

CASE REPORT

A Rare Case of Progressive Dyspnea and Bilateral Lung Infiltration in a Young Male

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Abstract

Pulmonary lymphangitic carcinomatosis (PLC) is defined as infiltration of the lymphatic vessels and perilymphatic connective tissue with tumor cells, which is secondary to malignancy. Therefore, it rarely appears as an initial finding preceding a diagnosis of malignancy. A 30-year-old male patient was hospitalized in our clinic with a pre-diagnosis of interstitial lung disease owing to the complaints of dry cough, progressive dyspnea, and acute respiratory insufficiency. He was diagnosed with signet ring cell carcinoma, which is a histologic subtype of adenocarcinoma, via gastroscopy, and lung involvement was consistent with PLC. Regardless of the patient age, PLC should be considered in differential diagnoses of progressive dyspnea, acute respiratory failure, and widespread interstitial lung involvement.

KEYWORDS: Progressive dyspnea, lymphangitic carcinomatosis, gastric cancer

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INTRODUCTION

Pulmonary lymphangitic carcinomatosis (PLC) is the infiltration of pulmonary lymphatic vessels and connective tissue adjacent to these vessels by malignant cells. PLC comprises 6-8% of all lung metastases. The most common underlying tumors found are those of the breast, stomach, lung, prostate, and pancreas. Irrespective of the location of the primary tumor, the prognosis is worse [1].

Involvement of the lymphatic vessels usually occurs following hematogenous seeding of the lungs. A less frequent mechanism is retrograde diffusion into the lymphatics of the mediastinal and hilar lymph nodes. Not only the central lymphatics consisting of the bronchovascular interstitium, but also the peripheral lymphatics consisting of the interlobular septa and beneath the pleura are involved. The radiologic features are similar to those of other interstitial lung diseases, which complicates a differential diagnosis. Thickening of bronchovascular bundles and interlobular septa, ground-glass opacity, pleural effusion, mediastinal lymphadenopathy, and nodular lesions are the common radiologic findings [2-5]. PLC may sometimes appear as the first finding before a diagnosis of tumor [6]. PLC is rarely reported as the first finding related to stomach tumor [7]. A 30-year-old male patient, who was diagnosed with signet cell gastric carcinoma after being admitted with PLC to the clinic and undergoing radiologic examination, is presented owing to his peculiar presentation.

CASE PRESENTATION

A 30-year-old male patient presented to our outpatient clinic with complaints of shortness of breath, dry cough, weight loss, and night sweats. His complaints had started 2 months previously with a mild dry cough, which was progressive and had been accompanied by dyspnea during the previous 2 weeks. He had lost 5 kg in weight. His general condition was moderate, he had difficulty talking, and he had an oxygen saturation of 90% on finger probe. On chest X-ray, bilateral reticulonodular infiltration was noted (Figure 1a). He was hospitalized for detailed evaluation and treatment. He did not have any other medical diseases. He had a cigarette smoking history of 5 packs/year, and he had not smoked for the previous 8 years. He was born and raised in İstanbul and had worked as an officer. He had no history of taking drugs, and he had no history of exposure to any antigen that causes hypersensitivity pneumonitis (HP). The patient was evaluated by another pulmonologist owing to complaints of dry cough. His physical examination and radiologic and spirometric findings were found to be normal, and he was referred to the internal medicine clinic (Figure 1b). Although he had no gastric complaints, owing to the unexplained etiology of the dry cough he underwent gastroscopy. The pathology results had not yet been reported at that time. He had used antibiotic treatment with amoxicillin-clavunate and clarithromycin in the previous 10 days. His brother had been diagnosed with Henoch-Schönlein purpura and his uncle had undergone treatment for pulmonary tuberculosis.

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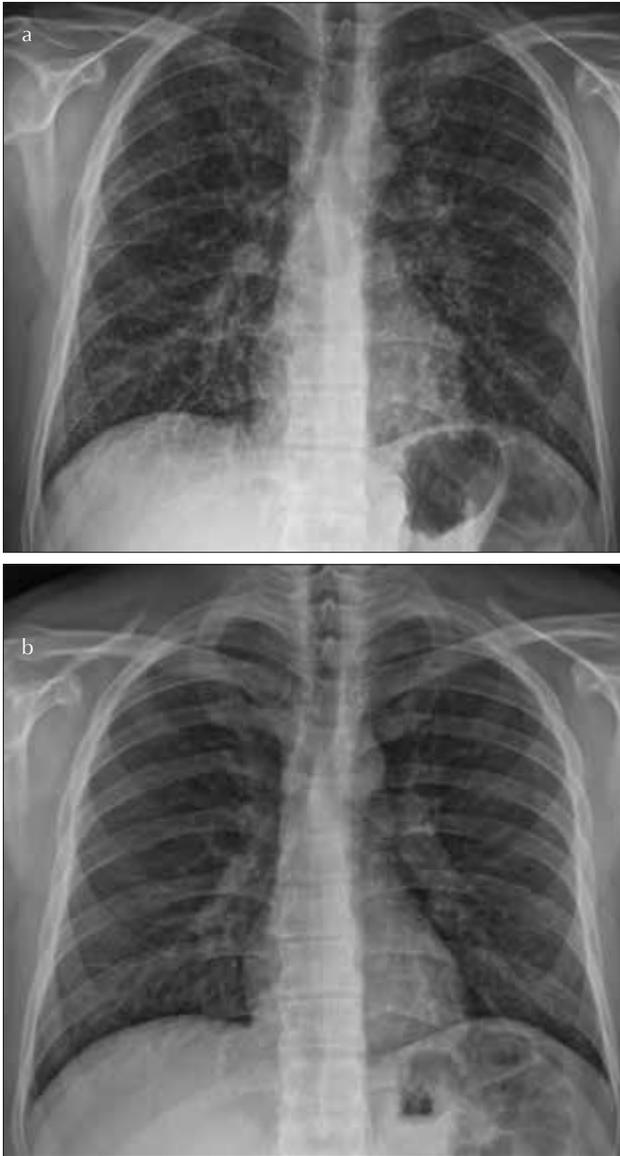


