**Patient:** Sophia Carter (DOB: 1990-05-06)  
**Medical Record Number:** 579236  
**Date of Admission:** 2025-03-17  
**Date of Discharge:** 2025-03-24  
**Admitting Physician:** Dr. R. Nelson (Hematology)  
**Consulting Physician:** Dr. J. Kim (Nephrology), Dr. T. Edwards (Gastroenterology)

**Discharge Diagnosis: Paroxysmal Nocturnal Hemoglobinuria with Breakthrough Hemolysis, Acute Kidney Injury (resolved)**

**1. Detailed Diagnosis:**

Primary Diagnosis: Paroxysmal Nocturnal Hemoglobinuria (PNH)  
Date of Initial Diagnosis**:** 2022-05-18  
Current Status: Active disease with breakthrough hemolysis on eculizumab

Flow Cytometry at Diagnosis:

* RBC PNH clone: 55% (Type III PNH cells, complete deficiency of GPI-anchored proteins)
* Granulocyte PNH clone: 68% (FLAER negative)
* Monocyte PNH clone: 72% (FLAER negative)

Molecular Genetics:

* PIGA gene mutation detected: c.756C>G (p.Tyr252\*), resulting in premature termination codon
* Next-generation sequencing panel: No additional mutations in genes associated with myeloid malignancies (ASXL1, DNMT3A, TET2, IDH1/2, RUNX1, TP53 all negative)
* Cytogenetics: Normal female karyotype (46,XX)

Bone Marrow Findings (2022-05-15):

* Hypocellular marrow (40%) for age
* Erythroid hyperplasia with left shift in maturation
* Dyserythropoiesis
* No dysplasia in myeloid or megakaryocyte lineages
* No increase in blasts
* No evidence of clonal evolution to MDS or AML
* Negative for fibrosis

Thrombotic Events:

* 2022-08-12: Mesenteric vein thrombosis (prior to eculizumab initiation)

**2. Current Treatment:**

Current PNH Clone Size Monitoring (2025-03-18):

* RBC PNH clone: 42% (Type III PNH cells)
* Granulocyte PNH clone: 70% (FLAER negative)
* Monocyte PNH clone: 74% (FLAER negative)

Parvovirus B19 mediated breakthrough hemolysis

* IVIGs (25g for 5 days)
* Piperacillin-tazobactam for 5 days
* Eculizumab 900 mg given on 2025-03-17 one week earlier than planned (last Eculizumab dose 2025-03-10)

**3. History of Previous Treatment:**

Initial Management (2022-05 to 2022-09):

* RBC transfusions (received approximately 12 units in total)
* Prednisone trial (60 mg daily × 1 week, then taper) with minimal response
* Hospitalization for mesenteric vein thrombosis (2022-08-12)
* Initial anticoagulation with enoxaparin, then transitioned to apixaban

Eculizumab Initiation (2022-09):

* Induction: 600 mg IV weekly × 4 weeks
* Maintenance: 900 mg IV every 2 weeks
* Meningococcal vaccination completed:
  + Meningococcal quadrivalent conjugate vaccine (MenACWY) 2 weeks prior to first dose
  + Meningococcal group B vaccine (MenB) series completed one month after starting eculizumab
* Annual meningococcal booster vaccinations maintained

Response to Eculizumab:

* Initial response: Excellent, with resolution of hemolysis and improvement in blood counts
* Maintenance response (until current breakthrough): Stable hemoglobin 9.8-10.5 g/dL, LDH 350-450 U/L, no clinically evident hemolysis, no transfusion requirement

Previous Breakthrough Episodes:

* One prior episode (2023-11-15): Resolved with additional eculizumab dose (900 mg)
* Associated with viral respiratory infection

**4. Secondary Illnesses (Comorbidities):**

* Iron deficiency (secondary to chronic intravascular hemolysis and urinary iron loss)
* History of anxiety disorder
* Hypothyroidism (well-controlled on levothyroxine)
* Gastroesophageal reflux disease (GERD)
* Vitamin D deficiency
* Mesenteric vein thrombosis (prior to eculizumab initiation 2022-08-12)

**5. Physical Exam at Admission:**

General: 34-year-old female appearing fatigued and pale.

