**Patient ID**: SYN219

**Caes Summary**

**Name**: Youssef Al-Saif **DOB**: 27 September 1955

**Primary Diagnosis**: Stage IV NSCLC, adenocarcinoma subtype **Date of Diagnosis**: 18 August 2021

## Clinical Presentation and Histopathology

The patient presented with a 4-month history of chronic non-productive cough, exertional dyspnea, and mild hemoptysis. He had a 30 pack-year smoking history but quit in 2005. Initial labs were notable for normocytic anemia (Hb 11.2 g/dL) and mildly elevated LDH. Chest CT with contrast demonstrated a 5.1 cm right upper lobe mass with right paratracheal and subcarinal lymphadenopathy, plus several left lower lobe pulmonary nodules suggestive of intrapulmonary metastases.

CT-guided biopsy of the right upper lobe lesion demonstrated moderately differentiated adenocarcinoma. Histologically, the tumor showed mixed architectural patterns—predominantly acinar and lepidic, with focal solid components. Tumor cells were cuboidal to columnar with moderate cytoplasm, hyperchromatic nuclei, and mitotic figures (10 per 10 HPF). Focal areas of necrosis were present.

Immunohistochemistry profile revealed:

- TTF-1: strongly positive
- Napsin A: positive
- CK7: positive
- CK20 and CDX2: negative
- p40, synaptophysin, chromogranin: negative

PD-L1 testing with the Dako 22C3 assay showed tumor proportion score of 35%. The Ki-67 index was 38%. Molecular profiling with the Oncomine Focus Assay revealed no actionable mutations; EGFR, ALK, ROS1, BRAF, RET, MET exon 14 skipping, KRAS G12C, and NTRK were negative. TMB was 4.1 mut/Mb, and MSI testing confirmed stability.

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## Treatment Course

He began first-line treatment on 09 September 2021 with a combination of carboplatin (AUC 5), pemetrexed (500 mg/m²), and pembrolizumab (200 mg q3w). Baseline ECOG was 1. Following four cycles, radiographic reassessment (December 2021) revealed a partial response, with shrinkage of the RUL mass to 2.7 cm and resolution of lymphadenopathy. His anemia improved slightly with supportive care (iron supplementation).

Maintenance pemetrexed and pembrolizumab were continued for 13 additional cycles. Fatigue, transaminitis (peak ALT 79 U/L), and cumulative anemia (Hb nadir 9.8 g/dL) were noted. He developed immune-related hypothyroidism (TSH 8.6 mU/L, FT4 low-normal), managed with levothyroxine 50 mcg daily.

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In early February 2023, new bilateral pleural thickening and growth of a left lower lobe lesion were observed. Biopsy reconfirmed NSCLC adenocarcinoma with no transformation. Second-line docetaxel plus nintedanib began in March 2023, leading to 9 months of stable disease.

In late 2023, clinical decline occurred with worsening dyspnea, ECOG 3, and oxygen dependence. Repeat imaging showed increased bilateral effusions and diffuse pulmonary infiltrates. He transitioned to hospice care and passed away peacefully on 31 May 2024.

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**Physician**: Dr. K. Elbaz, MD, Thoracic Oncology
**Date of Discharge Note**: 14 June 2024