The Evolving Context of Driver Mutations: ROS1 Rearrangement in Metastatic Non-Small Cell Lung Cancer

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A previously healthy, 30-year-old Filipino woman presented to an emergency department with complaints of shortness of breath and mild cough. She denied constitutional symptoms, such as night sweats, fevers, loss of appetite, or weight loss. Additional investigation revealed bilateral pleural and pericardial effusions with no obvious lung lesions or masses. The pericardial fluid was drained and preliminary cytology revealed atypical carcinoma cells.

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Her past medical history included an embryonic pregnancy and a benign breast cyst that was biopsied in the Philippines. She had immigrated to Canada two years earlier, was working full-time, and was living with her sister. She was planning on returning to the Philippines to wed and had a strong support system in Canada. She had never smoked cigarettes or consumed alcohol and had no family history of cancer. The patient was exposed to secondhand smoke as a child.

The patient was seen in an outpatient oncology clinic shortly after hospital discharge to review her final test results. Her Eastern Cooperative Oncology Group status was 0–1. Her pericardial fluid was positive for adenocarcinoma and immunohistochemistry (IHC) confirmed epidermal growth factor receptor (EGFR) negativity with no ALK rearrangement and negative KRAS. She was diagnosed with stage IV non-small cell lung cancer (NSCLC); however, the thoracic tumor board recommended a thoracoscopy and tissue biopsy to ensure that negative EGFR status was not a false-negative result—because the patient fit the clinical profile for EGFR positivity—and the limited sample may have been inaccurate.

Further tissue testing by polymerase chain rearrangement (PCR) confirmed EGFR and ALK negativity, and the decision was made to treat with the standard four cycles of cisplatin (Platinol®) and gemcitabine (Gemzar®) chemotherapy followed by pemetrexed (Alimta®) maintenance therapy. She tolerated induction and maintenance treatment with stable disease for a year and a half, at which time she began complaining of headaches. An urgent computed tomography scan of the brain confirmed the presence of brain metastases. She received whole-brain radiation and, after a two-week wash out period, started third-line docetaxel (Taxotere®) treatment. After only two cycles, she was clinically deteriorating and was admitted to the hospital with fatigue and hypoxia. She was enrolled into the palliative care program after reimaging confirmed further progression. Despite her poor prognosis, she continued to verbalize her desire to live and get married. She was not ready to die and hoped for some other treatment option.