ONCOLOGY CLINIC NOTE April 13, 2024

DIAGNOSIS

- Stage IV non-small cell lung cancer (adenocarcinoma)
- Wild-type for actionable mutations (EGFR, ALK, ROS1, BRAF, KRAS G12C, MET, RET, NTRK all negative)
- PD-L1 expression: TPS 35% (intermediate range: 1-49%)
- CPS: 45%, IC: 5%
- Metastatic sites: Multiple bone lesions, pleural disease
- Diagnosed: July 20, 2023
- Treatment start date: August 11, 2023
- Current status: Ongoing response to first-line therapy

PATIENT DETAILS Name: Jessica Miller DOB: 04/04/1970 MRN: SYN018 Address: 14287 Willow Creek Lane, Greenville, OH 45331 Primary Insurance: Anthem Blue Cross Blue Shield Secondary Insurance: None Primary Care Physician: Dr. Thomas Blackwell

DETAILED HISTORY OF PRESENTING ILLNESS Mrs. Miller is a 55-year-old female with 15 pack-year smoking history (quit 2010) who initially presented to her primary care physician in June 2023 with persistent right shoulder pain unresponsive to conservative measures including physical therapy and NSAIDs. She also reported increasing dyspnea on exertion and fatigue for approximately 3 months prior to presentation. Patient initially attributed these symptoms to her work as a dental hygienist and the physical demands of her position.

Initial chest x-ray ordered by PCP revealed a right pleural effusion and right upper lobe mass. Patient was referred to pulmonology for further evaluation. Diagnostic thoracentesis performed on June 28, 2023, yielded 850ml of serosanguineous fluid. Cytologic examination showed malignant cells consistent with adenocarcinoma of lung origin (TTF-1 positive, Napsin-A positive). Cell block from pleural fluid was sent for next-generation sequencing.

CT chest/abdomen/pelvis on July 5, 2023, confirmed a 4.3cm spiculated right upper lobe mass with direct extension to parietal pleura, moderate right pleural effusion, and multiple bone metastases affecting T4, T8, right scapula, and left iliac crest. Brain MRI on July 10, 2023, was negative for intracranial metastases. PET/CT on July 15, 2023, demonstrated intense FDG uptake in the primary lung mass (SUV 15.2) and in all previously identified bone lesions (SUV range 7.4-11.2), without additional sites of metastatic disease.

Molecular testing results returned on July 25, 2023, revealed no actionable mutations (EGFR, ALK, ROS1, BRAF, KRAS G12C, MET, RET, NTRK all negative). Comprehensive genomic profiling identified TP53 R273H mutation and CDKN2A/B loss, but no targetable alterations. PD-L1 testing showed TPS 35%, CPS 45%, IC 5%.

Given the PD-L1 status and absence of driver mutations, the patient was recommended first-line therapy with platinum-doublet chemotherapy plus immunotherapy. After discussion of risks, benefits, and alternatives, patient elected to proceed with Carboplatin/Pemetrexed/Pembrolizumab, which was initiated on August 11, 2023.

Patient completed 4 cycles of triplet therapy with excellent radiographic response (partial response by RECIST 1.1 criteria) and significant symptomatic improvement. She was then transitioned to maintenance Pemetrexed/Pembrolizumab on November 3, 2023, which she continues to receive with ongoing clinical benefit.

ONCOLOGIC TREATMENT HISTORY

First-line Therapy:

- Regimen: Carboplatin AUC 5 + Pemetrexed 500mg/m² + Pembrolizumab 200mg q3weeks
- Start date: August 11, 2023
- End date: October 13, 2023 (4 cycles completed)
- Best response: Partial response (primary tumor decreased from 4.3cm to 2.0cm, decreased pleural effusion, stable bone metastases)
- Toxicities: Grade 2 fatigue, Grade 1 nausea, Grade 1 anemia, Grade 1 thrombocytopenia

Maintenance Therapy:

