Patient: Freddy Wilson (DOB 1954-08-22)
Medical Record Number: SYN129
Date of Admission: 2025-04-07
Date of Discharge: 2025-04-14
Admitting Physician: Dr. B. Cohen (Medical Oncology)
Consulting Physicians: Dr. L. Rivera (Radiation Oncology), Dr. S. Kim (Neurosurgery), Dr. M. Ahmed (Palliative Care)

Discharge Diagnosis: Progressive CNS Metastases With Leptomeningeal Disease Due to EGFR T790M-Mediated Osimertinib Resistance

1. Detailed Oncological Diagnosis:

Primary Diagnosis: Non-Small Cell Lung Cancer (NSCLC), Adenocarcinoma, Stage IVB
Date of Initial Diagnosis: June 9, 2020

Histology:

- CT-guided biopsy of right lower lobe mass (June 2020) revealed moderately to poorly differentiated adenocarcinoma.
- Immunohistochemistry: Positive for TTF-1, CK7, Napsin A. Negative for p40, CK20, Synaptophysin.
- Original Molecular testing:
    - EGFR: L858R mutation positive
    - ALK: No rearrangement
    - ROS1: No rearrangement
    - BRAF: Wild-type
    - KRAS: Wild-type
    - MET: No amplification or exon 14 skipping mutation
    - RET: No rearrangement
    - NTRK: No fusion
- PD-L1 expression: 60% Tumor Proportion Score (TPS), CPS 65, IC 15%

Staging at Diagnosis:

- TNM (8th edition): cT2bN2M1c (Stage IVB)
- Imaging Studies at Diagnosis (June 2020):
    - Chest CT: 4.2 cm mass in right lower lobe with ipsilateral hilar and mediastinal lymphadenopathy.
    - Brain MRI: Three parenchymal brain metastases (right frontal 1.8 cm, left parietal 1.2 cm, right cerebellar 0.9 cm) with associated edema.
    - PET/CT: FDG-avid primary mass (SUVmax 14.5), mediastinal lymphadenopathy, and mild uptake in known brain metastases.

2. History of Oncological Treatment:

First-line Therapy:

- Osimertinib 80 mg PO daily
- Initiated July 1, 2020

- Initial excellent response in CNS and systemic disease
- Disease progression documented November 2022 (PFS 28 months)
- Liquid biopsy at progression revealed EGFR T790M resistance mutation

Radiation Therapy:

- Stereotactic radiosurgery (SRS) to initial three brain metastases (July 2020)
  - Right frontal: 21 Gy in 1 fraction
  - Left parietal: 21 Gy in 1 fraction
  - Right cerebellar: 21 Gy in 1 fraction
- Repeat SRS to two new brain metastases (November 2022)
  - Left temporal: 20 Gy in 1 fraction
  - Right parietal: 20 Gy in 1 fraction
- Whole brain radiation therapy (WBRT) for multiple new lesions (October 2023)
  - 30 Gy in 10 fractions

Second-line Therapy:

- Carboplatin AUC 5 + Pemetrexed 500 mg/m² IV every 3 weeks
- Initiated December 2022
- Completed 6 cycles (through May 2023)
- Followed by pemetrexed maintenance
- Progressive disease after 6 months of maintenance (November 2023)

Third-line Therapy:

- Docetaxel 75 mg/m² + Ramucirumab 10 mg/kg IV every 3 weeks
- Initiated December 2023
- Clinical benefit for 3 cycles
- Progressive disease documented February 2024

Fourth-line Therapy:

- Clinical trial of novel 4th generation EGFR TKI (PROT-EGFR-7742)
- Initiated March 2024
- Initial disease stabilization
- CNS progression documented December 2024
- Discontinued from trial January 2025

Supportive Procedures:

- Ventriculoperitoneal (VP) shunt placement (February 2025) for hydrocephalus secondary to leptomeningeal disease

3. Imaging:

- Brain MRI (April 5, 2025): Extensive leptomeningeal enhancement throughout basilar cisterns, sylvian fissures, and along the cerebellar folia. Multiple new parenchymal enhancing lesions (>15 lesions). Stable VP shunt with no evidence of obstruction.

- CT Chest/Abdomen/Pelvis (March 2025): Progression of primary lung mass (now 5.2 cm) and new liver metastases in segments 4a and 8 (2.3 cm and 1.8 cm).
- Spine MRI (April 8, 2025): Extensive leptomeningeal enhancement throughout the spinal cord with nodular thickening at L2-L3 and L5-S1 levels.

4. Comorbidities:

- Coronary artery disease s/p MI and PCI (2017)
- Hypertension (diagnosed 2012)
- Type 2 diabetes mellitus (diagnosed 2015)
- Hyperlipidemia (diagnosed 2012)
- Atrial fibrillation (diagnosed 2018, rate-controlled)
- Chronic kidney disease stage II (eGFR 60-89)
- History of DVT (2020, associated with malignancy)
- Former smoker (30 pack-year history, quit 2018)

5. Physical Exam at Admission:

General: 70-year-old male appearing chronically ill and cachectic, with evident fatigue and confusion.

Vitals: BP 142/85 mmHg, HR 92 bpm (irregular), RR 18/min, Temp 37.0°C, SpO2 95% on room air.

