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Diagnostic Dilemma: Pulmonary Lymphangiocarcinomatosis as a Manifestation of Occult Signet Ring Cell Carcinomatosis

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ABSTRACT

Background: This case underscores the diagnostic challenges posed by pulmonary lymphangitic carcinomatosis (PLC) as an initial manifestation of occult signet ring cell adenocarcinoma.

Case Presentation: A 69-year-old female presented to the emergency department with exertional shortness of breath and severe anemia with a hemoglobin of 5.8. CXR showed extensive interstitial opacities thought to be atypical pneumonia. Treatment was started with azithromycin but with no improvement of her clinical status. CT scan of chest was suggestive of interlobular septal thickening, bilateral ground glass opacities, pleural effusion and mediastinal lymphadenopathy. Patient trialed with diuresis due to suspicion of pulmonary edema but had no improvement in her clinical status and on repeat imaging. Endoscopy was performed for evaluation of anemia which showed a mass on the lesser curvature of the stomach. Biopsy showed adenocarcinoma with signet ring cells. Given the new diagnosis of gastric cancer, pulmonary findings were highly suggestive of lymphangitic carcinomatosis of the lungs making it Stage IV. Patient was found to be not a candidate for targeted therapies because HER 2 mutation was negative on FISH.

Outcome: She presented to the hospital one week after discharge with hypoxic respiratory failure requiring admission to the MICU. Patient and family decided to pursue comfort measures. She was eventually discharged to a hospice facility but needed to be admitted to the hospital again. She was started on a morphine drip to keep her comfortable. Patient passed away 6 weeks after diagnosis.

Discussion: The prevalence of signet cell carcinoma seems to be rising as prevalence of adenocarcinoma of the stomach has fallen since the advent of H. pylori eradication antibiotics. Pulmonary lymphangitic carcinomatosis represents amount 6-8% of all pulmonary metastasis with stomach cancer representing 0.6% of these. Diagnosis of PLC is considered to represent end-stage malignancy, with the life expectancy being about six months. This case underscores the diagnostic challenges posed by PLC as an initial manifestation of occult signet ring cell adenocarcinoma. The nonspecific respiratory symptoms and imaging findings can mimic more common conditions, leading to potential delays in diagnosis. A high index of suspicion is essential in patients presenting with unexplained dyspnea, cough, interstitial lung patterns unresponsive to standard treatments.

Introduction

Pulmonary Lymphangitic Carcinomatosis (PLC) is a rare manifestation of metastatic spread, most commonly associated with adenocarcinomas from primary sites such as the breast, lung, and gastrointestinal tract. It involves infiltration of malignant cells into the pulmonary lymphatics, leading to progressive respiratory symptoms and characteristic imaging findings. Due to its nonspecific and insidious presentation, PLC is often misdiagnosed as pneumonia or interstitial lung disease, delaying appropriate diagnosis and management. For many cases, PLC is diagnosed on autopsy especially if underlying malignancy is not known. Its presence typically signifies advanced-stage disease with a poor prognosis.

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Case Presentation:

A 69-year-old woman with a history of Dyke–Davidoff syndrome presented to urgent care with a dry cough and exertional shortness of breath for past two weeks. Her vitals were within normal limits. Physical examination revealed a cachectic habitus, conjunctival pallor and normal sounds on auscultation.

Laboratory workup (Table 1) revealed a hemoglobin level of 5.8 g/dL with low MCV, high RDW, and iron studies diagnosing iron deficiency anemia. She reported occasional black stools in the past. A chest X-ray showed bilateral interstitial opacities, raising concern for an atypical viral pneumonia (Figure 1).

Initial differentials for acute-onset exertional dyspnea included symptomatic anemia from an upper GI bleed, possible high-output heart

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Table 1: Laboratory Finding.

