is within normal limit and ultrasonography of abdomen revealed prostatic enlargement which means it's a benign enlargement with LUTS. This patient was suffering from COVID-19 with bilateral pneumonia but oxygen saturation was within normal limit that means it was a case of mild COVID-19 pneumonia.

Conclusion

COVID-19 infection may be dangerous other than involving lung or reducing oxygen saturation rather involving kidney following massive hemolysis and development of acute tubular necrosis (ATN) in a patient with Paroxysmal nocturnal Hemoglobulinemia with super added COVID-19 infection. Early recognition of this devastating effect is very important when COVID-19 infection occurs in a patient with Paroxysmal nocturnal Hemoglobulinemia. Eculizumab is the targeted therapy for this condition but timely intervention is the key of success.

Conflict of Interest

None.

Author Contribution

He was the treating physician and contributed to writing and editing of the final manuscript.

Ethical Approval

This manuscript has not been previously published elsewhere. The paper is not currently under process of publication elsewhere. The paper properly credits the contributions of the co-authors. All sources have been disclosed properly in references.

Patient Consented Statement

The patient gave consent for publication of this case.

Data Availability Statement

No datasets were generated or analyzed during the current study.

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