**Patient:** Peter Mitchell (DOB 1955-11-13)  
**Medical Record Number:** 629384  
**Date of Admission:** 2025-03-15  
**Date of Discharge:** 2025-03-22  
**Admitting Physician:** Dr. A. Sharma (Hematology/Oncology)  
**Consulting Physician:** Dr. L. Washington (Gastroenterology), Dr. C. Rodriguez (Neurology)

**Discharge Diagnosis: Primary Myelofibrosis (PMF) Transitioning from Fedratinib to Momelotinib due to Thiamine Deficiency and Encephalopathy**

**1. Detailed Diagnosis:**

Primary Diagnosis: Primary Myelofibrosis (PMF)  
Date of Initial Diagnosis: 2023-08-15  
Current Status: Active disease, DIPSS-Plus High risk

Laboratory Findings at Diagnosis:

* Hemoglobin: 9.2 g/dL (Reference: 13.5-17.5 g/dL)
* White Blood Cell Count: 18.2 × 10^9/L (Reference: 4.0-11.0 × 10^9/L)
* Platelets: 85 × 10^9/L (Reference: 150-400 × 10^9/L)
* Peripheral blood leukoerythroblastosis (nucleated RBCs, immature myeloid cells), peripheral blasts 1%
* Tear-drop shaped red blood cells (dacrocytes)
* LDH: 458 U/L (Reference: 135-225 U/L)
* Serum ferritin: 380 ng/mL (Reference: 30-400 ng/mL)

Bone Marrow Findings (2023-08-12): Bone marrow biopsy: Hypercellular marrow (80%) with marked megakaryocytic proliferation and atypia. Megakaryocytes with abnormal nuclear/cytoplasmic ratio and hyperchromatic, bulbous, and deeply lobulated nuclei. Reticulin fibrosis: Grade 3 (on scale 0-3), Collagen fibrosis: Present. Increased osteosclerosis

Molecular Studies:

* JAK2 V617F mutation: Positive (VAF 42%)
* CALR and MPL mutations: Negative
* Additional mutations detected: ASXL1, EZH2

Cytogenetic Analysis:

* Karyotype: 46,XY,del(13)(q12q22)[15]/46,XY[5]
* FISH: Deletion of 13q confirmed

Risk Stratification:

* Dynamic International Prognostic Scoring System (DIPSS):
  + Age >65 years: 1 point
  + Hemoglobin <10 g/dL: 2 points
  + WBC >25 × 10^9/L: 0 points
  + Circulating blasts ≥1%: 1 point
  + Constitutional symptoms: 1 point
  + Total DIPSS score: 5 points (High risk)
* DIPSS-Plus:
  + DIPSS High risk: 3 points
  + Platelets <100 × 10^9/L: 1 point
  + RBC transfusion need: 1 point
  + Unfavorable karyotype: 0 points
  + Total DIPSS-Plus score: 5 points (High risk)

Clinical Manifestations:

* Hematologic: Anemia requiring intermittent transfusions, moderate thrombocytopenia, leukocytosis
* Splenomegaly: Marked enlargement (22 cm craniocaudal dimension by ultrasound)
* Constitutional symptoms: Night sweats, unintentional weight loss (10 kg over 6 months), fatigue
* Early satiety and left upper quadrant discomfort due to splenomegaly

**2. Current Treatment:**

Encephalopathy suspected due to thiamine deficiency

* Thiamine deficiency (thiamine level 45 nmol/L at admission)
* High-dose substitution of thiamine
* Fedratinib stopped

New Treatment Plan:

* Transition to momelotinib 200 mg PO daily (started on day of discharge)
* Selected due to potential benefits for anemia and lower risk of thiamine-related complications

**3. History of Previous Treatment:**

Ruxolitinib Trial (2023-09-15 to 2024-10-20):

* Initial dose: 20 mg PO BID
* Dose reductions due to thrombocytopenia: 15 mg BID → 10 mg BID → 5 mg BID
* Best response: Minimal spleen reduction (~10%), modest symptom improvement
* Reason for discontinuation: Progressive disease with worsening splenomegaly and constitutional symptoms

