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Case report

Diffuse pulmonary infiltrates: A guise of adenocarcinoma



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ABSTRACT

Small and non-small cell lung cancer present in a variety of radiologic and clinical patterns, and have been linked to smoking. Primary adenocarcinoma of the lung has been increasingly recognized in females and nonsmokers, often presenting a diagnostic challenge.

In the absence of smoking history, these radiographic patterns may be initially misdiagnosed as an infectious or inflammatory condition, often delaying the diagnosis of malignancy.

We report two cases of female patients with relatively short or no smoking history presenting with diffuse pulmonary infiltrates not typically seen in primary lung cancer, which created a diagnostic challenge, ultimately diagnosed as primary lung adenocarcinoma. Each case had different subtype patterns of adenocarcinoma. The first case described adenocarcinoma of mostly acinar pattern; while the second case was noted to have adenocarcinoma of micropapillary pattern.

Given lung adenocarcinoma's nonspecific presentation, which may mimic infectious and diffuse interstitial lung disease, the above cases highlight the importance of entertaining lung adenocarcinoma as part of the differential diagnosis of such presentations.

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1. Introduction

Lung cancer is broadly categorized into two main types, small cell and non-small cell Lung cancer, presenting in a variety of different radiologic and clinical patterns, and has classically been linked to smoking. Despite this association, primary adenocarcinoma of the lung has been increasingly recognized in females and nonsmokers, often presenting a diagnostic challenge.

Classification of adenocarcinoma has recently changed providing detailed histology to allow accurate and timely diagnosis, and thus provide therapy options [1]. On imaging, adenocarcinoma can present unilaterally as solid or ground glass nodules, or masses [2] and less frequently, as bilateral nodular, interstitial, or ground glass opacities. In the absence of smoking history, these opacities may be initially misdiagnosed as an infectious or inflammatory condition, often delaying the diagnosis of malignancy. We report two cases which presented a diagnostic challenge, involving female patients with relatively short or no smoking history, presenting with diffuse pulmonary infiltrates, ultimately diagnosed as primary lung adenocarcinoma.

2. Case 1

A 53-year-old African American female nonsmoker with past medical history of diabetes and hypertension presented with complaints of cough and shortness of breath. She was in her usual state of health until two weeks earlier when she began to notice progressive dyspnea associated with cough. Her cough was described as minimally productive associated with subjective fever and chills. The patient was treated by her primary physician with an unknown antibiotic for one week prior to presentation. There were no symptoms of hemoptysis, rash, or joint swelling. She denied history of sick contacts, alcohol or drug abuse. Patient denied previous history of malignancy. She was born and raised in the United States of America (USA) with no recent travel, and worked as a manager at a local convenience store.

On presentation, patient had a heart rate (HR) of 110 beats per minute, respiratory rate (RR) of 25 breaths per minute, oxygen saturation (SpO₂) of 92% on ambient air and blood pressure (BP) of 135/82 mm Hg. Abnormal physical findings were confined to the chest, which evidenced coarse vesicular breath sounds and bibasilar rales. Cardiac exam on auscultation revealed normal S1/S2 sounds with normal P2. Laboratory studies revealed a white blood cell (WBC) count of 11,800/mm³ with 79% polymorphonuclear leucocytes (PMN), 15% lymphocytes, 3% monocytes and 2% eosinophils.

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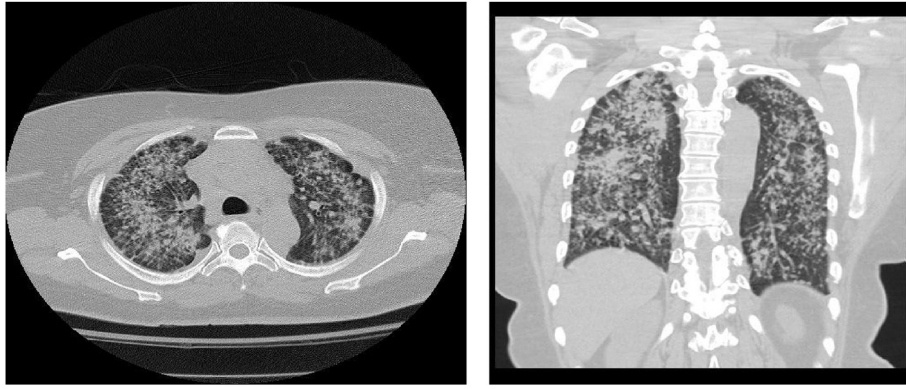


Fig. 1. CT Chest axial (left) and coronal (right) images showing diffuse bilateral confluent nodular and air space opacities with areas of consolidations.

