ROCKY MOUNTAIN ONCOLOGY INSTITUTE

DISCHARGE SUMMARY

PATIENT INFORMATION
Name: Jennifer Martinez
Medical Record Number: SYN048
Date of Birth: 11/16/1968

Admission Date: 04/03/2024
Discharge Date: 04/09/2024
Attending Physician: Dr. David Wilson, MD

PRINCIPAL DIAGNOSIS
Stage IV non-small cell lung cancer (adenocarcinoma) with KRAS G12D mutation, metastatic to contralateral lung

SECONDARY DIAGNOSES

1. Immune-mediated colitis (Grade 3)
2. Dehydration (resolved)
3. Hypokalemia (resolved)
4. Fibromyalgia
5. Asthma
6. Hypothyroidism
7. Generalized anxiety disorder

HISTORY OF PRESENT ILLNESS
Ms. Martinez is a 56-year-old female with KRAS G12D-mutated metastatic NSCLC diagnosed in September 2023, currently receiving first-line carboplatin/pemetrexed/pembrolizumab. She presented to the emergency department with a 5-day history of progressively worsening diarrhea (up to 8-10 watery stools per day), diffuse abdominal pain, nausea, and fatigue. She reported one episode of hematochezia the day prior to admission. She denied fever, vomiting, or recent travel. She had completed her 6th cycle of carboplatin/pemetrexed/pembrolizumab 10 days prior to symptom onset and was scheduled to transition to maintenance pemetrexed/pembrolizumab.

On presentation, she was hemodynamically stable but showed signs of dehydration with dry mucous membranes, decreased skin turgor, and orthostatic hypotension. Laboratory studies revealed leukocytosis, hypokalemia, elevated CRP, and normal liver function tests. Stool studies were negative for infectious etiology. Based on the timing of symptoms in relation to

immunotherapy and negative infectious workup, the patient was diagnosed with grade 3 immune-mediated colitis.

DETAILED ONCOLOGIC HISTORY

Date of Diagnosis: September 29, 2023

Presentation: The patient initially presented with persistent cough, shortness of breath, and unintentional weight loss of 12 pounds over 2 months. Chest CT revealed a 4.1 cm left upper lobe mass and multiple bilateral pulmonary nodules suspicious for metastatic disease. PET/CT confirmed hypermetabolic activity in the left upper lobe mass (SUVmax 16.4) and multiple bilateral pulmonary nodules (SUVmax 4.2-7.8). Brain MRI was negative for metastatic disease.

Diagnostic Procedures:

- CT-guided biopsy of left upper lobe mass (09/14/2023): Non-small cell lung adenocarcinoma, moderately differentiated
- Endobronchial ultrasound with transbronchial needle aspiration of station 4R lymph node (09/18/2023): Positive for metastatic adenocarcinoma

Pathology Details:

- Histology: Adenocarcinoma, acinar and solid pattern
- Immunohistochemistry: Positive for TTF-1, Napsin A, and CK7; Negative for p40, CK20, and CDX2
- Molecular Testing:
    - KRAS G12D mutation detected
    - EGFR, ALK, ROS1, BRAF, MET, RET, NTRK: Wild-type/negative
    - PD-L1 (22C3 assay): TPS 30%, CPS 35%, IC 10%
    - TMB: 8 mutations/Mb
    - Next-Generation Sequencing: KRAS G12D, TP53 R273H, STK11 Q37*, CDKN2A deletion

Staging:

- Clinical Stage: cT2bN2M1a (Stage IVA)
- TNM: Primary tumor 4.1 cm (T2b), ipsilateral mediastinal lymph node involvement (N2), contralateral lung metastases (M1a)

Treatment History:

- First-line therapy: Carboplatin AUC 5 D1 + Pemetrexed 500 mg/m² D1 + Pembrolizumab 200 mg D1, q3 weeks
    - Started: October 21, 2023
    - Cycles completed: 6 (last cycle on March 19, 2024)
    - Response assessment after cycle 4 (01/28/2024): Partial response (PR)
        - Left upper lobe primary tumor decreased from 4.1 cm to 2.3 cm (44% reduction)