Fedratinib Therapy (Started: 2024-11-10

* Last dose: 2025-03-14 (discontinued during admission)
* Duration of therapy prior to admission: 4 months
* Dose at discontinuation: 400 mg PO daily
* Response
  + Spleen size reduction: Approximately 30% reduction by physical examination, confirmed by ultrasound (22 cm → 15 cm)
  + Improvement in constitutional symptoms: Significant reduction in night sweats, weight stabilization
  + Hematologic response: Hgb 8.6 → 10.0 g/dL, WBC 22.4 → 12.6 × 10^9/L, Platelets 70 → 98 × 10^9/L

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

* Hypertension (well-controlled on medication)
* Type 2 diabetes mellitus (diet-controlled, HbA1c 6.8%)
* Coronary artery disease (history of non-ST elevation myocardial infarction 2018, medical management)
* Dyslipidemia
* Chronic kidney disease
* Gout (last flare 2024-12)
* Benign prostatic hyperplasia

**5. Physical Exam at Admission:**

General: 69-year-old male appearing chronically ill with signs of confusion.

Vitals: Temperature 37.2°C, Heart Rate 86 bpm, Respiratory Rate 16/min, Blood Pressure 142/82 mmHg, Oxygen Saturation 97% on room air, Weight 72 kg, Height 178 cm, BMI 22.7 kg/m².

HEENT: Normocephalic, atraumatic. Conjunctivae pale. Sclera anicteric. Mucous membranes dry.

Neck: Supple, no lymphadenopathy, no thyromegaly.

Cardiovascular: Regular rate and rhythm, normal S1/S2, no murmurs, rubs, or gallops.

Respiratory: Clear to auscultation bilaterally.

Abdomen: Soft, mild tenderness in left upper quadrant. Spleen palpable 8 cm below left costal margin. No hepatomegaly.

Extremities: No edema. No joint swelling or erythema.

Skin: Pale, no petechiae, ecchymoses, or jaundice.

Neurological: Oriented to person only, disoriented to place and time. Mild confusion present. Cranial nerves II-XII grossly intact. Motor strength 5/5 in all extremities. Sensory intact. Deep tendon reflexes 2+ throughout. Mildly unsteady gait. No focal motor deficits. Mild horizontal nystagmus noted on lateral gaze.

Lymphatic: No cervical, axillary, or inguinal lymphadenopathy.

**6. Epicrisis:**

Mr. Mitchell is a 69-year-old male with primary myelofibrosis (PMF), DIPSS-Plus high risk, who was admitted due to persistent nausea, vomiting, and diarrhea for 5 days, as well as progressive confusion noted by family members. These symptoms were concerning for potential Wernicke's encephalopathy, a rare but serious complication of fedratinib therapy due to thiamine depletion.

On admission, the patient was disoriented to place and time with mild horizontal nystagmus, along with moderate dehydration and acute kidney injury (creatinine 1.8 mg/dL from baseline 1.2 mg/dL). Thiamine level was ordered urgently and returned low at 45 nmol/L (reference 70-180 nmol/L), confirming thiamine deficiency. Review of outpatient records revealed that while thiamine monitoring was ordered monthly, the most recent level from 3 weeks prior had not been followed up on due to a system error.

The patient was immediately started on IV thiamine replacement (500 mg IV TID for 3 days, then 250 mg IV daily for 5 days) along with aggressive fluid resuscitation. Fedratinib was permanently discontinued due to the neurologic toxicity. Neurology consultation confirmed encephalopathy consistent with early Wernicke's secondary to thiamine deficiency. MRI brain showed mild non-specific periventricular white matter changes but no acute abnormalities.

Gastroenterology was consulted for management of persistent GI symptoms. Upper endoscopy revealed mild gastritis but no evidence of malignancy or bleeding. The patient's GI symptoms were attributed to fedratinib side effects, exacerbated by thiamine deficiency. Symptoms improved with ondansetron, famotidine, and loperamide.

With thiamine supplementation, IV hydration, and supportive care, the patient's mental status gradually improved, returning to his baseline by hospital day 5. Renal function also improved with hydration. After extensive discussion with the patient regarding risk-benefit considerations of the various JAK inhibitors, the decision was made to transition to momelotinib, which has a more favorable anemia profile and no reported association with thiamine deficiency or Wernicke's encephalopathy.

Momelotinib was initiated at 200 mg daily on the day of discharge, with a plan for close monitoring of clinical response and potential side effects. The patient received education regarding the new medication, continued thiamine supplementation, and signs/symptoms that would warrant immediate medical attention.