Hb	5.8
WBC	7.57
PLT	316
MCV	67.4
RDW	21.7
Iron	16
TIBC	343
Iron Saturation	4.7%
Ferritin	20
Procalcitonin	0.14
Streptococcus pneumonia antigen, urine	Negative
Legionella antigen, urine	Negative
Pro BNP	810

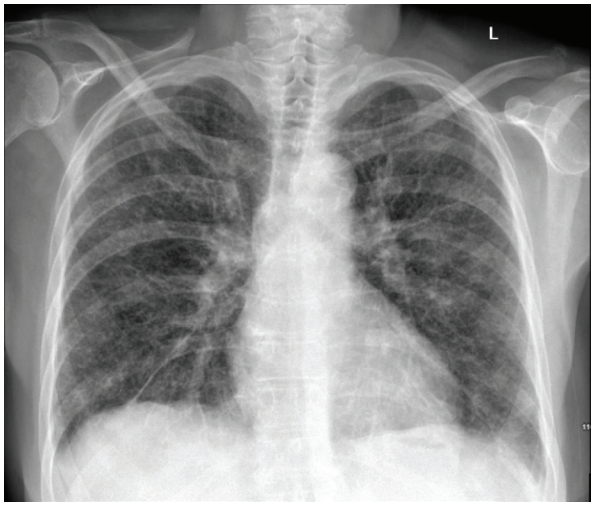

Figure 1: Chest X-Ray with bilateral interstitial reticular opacities.

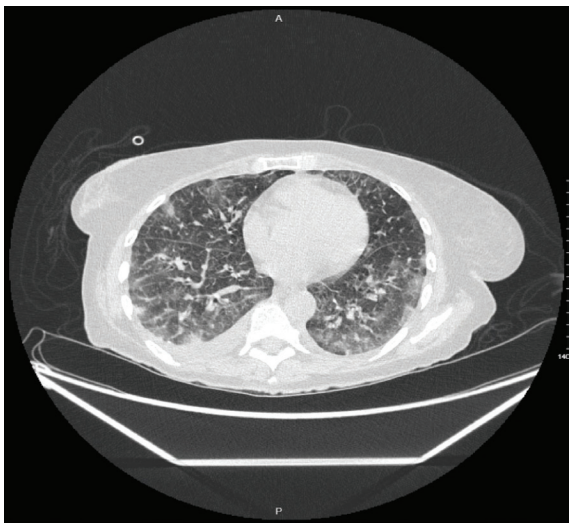

Figure 2: CT chest showcasing bilateral pleural effusions, ground glass opacities and interlobular septal thickening.

failure due to anemia, and an atypical pneumonia. Empirical treatment with azithromycin was initiated, and two units of PRBCs were transfused. Transthoracic echocardiogram (TTE) was within normal limits. CT chest (Figure 2) revealed interlobular septal thickening, bilateral ground-glass opacities, pleural effusion, and mediastinal lymphadenopathy. Pulmonology was consulted to evaluate for possible interstitial lung disease, and GI was consulted for evaluation of a possible upper GI bleeding. The patient completed a five-day course of azithromycin without clinical improvement. A trial of diuresis was attempted for suspected pulmonary edema but led to no change in clinical status or on imaging studies. Rheumatologic workup including ANA, ANCA, MPO, RF, Anti-Jo 1, ACE, SSA, Anti-Mi 2, and Anti-RNP was negative.

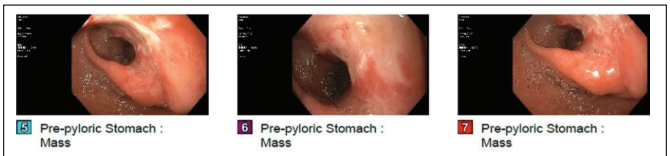

Figure 3: Endoscopy findings.

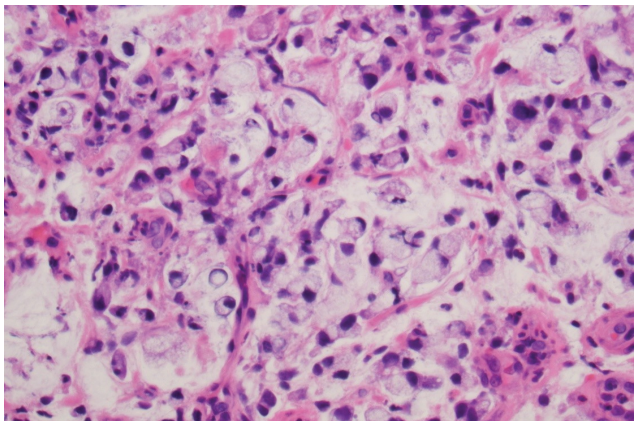

Figure 4: Gastric biopsy showcasing signet ring cells.