        - Bilateral pulmonary metastases decreased in size and number
    - Planned transition to maintenance pemetrexed/pembrolizumab after cycle 6

Adverse Events Prior to Current Admission:

- Grade 1 fatigue
- Grade 2 anemia requiring one packed red blood cell transfusion after cycle 3
- Grade 1 nausea
- Grade 1 peripheral neuropathy

PAST MEDICAL HISTORY

1. Fibromyalgia (diagnosed 2015)
2. Asthma (mild, intermittent)
3. Hypothyroidism
4. Generalized anxiety disorder
5. Iron deficiency anemia (pre-existing prior to cancer diagnosis)
6. Migraines with visual aura
7. History of smoking (15 pack-years, quit 2018)

PRIOR SURGICAL HISTORY

1. Laparoscopic cholecystectomy (2010)
2. Cesarean section (2002)
3. Tonsillectomy (childhood)

HOME MEDICATIONS PRIOR TO ADMISSION

1. Levothyroxine 112 mcg PO daily
2. Duloxetine 60 mg PO daily
3. Montelukast 10 mg PO daily
4. Albuterol inhaler 2 puffs PRN wheezing
5. Fluticasone/salmeterol 250/50 mcg inhaled BID
6. Ferrous sulfate 325 mg PO daily
7. Vitamin D3 2000 IU PO daily
8. Calcium carbonate 600 mg PO BID
9. Sumatriptan 50 mg PO PRN migraine (max 200 mg/24h)
10. Ondansetron 4 mg PO q8h PRN nausea
11. Lorazepam 0.5 mg PO PRN anxiety
12. Acetaminophen 650 mg PO q6h PRN pain

ALLERGIES

1. Penicillin (hives)
2. NSAIDs (asthma exacerbation)
3. Shellfish (anaphylaxis)

SOCIAL HISTORY
Former smoker (15 pack-years, quit 2018). Elementary school art teacher, currently on

medical leave. Divorced, lives alone. Two adult children who live nearby. No alcohol use. No recreational drug use.

FAMILY HISTORY
Mother: Breast cancer at age 62, died of complications at age 67 Father: Hypertension, died of myocardial infarction at age 78 Sister: Hypothyroidism, anxiety disorder Brother: No significant medical issues No known family history of lung cancer

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PHYSICAL EXAMINATION ON ADMISSION

Vital Signs:

- Temperature: 37.2°C
- Heart Rate: 104 bpm
- Blood Pressure: 104/68 mmHg (orthostatic drop from 118/74 mmHg when supine)
- Respiratory Rate: 18/min
- SpO_2: 96% on room air

General: Moderately distressed female appearing stated age, lying still in bed due to abdominal discomfort.

HEENT: Normocephalic, atraumatic. Mucous membranes dry. No oral lesions.

Cardiovascular: Tachycardic, regular rhythm. No murmurs, rubs, or gallops.

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

Abdominal: Soft, diffusely tender to palpation, most pronounced in left lower quadrant. No rebound tenderness or guarding. Normal bowel sounds. No hepatosplenomegaly.

Extremities: No edema, cyanosis, or clubbing. Capillary refill <3 seconds.

Skin: No rashes or lesions. Decreased skin turgor.

Neurological: Alert and oriented x3. Cranial nerves II-XII intact. 5/5 strength in all extremities. Sensation intact.

DIAGNOSTIC STUDIES

Laboratory Studies on Admission:

Complete Blood Count:

- WBC: 14.2 × 10^9/L (elevated)
- Hemoglobin: 10.6 g/dL (low)
- Hematocrit: 31.8% (low)
- Platelets: 286 × 10^9/L

- Absolute Neutrophil Count: 10.8 × 10^9/L (elevated)
- Lymphocytes: 2.1 × 10^9/L

Comprehensive Metabolic Panel:

- Sodium: 136 mmol/L
- Potassium: 3.2 mmol/L (low)
- Chloride: 102 mmol/L
- Bicarbonate: 22 mmol/L
- BUN: 24 mg/dL (elevated)
- Creatinine: 0.9 mg/dL
- Glucose: 114 mg/dL
- Calcium: 8.8 mg/dL
- Total Protein: 6.4 g/dL
- Albumin: 3.6 g/dL
- Total Bilirubin: 0.6 mg/dL
- AST: 28 U/L
- ALT: 32 U/L
- Alkaline Phosphatase: 88 U/L