- Regimen: Pemetrexed 500mg/m² + Pembrolizumab 200mg q3weeks
- Start date: November 3, 2023
- Current status: Ongoing (Cycle 10 of maintenance today)
- Best response: Continued partial response (primary tumor decreased from 2.0cm to 1.2cm, resolution of pleural effusion, sclerotic healing of bone metastases)
- Toxicities: Grade 1 fatigue, Grade 1 anemia, Grade 1 hypothyroidism (on replacement therapy)

Supportive Therapies:

- Zoledronic acid 4mg IV q3months (initiated August 2023)
- Radiation therapy to right scapula (September 5-12, 2023): 30 Gy in 10 fractions for pain control
- Pleural catheter (PleurX) inserted August 15, 2023, removed November 20, 2023, after pleurodesis achieved

CURRENT VISIT SUMMARY Today's visit is for cycle 10 of maintenance therapy. Patient reports continued improvement in breathing and resolution of bone pain. She notes mild fatigue for 2-3 days following treatment but remains able to work part-time (3 days/week) as a dental hygienist. She is walking 30 minutes daily and has resumed most normal activities including gardening and caring for her grandchildren. Her performance status remains excellent at ECOG 1.

Patient denies cough, hemoptysis, chest pain, dyspnea at rest, or new sites of pain. She reports occasional mild arthralgias that respond well to acetaminophen. Sleep and appetite are good. She has maintained stable weight at 142 pounds for the past 4 months.

The patient takes levothyroxine 50mcg daily for immune-related hypothyroidism, which developed in February 2024. Thyroid function is now well-controlled on replacement therapy.

Patient completed survivorship education program in March 2024 and has been participating in our institution's cancer support group. She reports good emotional coping and has declined referral for individual psychological counseling.

REVIEW OF SYSTEMS Constitutional: Denies fever, chills, night sweats. Reports mild fatigue. HEENT: Denies headache, visual changes, hearing changes, sinus congestion. Respiratory: Denies cough, hemoptysis, wheezing. Previous dyspnea resolved. Cardiovascular: Denies chest pain, palpitations, orthopnea, peripheral edema. Gastrointestinal: Denies nausea, vomiting, diarrhea, constipation, abdominal pain. Genitourinary: Denies dysuria, hematuria, incontinence. Musculoskeletal: Previous bone pain resolved. Reports mild arthralgias. Skin: Denies rash, pruritus, skin changes. Neurological: Denies headache, dizziness, focal weakness, sensory changes. Psychiatric: Denies depression, anxiety, insomnia. Endocrine: Reports stable weight. Denies polydipsia, polyuria. Hematologic: Denies easy bruising, bleeding. Allergic/Immunologic: Denies allergies, recurrent infections.

PHYSICAL EXAMINATION Vital Signs: Temperature 98.2°F, Heart Rate 72 BPM, Respiratory Rate 16, Blood Pressure 126/72 mmHg, Oxygen Saturation 97% on room air, Weight 142 lbs (stable), Height 5'4", BMI 24.4

General: Well-appearing woman in no acute distress. Alert, oriented, and conversant.

HEENT: Normocephalic, atraumatic. Pupils equal, round, reactive to light. Extraocular movements intact. Sclerae anicteric, conjunctivae pink. Oropharynx moist, no lesions.

Neck: Supple, no lymphadenopathy, thyroid not enlarged or nodular.

Lungs: Clear to auscultation bilaterally. No wheezes, rhonchi, or crackles. No dullness to percussion. Respiratory effort normal.

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

Abdomen: Soft, non-tender, non-distended. No hepatosplenomegaly. Normal bowel sounds.

Extremities: No clubbing, cyanosis, or edema. Full range of motion of all joints without pain. Well-healed scar over right scapula at previous radiation site.

Skin: Warm, dry, no rashes or lesions. No radiation dermatitis.

Lymphatic: No cervical, supraclavicular, axillary, or inguinal lymphadenopathy.

Neurological: Alert and oriented to person, place, and time. Cranial nerves II-XII intact. Motor strength 5/5 in all extremities. Sensation intact to light touch and pinprick throughout. Reflexes 2+ and symmetric. Gait normal.

