PATIENT INFORMATION: Name: Albert Gray DOB: 08/14/1948 (76 years) MRN: SYN217 Admission Date: 04/04/2022 Discharge Date: 04/14/2022 Attending Physician: Dr. Jonathan Hayes, Palliative Medicine Consulting Services: Medical Oncology, Interventional Pain Management

PRINCIPAL DIAGNOSIS: Terminal care for extensively pretreated metastatic non-small cell lung cancer with widespread bone metastases and spinal cord compression.

SECONDARY DIAGNOSES:

1. Malignant spinal cord compression at T8-T10 (status post palliative radiation)
2. Severe cancer-related pain
3. Cancer cachexia
4. Opioid-induced constipation
5. Steroid-induced hyperglycemia
6. History of COPD, moderate (40 pack-year smoking history)

DETAILED ONCOLOGICAL HISTORY:

Initial Diagnosis (April 2020): Patient initially presented with unexplained weight loss, persistent cough, and severe back pain. Chest CT revealed a 6.2 cm left lower lobe mass with retroperitoneal and mediastinal lymphadenopathy and multiple lytic bone lesions in the thoracic spine, ribs, and pelvis.

Histopathology (Initial Diagnosis): CT-guided Biopsy of Left Lower Lobe Mass (04/04/2020):

- Gross Description: Three cores of tan-white tissue measuring 0.8-1.5 cm in length
- Microscopic Findings:
  - Poorly differentiated squamous cell carcinoma
  - Predominantly solid growth pattern
  - Infiltrating nests and sheets of tumor cells with focal keratinization
  - Intercellular bridges visible in well-preserved areas
  - Central necrosis present in larger tumor nests
  - Marked nuclear pleomorphism with coarse chromatin
  - Prominent eosinophilic cytoplasm
  - Brisk mitotic activity (18 mitoses/10 HPF)
  - Stromal desmoplasia with moderate inflammatory infiltrate
  - Perineural invasion present
  - Lymphovascular invasion identified
- Immunohistochemical Profile:
  - p40: Strongly positive (diffuse nuclear)
  - p63: Positive (diffuse nuclear)
  - CK5/6: Positive (cytoplasmic and membranous)
  - TTF-1: Negative
  - Napsin A: Negative
  - CK7: Focally positive
  - Synaptophysin: Negative
  - Chromogranin: Negative
  - CD56: Negative
  - Ki-67: 60% proliferation index
- Molecular Testing:
  - Next-Generation Sequencing Panel:
    - No actionable driver mutations
    - PI3KCA E545K mutation (allelic frequency 38%)
    - TP53 R158L mutation (allelic frequency 45%)
    - NFE2L2 exon 2 mutation
    - CDKN2A homozygous deletion
  - PD-L1 (22C3): TPS <1%, CPS 15, IC 5%
  - TMB: High (15 mutations/Mb)
  - MSI Status: Stable

Bone Biopsy T9 Vertebral Body (04/10/2020):

- Metastatic squamous cell carcinoma with identical morphology and immunophenotype
- Extensive bony destruction with tumor replacing normal marrow elements

Treatment Course:

1. First-Line Therapy:
    - Carboplatin AUC 5 + Pemetrexed 500 mg/m² + Pembrolizumab 200 mg IV q3 weeks
    - Initiated 04/27/2020
    - Partial response after 4 cycles with 30% reduction in primary tumor
    - Progressive disease documented after 7 months (11/2020)
2. Second-Line Therapy:
    - Docetaxel 75 mg/m² q3 weeks
    - Initiated 12/2020
    - Disease stabilization for 4 months
    - Progressive disease documented 04/2021
3. Third-Line Therapy:
    - Gemcitabine 1000 mg/m² days 1 and 8, q3 weeks
    - Initiated 05/2021
    - Progressive disease after 2 cycles
4. Fourth-Line Therapy:
    - Afatinib 40 mg PO daily (off-label use)
    - Initiated 07/2021
    - Disease stabilization for 2 months
    - Discontinued due to severe diarrhea and skin toxicity
5. Radiation Therapy:
    - T8-T10 (08/2020): 30 Gy in 10 fractions
    - Left hip (01/2021): 20 Gy in 5 fractions
    - T8-T10 (re-irradiation) (04/2022): 20 Gy in 5 fractions for cord compression

Current Disease Status Prior to Admission: Widespread metastatic disease with primary LLL mass, bilateral pulmonary nodules, extensive bone metastases (spine, ribs, pelvis, long bones), and malignant spinal cord compression at T8-T10. No evidence of brain metastases on recent MRI (02/2022).

HISTORY OF PRESENT ILLNESS: Patient was transferred from an outside hospital where he presented with progressive weakness and numbness in bilateral lower extremities and severe back pain. MRI revealed progression of T8-T10 vertebral metastases with epidural extension causing cord compression. Patient received emergency dexamethasone and underwent palliative radiation therapy (20 Gy in 5 fractions, completed on 04/09/2022). Despite radiation, neurological status continued to deteriorate with development of urinary retention requiring catheterization and complete loss of motor function in the lower extremities.

Prior to transfer, the patient and family had extensive goals of care discussions and elected to transition to comfort-focused care. Patient was transferred to our facility for specialized palliative care and end-of-life management.

