Michelle Lawson (MRN SYN088) born May 9, 1974 fem.

ADMISSION DATE: 04/06/2024 **DISCHARGE DATE:** 04/11/2024

- **ATTENDING PHYSICIAN:** Dr. Sarah Wilson (Neuro-Oncology)

PRIMARY DIAGNOSIS: Stage IV KRAS G12D-mutated non-small cell lung cancer with brain and bone metastases

SECONDARY DIAGNOSES:

1. Status post intracranial hemorrhage (left parietal brain metastasis)
2. Seizure disorder secondary to brain metastases
3. Steroid-induced hyperglycemia (resolved)
4. Migraine with visual aura
5. Hypothyroidism
6. Anxiety disorder

REASON FOR ADMISSION: Acute onset of severe headache, right-sided weakness, and confusion due to hemorrhagic transformation of left parietal brain metastasis.

HISTORY OF PRESENT ILLNESS: Ms. Lawson is a 50-year-old female with KRAS G12D-mutated NSCLC diagnosed in June 2023, currently receiving first-line treatment. On the evening of 04/05/2024, she developed sudden-onset severe headache, described as "the worst headache of my life," accompanied by right-sided weakness, slurred speech, and confusion. Her husband called emergency services, and upon arrival to the Emergency Department, a stat head CT revealed a 2.3 cm left parietal hemorrhagic metastasis with surrounding edema and 3mm midline shift. The patient had completed her 9th cycle of pemetrexed/pembrolizumab 6 days prior to presentation.

ONCOLOGIC HISTORY:

Date of Diagnosis: June 14, 2023

Presenting Symptoms: Persistent cough, fatigue, and right shoulder pain. Initial brain MRI ordered for evaluation of headaches revealed multiple brain metastases.

Diagnostic Studies at Diagnosis:

- Brain MRI (06/10/2023): Three enhancing lesions - left parietal (1.8 cm), right frontal (0.9 cm), right cerebellar (1.1 cm)
- CT Chest/Abdomen/Pelvis (06/12/2023): 4.2 cm left upper lobe mass with ipsilateral hilar and mediastinal lymphadenopathy

- PET/CT (06/13/2023): Hypermetabolic primary lung mass (SUVmax 12.8), hypermetabolic mediastinal lymphadenopathy, and multiple bone metastases (T4, T7, left iliac crest, right femur)
- CT-guided lung biopsy (06/14/2023): Non-small cell lung adenocarcinoma

Molecular Testing:

- KRAS G12D mutation: Positive
- EGFR, ALK, ROS1, BRAF, MET, RET, NTRK: All negative
- PD-L1 (22C3 assay): TPS 35%, CPS 40%, IC 10%
- Next-Generation Sequencing: KRAS G12D, STK11 mutation, TP53 mutation

Initial Staging: cT2bN2M1c (Stage IVB) with metastases to brain and bone

Treatment History:

- First-line therapy: Carboplatin AUC 5 D1 + Pemetrexed 500 mg/m² D1 + Pembrolizumab 200 mg D1, q3 weeks
    - Started: July 6, 2023
    - Current status: Pemetrexed/Pembrolizumab maintenance
    - Best response: Partial response (50% reduction in primary tumor, stable bone metastases)
    - Notable adverse events: Grade 1 fatigue, Grade 2 anemia, Grade 1 neuropathy

Brain-Directed Therapy:

- Whole Brain Radiation Therapy (07/17/2023 - 07/28/2023): 30 Gy in 10 fractions
- Dexamethasone 4mg BID during WBRT, tapered and discontinued by 08/15/2023
- Levetiracetam 500mg BID started 06/15/2023 for seizure prophylaxis

Most Recent Imaging Prior to Admission:

- Brain MRI (03/15/2024): Left parietal lesion decreased to 1.2 cm (previously 1.4 cm), right frontal lesion stable at 0.5 cm, right cerebellar lesion stable at 0.6 cm
- CT Chest/Abdomen/Pelvis (03/15/2024): Primary tumor decreased to 2.1 cm (previously 2.3 cm). Stable bone metastases.

PAST MEDICAL HISTORY:

1. Migraine with visual aura (diagnosed 2010)
2. Hypothyroidism (diagnosed 2018)
3. Generalized anxiety disorder (diagnosed 2015)
4. Iron-deficiency anemia (diagnosed 2020)
5. Gastroesophageal reflux disease

PAST SURGICAL HISTORY:

1. Cesarean section (2009)
2. Cholecystectomy (2015)

SOCIAL HISTORY: Never-smoker. Works as a high school counselor (currently on medical leave). Married with one child (16 years old). No alcohol use. No recreational drug use.