Figure 1. a, b. Chest x-ray at admission, bilateral generalized reticulonodular infiltration (a). Normal chest X-ray: 1 month before admission (b)

On physical examination, his body temperature was 36.0°C, his blood pressure was 130/80 mmHg, and his heart rate was 130/min. On complete blood count, leukocytes were 9.5/mm³, hemoglobin was 15.4 g/dL, and platelets were found to be 160/mm³. On routine biochemical evaluation, blood glucose was 105 g/dL and blood urea nitrogen was 83 mg/dL. Other biochemical parameters were within the normal ranges. Angiotensin-converting enzyme (ACE) was 18 U/L (normal: 66-114), D-dimer was 5 µg/mL (normal: 0-0.5), C-reactive protein was 28 mg/dL (normal: 0-5), and erythrocyte sedimentation rate was 28 mm/hr. Arterial blood gas parameters in room air were pH 7.48, PaCO₂ 29.9 mmHg, and PaO₂ 64.7 mmHg. Despite the low levels of the infection parameters, broad-spectrum antibiotics were initiated, which consisted of piperacillin-tazobactam, ciprofloxacin, and oseltamivir, because pneumonia cannot be excluded in a young patient having progressive bilateral infiltration and progressive respiratory failure. On thorax computed tomogra-

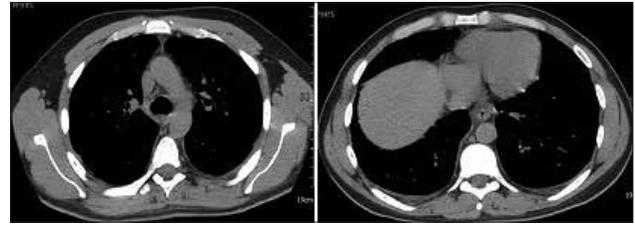


Figure 2. Thorax computed tomography: bilateral minimal effusion, no lymphadenomegaly

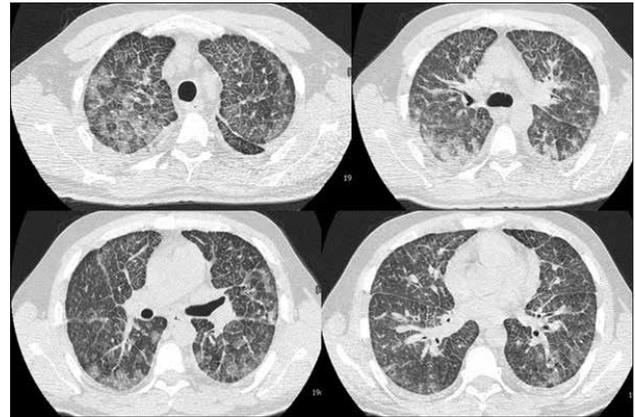


Figure 3. High Resolution Computed Tomography; bilateral ground-glass opacity and prominence of interlobular septum

phy, minimal bilateral effusion (3 mm pleural effusion in the right hemithorax and 5 mm in the left hemithorax), generalized ground-glass opacity, and interlobular septal thickenings were identified. He had no lymphadenomegaly (Figure 2). Echocardiographic evaluation was normal. On the third day of hospitalization, his general condition worsened, his respiratory rate increased to >32/min, and his oxygen saturation decreased to 82% of that of the room air. High-resolution computed tomography (HRCT) was performed with an initial diagnosis of acute interstitial pneumonia. On HRCT, generalized ground-glass opacity, thickening of the bronchovascular interstitium, and significant interlobular septal thickenings were seen bilaterally (Figure 3). Flexible fiber optic bronchoscopy was performed for endobronchial evaluation, and a bronchoalveolar lavage (BAL) fluid sample was obtained for the pre-diagnoses of acute interstitial pneumonia and lymphangitic carcinomatosis. No endobronchial lesion was identified, and BAL was performed on the middle lobe. Transbronchial biopsy (TBB) was not performed owing to the general deterioration in the patient condition and hypoxemic respiratory failure. BAL fluid analysis revealed cell ratios of lymphocytes 24%, neutrophils 35%, and eosinophils 1%, and a CD4/CD8 ratio of 3.11. In the lavage samples, acid-fast bacilli staining was negative, *Mycobacterium tuberculosis* by polymerase chain reaction was negative, and lavage cultures did not yield any specific microorganism; galactomannan antigen was also negative. Cytological evaluation of lavage fluid reported atypical epithelial cells that suggested malignancy. Moreover, the pathology results of the gastroscopy procedure were reported as signet cell carcinoma. The radiologic findings were found to be compatible with PLC by an expert thorax radiologist. The patient was referred to the oncology clinic for a chemotherapy program.