Inflammatory Markers:

- C-Reactive Protein: 68 mg/L (elevated)
- ESR: 46 mm/hr (elevated)
- Procalcitonin: 0.4 ng/mL (mildly elevated)

Stool Studies:

- C. difficile toxin PCR: Negative
- Stool culture: Negative for Salmonella, Shigella, Campylobacter, E. coli O157:H7
- Stool ova and parasites: Negative
- Fecal leukocytes: Positive
- Fecal occult blood: Positive

Imaging Studies:

Abdominal X-ray (04/03/2024): Mildly dilated loops of small and large bowel without evidence of obstruction or free air.

CT Abdomen/Pelvis with IV contrast (04/04/2024): Diffuse wall thickening of the colon, most pronounced in the descending and sigmoid colon, with pericolonic fat stranding and mesenteric lymphadenopathy. Findings consistent with colitis. No evidence of perforation, obstruction, or abscess. No new metastatic disease identified within the abdomen or pelvis.

Chest CT without contrast (04/04/2024): Left upper lobe mass decreased to 2.1 cm (previously 2.3 cm on 01/28/2024). Bilateral pulmonary nodules stable to slightly decreased in size. No new pulmonary lesions. No pleural effusion.

Endoscopic Studies:

Flexible Sigmoidoscopy (04/05/2024): Diffuse continuous inflammation from rectum to descending colon with erythema, friability, loss of vascular pattern, and superficial ulcerations. Multiple biopsies obtained.

Sigmoidoscopy Pathology (04/06/2024): Colonic mucosa with moderate to severe active inflammation, crypt abscesses, and focal ulceration. No viral inclusions, granulomas, or dysplasia identified. Immunohistochemistry for CMV negative. Findings consistent with immune-mediated colitis.

HOSPITAL COURSE

Ms. Martinez was admitted with clinical presentation consistent with grade 3 immune-mediated colitis secondary to pembrolizumab therapy. She was started on intravenous fluids for dehydration, electrolyte replacement for hypokalemia, and bowel rest with clear liquid diet.

Infectious etiologies were ruled out with negative stool studies. Flexible sigmoidoscopy confirmed colitis with biopsies consistent with immune-mediated inflammation. She was initiated on methylprednisolone 1 mg/kg IV BID (80 mg BID) on hospital day 2, with significant improvement in symptoms by day 3.

The frequency of diarrhea decreased from 8-10 episodes daily on admission to 3-4 episodes daily by discharge, with resolution of hematochezia and substantial improvement in abdominal pain. Inflammatory markers trended downward, and electrolyte abnormalities were corrected.

Gastroenterology recommended transitioning to oral prednisone 60 mg daily upon discharge, with a prolonged taper over 8 weeks. Due to the grade 3 severity of the immune-related adverse event, pembrolizumab was permanently discontinued. After multidisciplinary tumor board discussion, the plan is to continue pemetrexed monotherapy after resolution of colitis.

The patient was counseled on the management of immune-related colitis, prednisone taper schedule, and potential symptoms requiring urgent medical attention. She demonstrated good understanding of her condition and management plan.

DISCHARGE MEDICATIONS

1. Prednisone 60 mg PO daily for 14 days, followed by taper:
    - 50 mg daily for 7 days
    - 40 mg daily for 7 days
    - 30 mg daily for 7 days
    - 20 mg daily for 7 days
    - 15 mg daily for 7 days
    - 10 mg daily for 7 days
    - 5 mg daily for 7 days, then discontinue
2. Pantoprazole 40 mg PO daily (while on corticosteroids)
3. Levothyroxine 112 mcg PO daily