Vitals: Temperature 38.1°C, Heart Rate 102 bpm, Respiratory Rate 18/min, Blood Pressure 132/82 mmHg, Oxygen Saturation 98% on room air, Weight 62 kg, Height 165 cm, BMI 22.8 kg/m².

HEENT: Normocephalic, atraumatic. Conjunctivae and mucosal surfaces pale. Sclera with mild icterus.

Neck: Supple, no lymphadenopathy, no thyromegaly.

Cardiovascular: Tachycardic with regular rhythm, 2/6 systolic flow murmur. No rubs or gallops.

Respiratory: Clear to auscultation bilaterally. No rales, rhonchi, or wheezes.

Abdomen: Soft, non-tender, non-distended. Normal bowel sounds. No hepatosplenomegaly. Extremities: No edema. No evidence of deep vein thrombosis. No petechiae. Skin: Pale with mild jaundice. No rashes.

Neurological: Alert and oriented ×3. Cranial nerves II-XII intact. Motor strength 5/5 in all extremities. Sensory intact. Deep tendon reflexes 2+ throughout. Normal gait.

**6. Epicrisis:**

Ms. Carter is a 34-year-old female with established PNH on standard eculizumab therapy who presented with a 3-day history of fatigue, cola-colored urine, abdominal pain, and low-grade fever. Laboratory studies confirmed breakthrough intravascular hemolysis with significant drops in hemoglobin, elevated LDH, undetectable haptoglobin, and hemoglobinuria.

The patient was admitted for management of breakthrough hemolysis and acute kidney injury. Piperacillin-tazobactam was started empirically. Extensive workup was performed to identify potential triggers. Blood cultures were obtained and returned negative. Viral studies showed positive PCR for human parvovirus B19. No evidence of recent medication changes or compliance issues with eculizumab was identified.

Treatment included hydration with IV fluids to protect renal function, red blood cell transfusion (2 units), and administration of an additional 900 mg dose of eculizumab on day of admission. Upon confirmation of parvovirus B19 infection, intravenous immunoglobulin (IVIG) therapy was initiated at a dose of 0.4 g/kg/day for 5 consecutive days (total 25 g daily) to control the viral infection. She was continued on her standard anticoagulation with apixaban.

Nephrology was consulted for acute kidney injury (creatinine 1.6 mg/dL). The etiology was attributed to hemoglobinuria causing tubular damage. With aggressive hydration and resolution of hemolysis, renal function improved to baseline (discharge creatinine 0.9 mg/dL).

The patient's hemolysis parameters gradually improved with LDH decreasing to 520 U/L by discharge. Her hemoglobin stabilized at 9.2 g/dL, and hemoglobinuria resolved. Repeat parvovirus B19 PCR showed significant reduction in viral load following IVIG therapy.

Given the breakthrough hemolysis with therapeutic dosing, her eculizumab regimen was modified to 1200 mg IV every 2 weeks, with a plan to monitor therapeutic efficacy closely. The possibility of switching to ravulizumab was discussed as an alternative if breakthrough hemolysis recurs on the intensified eculizumab regimen.

Patient education was provided regarding signs and symptoms of breakthrough hemolysis, the importance of prompt reporting of symptoms, and adherence to scheduled infusions. The patient verbalized understanding of the modified treatment plan and follow-up arrangements.