FAMILY HISTORY: Mother: Breast cancer at age 62 (survivor) Father: Hypertension Maternal aunt: Lung cancer at age 55 (never-smoker, deceased)

HOME MEDICATIONS:

1. Levetiracetam 500mg PO BID
2. Levothyroxine 112mcg PO daily
3. Escitalopram 10mg PO daily
4. Omeprazole 20mg PO daily
5. Ferrous sulfate 325mg PO daily
6. Sumatriptan 50mg PO PRN for migraine
7. Acetaminophen 650mg PO q6h PRN for pain
8. Zoledronic acid 4mg IV every 3 months (last dose: 03/01/2024)

ALLERGIES: Penicillin (hives) Sulfa drugs (rash)

PHYSICAL EXAMINATION AT ADMISSION:

Vital Signs:

- Temperature: 37.2°C
- Heart Rate: 94 bpm
- Blood Pressure: 162/94 mmHg
- Respiratory Rate: 18/min
- SpO_2: 96% on room air

General: Alert but disoriented, in moderate distress due to headache.

HEENT: Pupils equal at 3mm, reactive to light. No papilledema on fundoscopic exam.

Cardiovascular: Regular rate and rhythm. Normal S1 and S2. No murmurs, rubs, or gallops.

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

Abdominal: Soft, non-tender, non-distended. Normal bowel sounds.

Musculoskeletal: No joint swelling or tenderness.

Neurological:

- Mental Status: Glasgow Coma Scale 14 (E4, V4, M6). Oriented to person, disoriented to place and time.
- Cranial Nerves: Intact except for mild right facial droop (CN VII).
- Motor: 3/5 strength in right upper and lower extremities, 5/5 strength in left extremities.

- Sensory: Decreased light touch and pin-prick sensation on right side.
- Reflexes: 3+ on right, 2+ on left. Positive Babinski on right.
- Coordination: Unable to test right side due to weakness. Normal on left.

Skin: No rashes or lesions.

DIAGNOSTIC STUDIES:

Laboratory Data on Admission (04/06/2024):

- Complete Blood Count:
  - WBC: 6.8 × 10^9/L
  - Hemoglobin: 10.8 g/dL
  - Platelets: 196 × 10^9/L
- Comprehensive Metabolic Panel:
  - Sodium: 138 mmol/L
  - Potassium: 4.1 mmol/L
  - Chloride: 102 mmol/L
  - CO_2: 25 mmol/L
  - BUN: 14 mg/dL
  - Creatinine: 0.8 mg/dL
  - Glucose: 138 mg/dL
  - Calcium: 9.2 mg/dL
  - Total protein: 6.7 g/dL
  - Albumin: 3.8 g/dL
  - AST: 24 U/L
  - ALT: 22 U/L
  - Alkaline phosphatase: 112 U/L
  - Total bilirubin: 0.6 mg/dL
- Coagulation Studies:
  - PT: 12.6 seconds
  - INR: 1.1
  - PTT: 30 seconds
- Thyroid Function:
  - TSH: 2.8 μIU/mL
  - Free T4: 1.2 ng/dL

Imaging Studies:

Head CT without contrast (04/06/2024): 2.3 cm left parietal hemorrhagic mass with surrounding edema and 3mm midline shift. Blood products within previously known metastatic lesion. No evidence of hydrocephalus.

Brain MRI with and without contrast (04/07/2024):

- Left parietal hemorrhagic metastasis measuring 2.3 cm with surrounding vasogenic edema and mass effect causing 3mm midline shift
- Stable right frontal lesion (0.5 cm) with minimal enhancement
- Stable right cerebellar lesion (0.6 cm)

- No new intracranial metastases

CT Chest/Abdomen/Pelvis with contrast (04/08/2024):

- Primary left upper lobe mass stable at 2.1 cm compared to 03/15/2024
- Stable mediastinal lymphadenopathy
- No new metastatic sites
- Stable sclerotic bone metastases

Electroencephalogram (04/07/2024): Focal slowing in the left parietal region without epileptiform discharges.

HOSPITAL COURSE:

Ms. Lawson was admitted to the Neuro-ICU for management of intracranial hemorrhage. Neurosurgery was consulted and determined that surgical evacuation was not indicated given the location and clinical stability. The patient was started on dexamethasone 10mg IV followed by 4mg IV q6h with significant improvement in edema and associated symptoms.

The patient experienced one focal seizure involving the right arm on hospital day 1, prompting increase in levetiracetam dosage from 500mg BID to 750mg BID. No further seizures occurred during hospitalization.

The patient's right-sided weakness and speech difficulties gradually improved with medical management. By hospital day 3, the patient's strength had improved to 4/5 in the right upper and lower extremities, and she was able to ambulate with minimal assistance.

Repeat head CT on hospital day 3 showed stable hemorrhage without expansion and decreased edema. Medical oncology recommended continuing pembrolizumab/pemetrexed maintenance therapy after recovery from the acute neurologic event, but skipping one dose of pembrolizumab.

Physical therapy and occupational therapy evaluations were completed, with recommendations for outpatient rehabilitation services. The patient participated in therapy sessions with gradual improvement in functional status.

The patient experienced steroid-induced hyperglycemia requiring temporary insulin therapy, which resolved with steroid taper initiated prior to discharge.

By discharge, the patient was alert and oriented x3 with improved right-sided strength (4+/5) and minimal residual dysarthria. She was ambulatory with a walker and independent in most activities of daily living.