Upper GI Endoscopy (Figure 3) revealed a malignant gastric tumor on the lesser curvature of the stomach. This finding raised high concern for metastatic gastric cancer with possible lymphangitic carcinomatosis of the lungs. Biopsy of the gastric lesion revealed poorly cohesive signet ring cell carcinoma (Figure 4). HER2 studies were ordered to guide treatment. The patient was discharged with outpatient oncology and pulmonology follow-up.

She presented to the emergency department one week later with acute hypoxic respiratory failure requiring BiPAP and brief ICU admission. CT chest revealed worsening of ground-glass opacities and interlobular thickening. Another trial of diuresis led to some clinical improvement, and she was started on a seven-day course of prednisone 40 mg for potential benefit in lymphangitic spread to the lungs. HER2 testing returned negative, and she was not considered a candidate for targeted therapy.

Further testing with PD-L1 and MSI was not pursued given her poor functional status (ECOG 4) and ongoing respiratory failure. In light of her overall poor condition and guarded prognosis, she was deemed not a candidate for chemotherapy (FOLFOX), and transitioned to comfort care after shared decision making. She was started on a morphine drip for control of pain, respiratory distress, and anxiety. While preparations were being made for transfer to a hospice facility, she passed away.

Discussion

Lymphangitic carcinomatosis refers to the spread of cancer cells in the lymphatic vasculature secondary to metastatic dissemination from a primary site. In most cases, lymphatic spread occurs in the pulmonary vasculature; however, lymphangitic spread has also been described in the skin, duodenum, and kidneys [1-3].

Most cases of pulmonary lymphangitic carcinomatosis have been described as metastatic from adenocarcinomas, commonly of the breast, lung, and stomach. It represents approximately 6–8% of all pulmonary metastases, with stomach cancer accounting for 0.6% of these cases. Calculating the true incidence and prevalence remains a challenge due to subtle symptoms and clinical mimicry with other pathologies, as highlighted in our case, often leading to diagnostic delays and post- mortem diagnoses.

Typical presentation involves gradually progressive dyspnea over days to weeks. An underlying malignancy is usually known, although in rare cases, PLC may be the first presentation of cancer, as in our patient. Imaging is generally obtained to rule out other differentials. Chest X-ray can reveal reticular, nodular, or reticulonodular patterns with coarse bronchovascular features, typically in advanced stages. CT thorax often shows interlobular septal and peribronchovascular interstitial thickening—either smooth (early) or nodular (late). Interstitial edema or parenchymal tumor extension may lead to ground- glass opacities. While nodular septal thickening can help differentiate PLC from other interstitial lung diseases, conditions like sarcoidosis and asbestosis may mimic similar patterns. Preservation of lobular and general lung architecture is another distinguishing feature of PLC.

Histopathologic confirmation remains the gold standard but is not always feasible. In practice, many patients with suspected PLC deteriorate rapidly, making invasive diagnostics intolerable. Therefore, a presumptive diagnosis is often made based on clinical history, imaging, and non-response to standard therapies, especially in patients with known or suspected malignancy and poor performance status.

Management includes symptom control and treatment of the underlying cancer. Definitive therapies may involve surgical resection, chemotherapy, and/or radiotherapy depending on the primary tumor. In gastric adenocarcinoma, standard regimens include combination chemotherapy (for example, a platinum-based doublet with a fluoropyrimidine). In HER2-positive cases, trastuzumab is added, and for tumors with high PD-L1 expression, checkpoint inhibitors (e.g. Nivolumab) may be used [4].

Supportive measures include supplemental oxygen and non-invasive ventilation. Antibiotics are often administered due to diagnostic uncertainty. Some clinicians use intravenous steroids for symptomatic relief, though this practice lacks robust evidence. Diuretics may be beneficial in cases with concurrent heart failure.

The diagnosis of pulmonary lymphangitic carcinomatosis typically signifies end-stage disease, with a life expectancy around six to twelve months even with treatment [5].

Conclusion

This case describes the diagnostic challenges of PLC due to its varied presentation and overlap with other pulmonary conditions. Our patient failed to respond to conventional treatment strategies for symptomatic anemia, pneumonia, or heart failure. Only after identifying the primary gastric malignancy was the possibility of PLC seriously considered. This emphasizes the importance of maintaining a high index of suspicion in elderly or debilitated patients who show no improvement with standard management, particularly when imaging suggests interstitial involvement.

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