**7. Medication at Discharge:**

* Eculizumab 1200 mg IV every 2 weeks (increased from 900 mg) (Next dose due: 2025-03-31)
* Penicillin VK 500 mg PO BID (Meningococcal prophylaxis)
* Apixaban 5 mg PO BID
* Levothyroxine 75 mcg PO daily
* Ferrous sulfate 325 mg PO daily
* Folic acid 1 mg PO daily
* Vitamin D3 2000 IU PO daily
* Pantoprazole 40 mg PO daily
* Acetaminophen 650 mg PO Q6H PRN pain or fever

**8. Further Procedure / Follow-up:**

Hematology Follow-up:

* Appointment with Dr. R. Nelson in 1 week (2025-03-31) for next eculizumab infusion and evaluation
* Laboratory monitoring: CBC, reticulocyte count, LDH, haptoglobin, and comprehensive metabolic panel prior to next infusion
* PNH clone size measurement in 3 months

Monitoring for Breakthrough Hemolysis:

* Weekly CBC, LDH for next 4 weeks, then biweekly if stable
* Urinalysis monthly to monitor for hemoglobinuria
* Patient instructed to report immediately if experiencing dark urine, increased fatigue, or fever

Ravulizumab Consideration:

* Will consider transition to ravulizumab (every 8 weeks dosing) if breakthrough hemolysis recurs despite increased eculizumab dosing
* Insurance pre-authorization in process

Nephrology Follow-up:

* Appointment with Dr. J. Kim in 2 weeks (2025-04-07)
* Renal function monitoring with weekly creatinine and urinalysis for 4 weeks

Infectious Disease Management:

* Follow-up parvovirus B19 PCR in 2 weeks to confirm viral clearance
* Consider additional course of IVIG if viral load persists or increases
* Meningococcal vaccination status:
  + Last MenACWY booster received: 2024-09-10
  + Next MenACWY booster due: 2025-09-10
  + MenB booster completed 2024-10, next due 2026-10
* Meningococcal Prophylaxis: Patient must continue Penicillin VK 500 mg PO BID for the entire duration of complement inhibitor therapy.

Patient Education:

* Instructions provided regarding:
  + Signs and symptoms of breakthrough hemolysis
  + Importance of compliance with anticoagulation
  + Recognition of thrombotic events
  + Avoiding triggers (infections, strenuous exercise during illness)
  + Importance of maintaining up-to-date meningococcal vaccinations
  + When to seek immediate medical attention

**9. Lab Values (Excerpt):**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Parameter** | **Admission (2025-03-17)** | **Discharge (2025-03-24)** | **Units** | **Reference Range** |
| WBC | 4.1 | 4.8 | ×10^9/L | 4.0-11.0 |
| Hemoglobin | 6.8 | 9.2 | g/dL | 12.0-15.5 |
| Hematocrit | 20.4 | 27.6 | % | 36.0-46.0 |
| MCV | 98 | 97 | fL | 80-100 |
| Platelets | 95 | 110 | ×10^9/L | 150-400 |
| Reticulocytes | 12.3 | 8.5 | % | 0.5-2.5 |
| Absolute Reticulocytes | 232 | 185 | ×10^9/L | 25-100 |
| LDH | 1,850 | 420 | U/L | 135-225 |
| Haptoglobin | <10 | 12 | mg/dL | 30-200 |
| Total Bilirubin | 3.6 | 1.8 | mg/dL | 0.1-1.2 |
| Direct Bilirubin | 0.5 | 0.3 | mg/dL | 0.0-0.3 |
| BUN | 32 | 16 | mg/dL | 7-20 |
| Creatinine | 1.6 | 0.9 | mg/dL | 0.5-1.1 |
| eGFR | 45 | 86 | mL/min/1.73m² | >90 |
| Serum Free Hemoglobin | 428 | 58 | mg/dL | <20 |
| D-dimer | 1.8 | 0.8 | mg/L | <0.5 |
| Ferritin | 18 | 65 | ng/mL | 15-150 |
| Parvovirus B19 PCR | Positive (high viral load) | Positive (very low viral load) | - | Negative |

**Urinalysis:**

* Admission: Large hemoglobin, 0-2 RBCs/HPF (consistent with hemoglobinuria, not hematuria)
* Discharge: Negative for hemoglobin, 0-2 RBCs/HPF

Electronically Signed By:  
Dr. R. Nelson (Hematology)  
Date/Time: 2025-03-24 15:30

Dr. J. Kim (Nephrology)  
Date/Time: 2025-03-24 14:45