A comprehensive metabolic panel was unremarkable. Echocardiogram results demonstrated preserved ejection fraction with no wall motion abnormalities. Chest radiograph was notable for diffuse bilateral infiltrates. As such, a computed tomography (CT) of the chest was performed which revealed diffuse bilateral confluent nodular and air space opacities with areas of consolidation. Based on these findings, empiric antibiotics were initiated in light of suspected infection. Further inpatient hospital workup revealed no isolated pathogens on sputum and blood cultures. Microbiology smear and culture for acid-fast bacteria were negative. Other workup included autoimmune serology and hypersensitivity panel which were within normal limits. Patient underwent a fiberoptic bronchoscopic (FOB) examination which showed trace mucopurulent secretions located in the basal segments of the lower lobe bronchi bilaterally. The airways were patent with no endobronchial lesions. Bronchial washings were sent for cytology, as well as fungal, bacterial, and viral gram stain and culture; these results were negative. Throughout the hospital course, patient had no fever, but continued to report dyspnea and cough, and remained hypoxemic requiring supplemental oxygen. Repeat CT Chest was performed after twelve days of her hospitalization which revealed extensive confluent nodular opacities in both lung fields with more focal area of mass-like consolidation in the left upper lobe and several mediastinal nodes (see Fig. 1). Due to the unknown etiology of the diffuse reticulonodular process, a CT guided biopsy of the left upper lobe consolidation was performed. Adenocarcinoma of mostly acinar pattern was confirmed using immunostains, which were positive for Transcription termination factor, RNA polymerase 1 (TTF-1), and fluorescence in-situ hybridization (FISH) was negative for rearrangement involving anaplastic lymphoma kinase (ALK) and c-ros oncogene 1 (ROS1) genes. These results reflect a

primary origin of the lung, which on biomarker analysis was noted to be epidermal growth factor receptor (EGFR) positive with p.L858R mutation in Exon 21 (see Fig. 2).

3. Case 2

A 36-year-old Caucasian female smoker, with no reported past medical history, presented with respiratory complaints of shortness of breath that originated two months prior. During this time period, patient had been treated with multiple courses of antibiotics, as well as steroids, due to what was believed to be a failure to resolve recurrent episodes of pneumonia. In addition to the shortness of breath, the patient also reported lower back pain that started six months prior to presentation, described as dull in nature and non-radiating, that she attributed to musculoskeletal strain. Otherwise, the patient denied cough, vision changes, hemoptysis, gait abnormality, bowel or urinary incontinence. She was born and raised in the USA. Patient stated she had a thirteen pack year history of smoking, but denied alcohol or drug abuse.

On presentation, her vital signs were as follows: HR 112 bpm, RR 20 bpm, SpO2 95% on ambient air, and BP 114/97 mmHg. Pulmonary examination revealed diffuse bronchial breath sounds with bibasilar rales located in posterior lung fields. Laboratory workup revealed a WBC count of 14,800/mm³ with 77% PMN, 12% lymphocytes, 9% monocytes and 2% eosinophils. Additional laboratory data was unremarkable. CT chest imaging showed diffuse bilateral interstitial infiltrates, most notable in the upper lungs intermixed with ground glass infiltrates (see Fig. 3). Further inpatient workup included bacterial, fungal, and viral cultures, immunological workup for connective tissue disease, acid-fast stains, and screening for immunodeficiency; results came back within normal

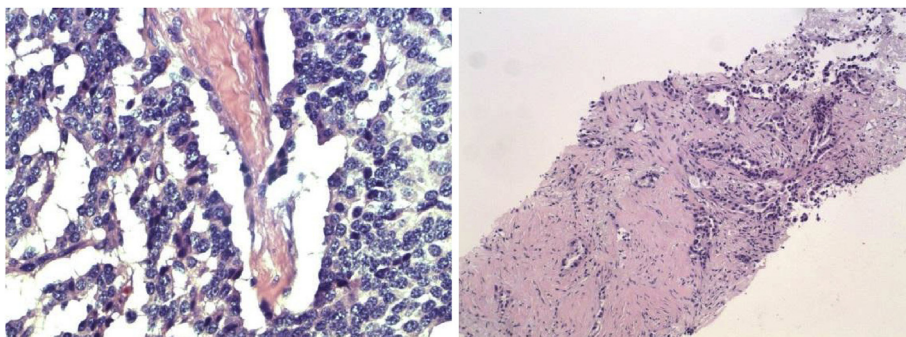


Fig. 2. Adenocarcinoma of acinar pattern, with immunostains of TTF-1 positive (left), and low-power micrograph (right).