HOSPITAL COURSE:

1. Pain Management:
    - Initial severe, poorly controlled pain (9/10) despite high-dose oral opioids
    - Converted to hydromorphone patient-controlled analgesia (PCA)
    - Pain specialty consultation resulted in addition of methadone 5 mg PO q8h for neuropathic component
    - Ketamine low-dose infusion added for 48 hours with good effect
    - Final regimen: Hydromorphone 0.8 mg/hr continuous with 0.5 mg q15min PRN, methadone 5 mg PO q8h
    - Pain adequately controlled (2-3/10) by discharge
2. Neurological Management:
    - Complete paraplegia at T10 level with no recovery after radiation
    - Bowel and bladder management protocols implemented

    - Patient and family counseled on irreversible nature of deficit
    - Positioning and skin care protocols implemented
3. Symptom Management:
    - Dyspnea managed with low-dose opioids and positioning
    - Anxiety treated with lorazepam PRN
    - Sleep disturbance improved with trazodone
    - Constipation managed with stimulant laxatives and stool softeners
4. End-of-Life Planning:
    - Multiple family conferences held to discuss prognosis and expectations
    - Spiritual care provided per patient's request
    - Hospice services arranged for home care
    - DNR/DNI status confirmed and documented

LABORATORY DATA (04/14/2022):

- Hemoglobin: 8.6 g/dL (decreased)
- WBC: 11.2 × 10⁹/L (elevated)
- Platelets: 156 × 10⁹/L
- Sodium: 133 mmol/L (decreased)
- Potassium: 4.3 mmol/L
- Creatinine: 0.9 mg/dL
- Calcium: 9.2 mg/dL (corrected for albumin)
- Albumin: 2.8 g/dL (decreased)
- Total bilirubin: 0.7 mg/dL
- Alkaline phosphatase: 342 U/L (elevated)

PATHOLOGY UPDATE (Re-review during current admission):

A comprehensive pathology review was conducted during this admission to inform prognostication and family discussions. Review confirmed the original diagnosis with additional insights:

Review of Original Specimen (04/04/2020) with Additional Staining:

- Tumor showed high expression of immune evasion markers:
    - PD-L1 (SP263): <1% of tumor cells (confirming original result)
    - VISTA: Strong positive (>50% of tumor cells)
    - B7-H3: Strong positive (>80% of tumor cells)
    - TIM-3: Positive on tumor-infiltrating lymphocytes
- Tumor microenvironment analysis:
    - CD8+ T-cells: Sparse (<5% of stromal cells)
    - FOXP3+ Tregs: Moderate infiltration
    - CD68+ macrophages: Abundant at tumor-stroma interface
    - PD-1+ lymphocytes: Rare
- Ultrastructural examination confirmed squamous differentiation with prominent desmosomes and cytoplasmic tonofilaments
- Findings consistent with "cold" tumor immune microenvironment and explaining poor response to immunotherapy

Recent Liquid Biopsy (04/06/2022):

- Circulating tumor DNA analysis showed:
    - Original PI3KCA and TP53 mutations at increased allelic frequencies
    - New PTEN truncating mutation
    - Increased tumor mutation burden (18 mutations/Mb)
    - Polyclonal resistance patterns typical of heavily pretreated disease

DISCHARGE PLAN:

Discharge Disposition: Home with hospice services (inpatient hospice bed unavailable)

Medications at Discharge:

1. Hydromorphone 2 mg PO q2h ATC (equivalent to current IV dose)
2. Hydromorphone 2 mg PO q1h PRN breakthrough pain
3. Methadone 5 mg PO q8h
4. Dexamethasone 4 mg PO BID × 3 days, then 2 mg BID × 3 days, then discontinue
5. Lorazepam 0.5 mg SL q4h PRN anxiety
6. Haloperidol 0.5 mg PO q6h PRN terminal agitation
7. Hyoscyamine 0.125 mg SL q4h PRN secretions
8. Senna 8.6 mg plus docusate 50 mg, 2 tablets PO BID
9. Bisacodyl suppository 10 mg PR daily PRN constipation
10. Trazodone 50 mg PO qHS PRN insomnia

Home Equipment:

1. Hospital bed
2. Pressure-relieving mattress
3. Hoyer lift
4. Bedside commode
5. Oxygen concentrator
6. Suction equipment

Home Services:

1. Hospice admission day of discharge
2. Nursing visits initially daily, then as needed
3. Home health aide 12 hours daily
4. Social work and chaplain services as requested
5. Volunteer respite care available

Follow-up:

1. Hospice physician home visit within 48 hours
2. Interdisciplinary team meeting scheduled in 1 week
3. 24/7 hospice nursing support available via telephone

PROGNOSIS: Poor, with estimated survival of days to weeks. This has been discussed transparently with the patient and family.

CONDITION AT DISCHARGE: Patient is comfortable with pain well-controlled on current regimen. Alert and oriented with periods of somnolence. Complete paraplegia with no motor or sensory function below T10. Hemodynamically stable. Overall condition is declining with reduced oral intake, increased fatigue, and periods of confusion consistent with end-stage disease.

Jonathan Hayes, MD Palliative Medicine 04/14/2022

INFO: Patient died on 04/28/2022