**7. Medication at Discharge:**

* Momelotinib 200 mg PO daily (initiated on discharge)
* Thiamine 100 mg PO TID
* Ondansetron 8 mg PO q8h PRN nausea/vomiting
* Loperamide 2 mg PO after each loose stool (max 16 mg/day)
* Famotidine 20 mg PO twice daily
* Amlodipine 5 mg PO daily
* Lisinopril 10 mg PO daily
* Atorvastatin 40 mg PO daily
* Aspirin 81 mg PO daily
* Allopurinol 100 mg PO daily
* Tamsulosin 0.4 mg PO daily at bedtime
* Acetaminophen 650 mg PO q6h PRN pain or fever

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

Hematology/Oncology Follow-up:

* Appointment with Dr. A. Sharma in 1 week (2025-03-29)
* Subsequent visits weekly for the first month to monitor transition to momelotinib, then biweekly for 2 months, then monthly
* CBC weekly for 4 weeks, then biweekly for 8 weeks, then monthly
* CMP, LDH, and uric acid weekly for 4 weeks, then monthly
* Thiamine level weekly for 4 weeks, then monthly
* Monitor for momelotinib-specific side effects: headache, dizziness, increased transaminases

Spleen Monitoring:

* Abdominal ultrasound in 3 months to assess spleen response to momelotinib
* Physical examination at each visit

Neurology Follow-up:

* Appointment with Dr. C. Rodriguez in 2 weeks (2025-04-05)
* Comprehensive cognitive and neurological assessment
* Further follow-up as needed based on symptoms

Gastroenterology Follow-up:

* Appointment with Dr. L. Washington in 1 month (2025-04-22)
* Assessment of GI symptoms and medication adjustment as needed

Bone Marrow Transplant Evaluation:

* Consideration for allogeneic hematopoietic stem cell transplantation given high risk disease
* Appointment with Transplant Center scheduled for 2025-04-10
* HLA typing to be completed prior to transplant consultation

Patient Education:

* Instructions provided regarding:
  + New medication regimen (momelotinib): administration, potential side effects
  + Importance of continued thiamine supplementation
  + Reporting signs of neurological symptoms immediately
  + Signs and symptoms of disease progression (increasing fatigue, fever, weight loss, night sweats)
  + When to seek immediate medical attention

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

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Parameter** | **Admission (2025-03-15)** | **Discharge (2025-03-22)** | **Units** | **Reference Range** |
| WBC | 12.6 | 11.8 | ×10^9/L | 4.0-11.0 |
| Hemoglobin | 10.0 | 9.8 | g/dL | 13.5-17.5 |
| Hematocrit | 30.0 | 29.4 | % | 40.0-52.0 |
| MCV | 96 | 97 | fL | 80-100 |
| Platelets | 98 | 105 | ×10^9/L | 150-400 |
| BUN | 32 | 18 | mg/dL | 7-20 |
| Creatinine | 1.8 | 1.3 | mg/dL | 0.7-1.2 |
| eGFR | 38 | 56 | mL/min/1.73m² | >60 |
| Sodium | 134 | 138 | mmol/L | 135-145 |
| Potassium | 3.6 | 4.0 | mmol/L | 3.5-5.0 |
| Chloride | 100 | 104 | mmol/L | 98-107 |
| Bicarbonate | 23 | 25 | mmol/L | 22-29 |
| Glucose | 156 | 132 | mg/dL | 70-99 |
| Calcium | 9.0 | 9.2 | mg/dL | 8.6-10.2 |
| Albumin | 3.4 | 3.6 | g/dL | 3.5-5.0 |
| Total Bilirubin | 1.2 | 1.0 | mg/dL | 0.1-1.2 |
| Alkaline Phosphatase | 96 | 92 | U/L | 45-115 |
| AST | 38 | 32 | U/L | 10-40 |
| ALT | 42 | 36 | U/L | 10-55 |
| LDH | 386 | 370 | U/L | 135-225 |
| Uric Acid | 7.6 | 6.8 | mg/dL | 3.7-8.0 |
| Thiamine | 45 | 120 | nmol/L | 70-180 |
| C-reactive protein | 2.2 | 0.8 | mg/dL | <0.5 |

Electronically Signed By:  
Dr. A. Sharma (Hematology/Oncology)  
Date/Time: 2025-03-22 14:45

Dr. L. Washington (Gastroenterology)  
Date/Time: 2025-03-22 13:30

Dr. C. Rodriguez (Neurology)  
Date/Time: 2025-03-22 12:15