LABORATORY FINDINGS CBC (04/13/2024):

- WBC: 5.2 K/uL (normal)
- Hgb: 12.1 g/dL (slightly low, stable)
- Hct: 36.3% (slightly low, stable)
- Plt: 189 K/uL (normal)

- ANC: 3.1 K/uL (normal)
- ALC: 1.4 K/uL (normal)

Chemistry (04/13/2024):

- Na: 138 mEq/L
- K: 4.2 mEq/L
- Cl: 104 mEq/L
- CO2: 25 mEq/L
- BUN: 14 mg/dL
- Cr: 0.9 mg/dL (normal, stable)
- Glucose: 92 mg/dL
- Ca: 9.4 mg/dL
- Phos: 3.6 mg/dL
- Mg: 2.0 mg/dL
- AST: 28 U/L (normal)
- ALT: 32 U/L (normal)
- Alk Phos: 86 U/L (normal)
- T. Bili: 0.8 mg/dL (normal)
- Albumin: 4.1 g/dL (normal)
- LDH: 168 U/L (normal)

Thyroid Function (04/13/2024):

- TSH: 3.2 mIU/L (normal on replacement)
- fT4: 1.1 ng/dL (normal)

Immune-related Monitoring:

- ANA: Negative
- Rheumatoid Factor: Negative
- CRP: 0.8 mg/dL (normal)
- ESR: 18 mm/hr (normal)

Tumor Markers:

- CEA: 2.4 ng/mL (normal, decreased from 18.6 ng/mL at diagnosis)
- CYFRA 21-1: 1.8 ng/mL (normal, decreased from 8.4 ng/mL at diagnosis)

RECENT IMAGING CT Chest/Abdomen/Pelvis (04/02/2024): FINDINGS:

1. Right upper lobe lung nodule measures 1.2 cm (decreased from 1.8 cm on previous study from 01/05/2024 and from 4.3 cm at baseline).
2. Complete resolution of previously noted right pleural effusion.
3. No pleural thickening or nodularity.
4. No mediastinal or hilar lymphadenopathy.
5. Liver, spleen, adrenals, and pancreas appear normal.
6. No intra-abdominal lymphadenopathy.
7. Previously noted bone metastases demonstrate sclerotic healing changes in T4, T8, right scapula, and left iliac crest without new lesions.
8. No new sites of metastatic disease identified.

IMPRESSION: Continued partial response to therapy with further decrease in size of primary tumor and stable sclerotic changes in known bone metastases. No evidence of disease progression.

Comparison with Prior Imaging:

- Initial CT (07/05/2023): 4.3 cm RUL mass, moderate right pleural effusion, multiple lytic bone lesions
- CT after 4 cycles (11/01/2023): 2.0 cm RUL mass, small right pleural effusion, stable bone metastases
- CT (01/05/2024): 1.8 cm RUL mass, resolved pleural effusion, early sclerotic changes in bone metastases
- Current CT (04/02/2024): 1.2 cm RUL mass, no pleural effusion, sclerotic healing of bone metastases

Brain MRI with contrast (04/02/2024): No evidence of intracranial metastases. No abnormal enhancement. No parenchymal lesions. Ventricles and sulci normal in size and configuration. No midline shift or mass effect.

ASSESSMENT & PLAN 55-year-old female with stage IV NSCLC (adenocarcinoma, wild-type, PD-L1 TPS 35%) diagnosed in July 2023, showing continued excellent response to Pemetrexed/Pembrolizumab maintenance therapy. She has tolerated treatment exceptionally well with minimal side effects and improving quality of life. Current disease status shows ongoing partial response with decreasing size of primary tumor, resolution of pleural effusion, and sclerotic healing of bone metastases. No new sites of metastatic disease.