4. Duloxetine 60 mg PO daily
5. Montelukast 10 mg PO daily
6. Fluticasone/salmeterol 250/50 mcg inhaled BID
7. Calcium carbonate 600 mg + Vitamin D 400 IU PO BID
8. Vitamin D3 2000 IU PO daily
9. Ferrous sulfate 325 mg PO daily
10. Trimethoprim-sulfamethoxazole 800/160 mg PO three times weekly (Pneumocystis prophylaxis while on high-dose corticosteroids)
11. Nystatin oral suspension 5 mL QID swish and swallow (thrush prophylaxis)
12. Loperamide 2 mg PO after each loose stool, maximum 16 mg/day
13. Ondansetron 4 mg PO q8h PRN nausea
14. Acetaminophen 650 mg PO q6h PRN pain

DISCHARGE INSTRUCTIONS

1. Low-residue diet for 2 weeks, then gradually advance to regular diet as tolerated
2. Monitor and record frequency and consistency of bowel movements daily
3. Take prednisone with food to minimize GI irritation
4. Continue PJP prophylaxis while on prednisone doses >20 mg daily
5. Check blood glucose daily while on high-dose corticosteroids
6. Drink plenty of fluids (at least 2-3 liters daily)
7. Avoid NSAIDs and other medications that may irritate the GI tract
8. Contact oncology team for:
    - Increased diarrhea (>4 episodes per day)
    - Blood in stool
    - Severe or worsening abdominal pain
    - Fever >100.4°F
    - Inability to maintain adequate oral intake
    - Signs of dehydration
9. Continue to avoid pembrolizumab permanently
10. Follow-up appointments as scheduled

FOLLOW-UP PLAN

1. Medical Oncology: Dr. David Wilson - April 16, 2024 (1 week)
2. Gastroenterology: Dr. Sarah Chen - April 23, 2024 (2 weeks)
3. Labs (CBC, CMP, TSH) - April 16, 2024 (with oncology appointment)
4. Restart pemetrexed monotherapy - Tentatively planned for May 2024, pending resolution of colitis
5. Next CT chest/abdomen/pelvis - July 2024 (3 months from current imaging)

ONCOLOGIC ASSESSMENT

Ms. Martinez has stage IV KRAS G12D-mutated non-small cell lung adenocarcinoma with metastases to the contralateral lung, diagnosed in September 2023. Her PDL1 status shows intermediate expression (TPS 30%, CPS 35%, IC 10%).

She has demonstrated good response to first-line carboplatin/pemetrexed/pembrolizumab with a partial response (44% reduction in primary tumor size) and is currently 6.5 months into treatment. The current admission for grade 3 immune-mediated colitis necessitates permanent discontinuation of pembrolizumab.

The presence of KRAS G12D mutation and concurrent STK11 mutation suggests potential resistance to immune checkpoint inhibition, although the patient did demonstrate initial response to combination therapy. Given the molecular profile and good initial response to chemotherapy component, continuation with pemetrexed maintenance monotherapy is recommended once colitis has resolved.

Recent imaging confirms ongoing disease response with slight additional decrease in the primary tumor since previous assessment (from 2.3 cm to 2.1 cm). There is no evidence of disease progression at this time.

The estimated progression-free survival for patients with KRAS-mutated NSCLC treated with platinum-based chemotherapy ranges from 4-7 months. Her ongoing response at 6.5 months is encouraging. Given the early onset of response and continued tumor shrinkage, we anticipate continued disease control with pemetrexed monotherapy, although duration of response may be shorter without the immunotherapy component.

PROGNOSIS

Ms. Martinez has responded well to initial therapy with ongoing partial response at 6.5 months. The need to discontinue pembrolizumab due to grade 3 immune-mediated colitis may impact long-term prognosis, as immune checkpoint inhibitors have been associated with improved overall survival in appropriate candidates.

However, given her continued response to therapy, good performance status (ECOG 1), and the availability of subsequent treatment options in the event of progression, her overall prognosis remains guarded but favorable in the intermediate term. Patients with KRAS-mutated NSCLC have median overall survival of approximately 9-12 months with platinum-based chemotherapy alone, though outcomes can vary significantly based on individual factors.

The resolution of immune-mediated colitis is expected with appropriate corticosteroid therapy, and this adverse event is not anticipated to have long-term effects on her overall health once resolved.

Electronically signed by:

David Wilson, MD
Medical Oncology

Rocky Mountain Oncology Institute
April 9, 2024 14:22