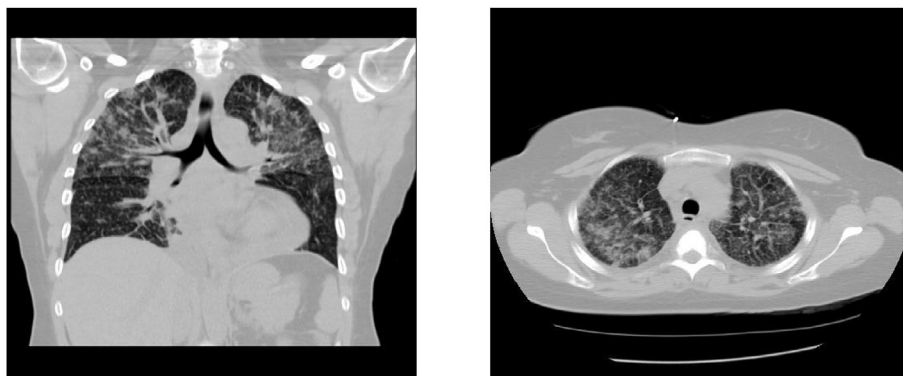


Fig. 3. CT chest with coronal (left), and axial (right) images showing diffuse bilateral interstitial infiltrates, worse in the upper lungs intermixed with ground glass infiltrates.

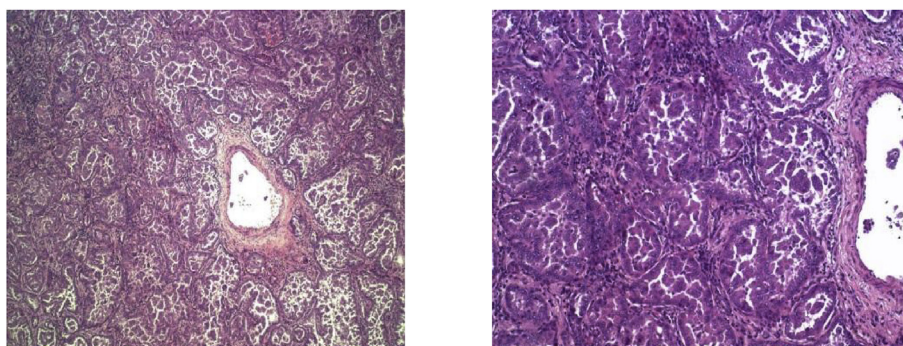


Fig. 4. Micrograph showing adenocarcinoma of micropapillary pattern.

limits. Patient underwent a FOB during which time an endobronchial lesion was seen partially obstructing the origin of the left lower lobe; this lesion was biopsied and bronchial washings were obtained. Transbronchial biopsies were obtained from the superior segment of the Lingula. The cytology and pathology results noted focal cells with marked atypia, and since a neoplastic process could not be ruled out, the patient was scheduled for a video-assisted thoracic surgery (VATS). During the VATS, multiple pleural nodules were seen on the parietal pleural surface and a biopsy was obtained. Frozen section returned as malignant favoring adenocarcinoma. Adenocarcinoma of micropapillary pattern was confirmed with immunostains of TTF-1 and cytokeratin-7 (CK-7) positive. FISH was positive for rearrangement involving ROS1 gene and negative for a rearrangement involving the ALK gene. V-Ki-ras2 Kirsten rat sarcoma (KRAS) and EGFR mutation analysis were negative (see Fig. 4).

4. Discussion

The cases described provide unique examples of how primary adenocarcinoma of the lung can be mistaken for interstitial and infectious processes. Specifically, both cases identified females with little or no smoking history who presented with radiological imaging not typically seen for primary lung malignancy. In addition, each case had different subtype patterns of adenocarcinoma. Case 1 described adenocarcinoma of mostly acinar pattern; while case 2 was noted to have adenocarcinoma of micropapillary pattern.

Lung cancer should be considered in patients who present with signs and symptoms suspicious for pneumonia, but with no improvement despite appropriate antibiotic coverage. Lung cancer as a differential diagnosis, especially in young females with

relatively little or no smoking history, can be important in the early investigative phase in order to implement timely treatment. Chang et al. has noted that neoplastic processes such as lymphoma and leukemia are more likely to present as diffuse pulmonary infiltrates of the lung, causing acute respiratory distress syndrome (ARDS), rather than primary lung carcinoma [3]. In our subset of cases, however, adenocarcinoma can have similar presentation, which in the absence of smoking history, may be initially misdiagnosed as infectious or inflammatory conditions, often delaying the diagnosis of malignancy. The rising incidence of adenocarcinoma can be partially attributed to the increasing use imaging techniques on hospitalized patients, and increasing aging population [4]. Accuracy of an early diagnosis of primary lung adenocarcinoma can help direct treatment planning and better overall patient outcomes.

5. Conclusion

Given lung adenocarcinoma's nonspecific presentation, which may mimic infectious and diffuse interstitial lung disease, the above cases highlight the importance of entertaining lung adenocarcinoma as part of the differential diagnosis of such presentations.

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