HEENT: Normocephalic. VP shunt visible behind right ear. No scleral icterus. Pupils equal but sluggishly reactive.

Neck: Supple. No cervical or supraclavicular lymphadenopathy. No JVD.

Cardiovascular: Irregularly irregular rhythm. Normal S1, S2. No murmurs, rubs, or gallops.

Respiratory: Decreased breath sounds in right lower lobe. Scattered rhonchi bilaterally. No wheezes.

Abdomen: Soft, mildly tender in right upper quadrant. Palpable liver edge 3 cm below costal margin. VP shunt reservoir palpable in right upper quadrant.

Extremities: 1+ bilateral lower extremity edema. No calf tenderness.

Skin: Pale with scattered ecchymoses on extremities.

Neurological: Fluctuating mental status, oriented to person only. Cranial nerves: Left facial droop and left lateral gaze palsy. Motor: Right-sided weakness (3/5 in right upper and lower extremities). Left-sided strength 4/5. Bilateral positive Babinski sign. Unable to assess coordination or gait due to weakness and confusion.

ECOG Performance Status: 3 (deteriorated from 2 over past month)

6. Hospital Course Summary:

Mr. Wilson was admitted for evaluation and management of progressive neurological symptoms including confusion, right-sided weakness, headache, and diplopia. MRI of the brain and spine revealed extensive leptomeningeal disease and multiple new parenchymal metastases despite prior whole brain radiation therapy. Lumbar puncture confirmed malignant cells in CSF.

The patient had previously been diagnosed with EGFR L858R positive metastatic NSCLC in June 2020 with brain metastases at presentation. He had an excellent initial response to osimertinib for 28 months, followed by progression with development of the T790M resistance mutation. Despite multiple subsequent lines of therapy, including chemotherapy and an investigational 4th generation EGFR TKI, his disease had progressed significantly with extensive CNS involvement.

During this admission, dexamethasone was initiated at 10 mg IV q6h with modest improvement in neurological symptoms. Neurosurgery assessed the VP shunt, which was functioning appropriately. The patient was not a candidate for Ommaya reservoir placement due to poor performance status and extensive disease burden.

A comprehensive multidisciplinary meeting including medical oncology, radiation oncology, neurosurgery, and palliative care determined that further anti-cancer therapy was unlikely to provide meaningful benefit given his poor performance status, extensive prior treatments, and aggressive disease biology. The team recommended transition to hospice care with focus on symptom management and quality of life.

Extensive discussions were held with the patient and family regarding prognosis and goals of care. After thoughtful consideration, the patient and family elected to pursue palliative care. His neurological symptoms were stabilized with high-dose dexamethasone and scheduled pain medication. Anti-seizure prophylaxis was initiated due to multiple brain metastases. Patient died peacefully on 2025-04-14.

9. Lab Values (Excerpt):

Parameter	Baseline (6/2020)	Previous Visit (3/2025)	Admission (4/7/2025)	Discharge (4/14/2025)	Units	Reference Range
WBC	8.5	12.8	14.2	15.1	× 10^9/L	4.0-11.0
Hemoglobin	13.5	10.2	9.8	9.5	g/dL	13.5-17.5 (M)
Hematocrit	40.5	30.6	29.4	28.5	%	41.0-53.0 (M)
Platelets	275	185	162	148	× 10^9/L	150-400
Creatinine	1.1	1.4	1.5	1.6	mg/dL	0.7-1.3
eGFR	72	52	48	45	mL/min	>60
BUN	16	28	32	34	mg/dL	7-20
Sodium	138	135	132	133	mmol/L	135-145
Potassium	4.2	4.5	4.7	4.6	mmol/L	3.5-5.0
Glucose	142	156	182	208	mg/dL	70-100
Albumin	3.8	3.0	2.8	2.7	g/dL	3.5-5.0

Parameter	Baseline (6/2020)	Previous Visit (3/2025)	Admission (4/7/2025)	Discharge (4/14/2025)	Units	Reference Range
Total Protein	6.8	5.8	5.6	5.5	g/dL	6.4-8.2
ALT	28	45	68	72	U/L	7-56
AST	32	52	78	84	U/L	8-48
Alk Phos	86	182	235	248	U/L	45-115
Total Bilirubin	0.8	1.2	1.6	1.8	mg/dL	0.2-1.2
INR	1.0	1.3	1.4	1.4	Ratio	0.8-1.1

Cerebrospinal Fluid Analysis (4/8/2025):

- Appearance: Cloudy, colorless
- Opening pressure: 24 cm H2O (elevated)
- RBC: 85/mm³
- WBC: 38/mm³ (predominantly lymphocytes)
- Protein: 128 mg/dL (elevated)
- Glucose: 42 mg/dL (decreased)
- Cytology: Positive for malignant cells consistent with adenocarcinoma
- Molecular testing on CSF: EGFR L858R and T790M mutations detected

Electronically Signed By:
Dr. B. Cohen (Medical Oncology)
Date/Time: 2025-04-14 16:25

Dr. L. Rivera (Radiation Oncology)
Date/Time: 2025-04-13 15:40

Dr. S. Kim (Neurosurgery)
Date/Time: 2025-04-13 14:15

Dr. M. Ahmed (Palliative Care)
Date/Time: 2025-04-14 11:30