Treatment Plan:

1. Continue maintenance Pemetrexed 500mg/m² + Pembrolizumab 200mg IV today (Cycle 11)
2. Standard premedications with dexamethasone 4mg PO BID day before, day of, and day after Pemetrexed
3. Continue vitamin B12 1000mcg IM every 9 weeks (last given 03/02/2024, next due 05/04/2024)
4. Continue folic acid 1mg PO daily
5. Continue zoledronic acid 4mg IV today (q3months for bone metastases)
6. Continue levothyroxine 50mcg PO daily for immune-related hypothyroidism
7. Next CT chest/abdomen/pelvis in 3 months (July 2024)
8. Brain MRI for surveillance in 3 months (July 2024)
9. Return for cycle 12 in 3 weeks (05/04/2024)

ADDITIONAL DISCUSSION POINTS

Duration of Therapy: We discussed the duration of maintenance therapy. Current standard of care supports continuation of Pemetrexed/Pembrolizumab for up to 2 years of pembrolizumab (35 cycles total), assuming continued benefit and absence of prohibitive toxicity. We reviewed emerging data suggesting consideration of discontinuation after prolonged disease control, particularly in patients with excellent and durable responses. However, this approach remains investigational, and the optimal duration of therapy is not definitively established.

Given Mrs. Miller's excellent tolerance of therapy, ongoing response, and preference, our plan is to continue current regimen through completion of 2 years (24 more cycles). We will reassess at that time based on disease status and emerging evidence.

Immune-related Adverse Events: Patient has experienced mild immune-related hypothyroidism requiring thyroid hormone replacement but no other significant immune-related adverse events. We reviewed potential signs and symptoms of immune-mediated toxicities affecting other organ systems (colitis, pneumonitis, hepatitis, endocrinopathies, dermatitis, nephritis) and instructed patient to report any new or concerning symptoms promptly. Thyroid function will continue to be monitored every 6 weeks during therapy.

Work and Lifestyle Considerations: Mrs. Miller has successfully maintained part-time employment throughout treatment. We discussed strategies to manage treatment-related fatigue, including energy conservation, prioritization of activities, and scheduled rest periods. Patient has implemented these strategies effectively and reports satisfaction with current work-life balance. She has resumed most normal activities and hobbies with minimal limitations.

Survivorship Planning: Patient has been participating in our institution's survivorship program. She has completed advance care planning documentation and has appointed her husband as healthcare power of attorney. We have engaged social work to assist with financial navigation and insurance considerations. Nutrition and exercise consultations have been completed with personalized recommendations. Patient reports adherence to Mediterranean diet and regular walking program.

Future Therapeutic Options: While current therapy continues to provide benefit, we discussed potential future treatment options if progression occurs. These include:

1. Docetaxel ± ramucirumab for second-line therapy
2. Consideration of clinical trials based on genomic profiling results
3. Evaluation for additional targetable mutations at progression through repeat biopsy or liquid biopsy
4. Local therapies for oligoprogressive disease if appropriate

Psychosocial Support: Patient is coping well emotionally with her diagnosis and treatment course. She attends our monthly lung cancer support group and has established connections with other survivors. She denies significant anxiety or depression symptoms. She has good family support from her husband of 30 years and two adult children who live nearby. Patient has declined formal psychological counseling at this time but understands this resource is available if needed.

TREATMENT ADMINISTERED TODAY

- Pembrolizumab 200mg IV over 30 minutes
- Pemetrexed 500mg/m² IV over 10 minutes
- Zoledronic acid 4mg IV over 15 minutes
- Standard premedications administered
- Treatment tolerated without acute complications

FOLLOW-UP PLAN

- Return to clinic in 3 weeks (05/04/2024) for cycle 12 of maintenance therapy
- Laboratory testing prior to next visit including CBC, CMP, TSH
- Call with any new or worsening symptoms
- Patient provided with after-hours contact information

CLINICAL TRIALS Patient was screened for eligibility in protocol INSPIRE-NSCLC-203 (Immunotherapy Continuation vs. Observation After 2 Years of PD-1 Inhibitor Therapy in NSCLC), but is not yet eligible as she has not completed 2 years of therapy. We will reassess eligibility as she approaches completion of planned therapy duration.

Signed,

Elizabeth Nguyen, MD Board Certified Medical Oncology Metro Cancer Center License #: MD65432 NPI: 1234567890 Phone: (555) 123-4567 Fax: (555) 123-4568

Reviewed and co-signed by: Jonathan Blackwell, MD, PhD Director, Thoracic Oncology Program