PROCEDURES: None

CONSULTATIONS:

1. Neurosurgery (Dr. James Chen): Recommended medical management without surgical intervention given stability and gradual improvement.
2. Medical Oncology (Dr. Maria Rodriguez): Recommended continuing pembrolizumab/pemetrexed maintenance after neurologic recovery, but skipping one dose of pembrolizumab.
3. Physical/Occupational Therapy: Recommended outpatient rehabilitation 3 times weekly for 4 weeks.
4. Endocrinology (Dr. Sarah Klein): Managed steroid-induced hyperglycemia, recommended glucose monitoring during steroid taper.

DISCHARGE MEDICATIONS:

1. Dexamethasone 2mg PO q12h with taper schedule:
    - 2mg q12h for 3 days
    - 1mg q12h for 3 days
    - 1mg daily for 3 days, then discontinue
2. Levetiracetam 750mg PO BID (increased from 500mg BID)
3. Omeprazole 40mg PO daily (while on dexamethasone)
4. Levothyroxine 112mcg PO daily
5. Escitalopram 10mg PO daily
6. Ferrous sulfate 325mg PO daily
7. Acetaminophen 650mg PO q6h PRN for pain
8. Sumatriptan 50mg PO PRN for migraine (avoid during acute post-hemorrhagic period)
9. Zoledronic acid 4mg IV every 3 months (next dose: 06/01/2024)

DISCHARGE INSTRUCTIONS:

1. Take all medications as prescribed, following dexamethasone taper schedule
2. No driving until cleared by neurology (minimum 3 months seizure-free)
3. Use walker for ambulation until cleared by physical therapy
4. Monitor blood glucose daily while on dexamethasone
5. Seizure precautions: no bathing unattended, no swimming, no operating dangerous machinery
6. Follow up with appointments as scheduled
7. Return to emergency department immediately for:
    - Increasing headache
    - New or worsening weakness
    - Changes in vision or speech
    - Seizure activity
    - Confusion or altered mental status

FOLLOW-UP PLAN:

1. Neurosurgery: Dr. James Chen - 04/25/2024 (2 weeks)
2. Medical Oncology: Dr. Maria Rodriguez - 04/21/2024 (10 days)
3. Radiation Oncology: Dr. Robert Davis - 05/09/2024 (4 weeks) for SRS planning
4. Neurology: Dr. Thomas Williams - 05/02/2024 (3 weeks)
5. Brain MRI: 05/09/2024 (prior to radiation oncology appointment)
6. Physical Therapy: Metropolitan Rehabilitation Center - Initial visit 04/15/2024
7. Occupational Therapy: Metropolitan Rehabilitation Center - Initial visit 04/15/2024

ONCOLOGIC ASSESSMENT:

Ms. Lawson has KRAS G12D-mutated NSCLC diagnosed in June 2023 with metastases to brain and bone. She has been receiving first-line carboplatin/pemetrexed/pembrolizumab and pemetrexed/pembrolizumab maintenance with partial response. Her PDL1 status was intermediately positive (TPS 35%, CPS 40%, IC 10%).

The presence of KRAS G12D and STK11 co-mutations suggests potential resistance to immunotherapy, though the patient has demonstrated partial response to combination therapy to date. The current hemorrhagic complication involving a known brain metastasis is likely related to tumor necrosis and/or underlying vascular fragility, rather than true disease progression, as other metastatic sites remain stable or improved on recent imaging.

Given the hemorrhagic event, pembrolizumab will be temporarily paused due to theoretical risk of enhanced inflammatory response, though a direct causal relationship between immunotherapy and hemorrhagic transformation is not clearly established.

Close surveillance with brain MRI every 2-3 months is recommended given the patient's history of brain metastases and recent hemorrhagic event.

The patient has received zoledronic acid for bone metastases, which will continue on the established schedule to reduce risk of skeletal-related events.

Overall prognosis remains guarded but favorable in the intermediate term, given the patient's good performance status prior to the current event, ongoing response to therapy, and absence of systemic disease progression. Careful management of neurologic complications and transition to appropriate maintenance therapy should allow for ongoing disease control.

PROGNOSIS:

Ms. Lawson has experienced a significant neurologic complication of her brain metastases but has demonstrated good recovery with appropriate medical management. The hemorrhagic event itself does not necessarily indicate disease progression, as other disease sites remain stable or improved on imaging.

Patients with KRAS G12D-mutated NSCLC with brain metastases typically have median survival of 10-14 months from diagnosis. However, the patient's good initial response to therapy, young age, never-smoking status, and good performance status prior to the current complication are favorable prognostic factors.

With appropriate management of the current neurologic complication, transition to pemetrexed maintenance therapy, and planned stereotactic radiosurgery to the hemorrhagic lesion, continued disease control for an additional 6-12 months or longer is reasonable to expect, though the presence of brain metastases remains a significant adverse prognostic factor requiring vigilant monitoring.

Electronically signed by:

Sarah Wilson, MD, PhD
Neuro-Oncology
Northside Medical Center
04/11/2024 15:30