DISCUSSION

The present case comprises a young male patient who was evaluated for progressive dry cough and respiratory insufficiency with a pre-diagnosis of acute interstitial pneumonia and was diagnosed with PLC due to gastric cancer. He had no gastrointestinal complaints. Thus, the present case is peculiar in its emphasis that PLC can be encountered prior to a diagnosis of malignancy at any age.

Pulmonary lymphangitic carcinomatosis was first described by Andral in a patient with uterine cancer in 1824 [8]. PLC mostly occurs secondary to malignancies of the breast, stomach, lung, prostate, and pancreas [1]. PLC may appear in the natural course of primary disease or may represent the very first finding, as in our case [7]. In nearly 50% of cases, the initial complaints are respiratory symptoms rather than symptoms of an underlying tumor. The most common clinical symptom is dyspnea, which typically starts and gradually progresses for 2-4 months before diagnosis. Dry cough often accompanies dyspnea [9].

It has been reported that 30-50% of cases have no abnormalities on chest X-ray. Therefore, for patients with a known malignancy having new-onset progressive dyspnea, HRCT is recommended as a more sensitive radiologic method [6]. HRCT findings are typically characterized by irregular and nodular thickening of the interstitial septum, subpleural nodules, prominent interstitial markings, ground-glass opacity, pleural effusion, and hilar and mediastinal lymphadenopathy [2].

Histopathologic examination is necessary for the diagnosis of PLC, but diagnosis is often made on the basis of clinical and radiologic findings because of a general deterioration in patient condition. Grenier et al. [10] reported that clinical and radiologic findings are accurate in the diagnosis of PLC in 92% of patients with diffuse interstitial pulmonary disease. Bronchoscopy should be performed in all patients who can tolerate the procedure. Cytological examination of sputum and bronchoscopic lavage, TBB, and thoracoscopic lung biopsy are the usual invasive diagnostic methods.

In a study including 31 cases, diagnoses were established by bronchial brushing, TBB, forceps biopsy, and bronchial lavage in order of frequency [11]. TBB was performed on a 24-year-old male patient similar to our case, and the pathology was reported to be metastatic carcinoma, which was thought to have originated from tumors of the stomach, pancreas, and biliary duct. This case was diagnosed as signet ring cell carcinoma by gastroscopy and whole-body magnetic resonance imaging (MRI). Whole-body MRI techniques are reported to be able to accurately identify gastric tumors, as well as liver and skeletal metastases. In addition, they are also suggested as preferable methods in patients with renal dysfunction and contrast allergy [7].

Interstitial pulmonary diseases and infectious diseases were considered as preliminary diagnoses in our case because of the patient's young age and clinical findings with acute and progressive onset. For the differential diagnosis of PCL, sarcoidosis, hypersensitivity pneumonia, vasculitis, pulmonary alveolar proteinosis (PAP), viral pneumonia, lymphoma, pulmonary edema, and Kaposi's sarcoma should be considered

[6]. In the present case, sarcoidosis was not considered because of the low levels of ACE, and the CD4/CD8 ratio on BAL analysis also did not suggest mediastinal lymphadenopathy. HP was not considered because the patient had no exposure suggestive of HP and the lymphocyte levels in BAL fluid were low. Vasculitis was not thought probable because his urine test analysis, renal test function, and acute-phase reactants were not increased. The BAL findings were not compatible with PAP. No response could be observed to broad-spectrum antibiotic therapy, and the fact that no mediastinal or peripheral lymphadenopathy was present rendered a diagnosis of lymphoma unlikely. Although his clinical complaints were compatible with tuberculosis, the HRCT findings were not suggestive of tuberculosis. His sputum and BAL fluid samples did not reveal any bacilli.

Bronchoscopy and BAL were performed in the present case, but TBB could not be performed owing to the deterioration in the patient's general condition, and atypical cells were seen on lavage pathology. Moreover, the pathology results of the previously performed gastroscopy were reported as signet ring cell carcinoma. Gastric tumors are the second most common cancers in males in Turkey and worldwide [12,13]. They constitute 7.4% of cancers in males in Turkey [12]. Their incidence increases with age, mostly during the sixth and seventh decades [13].

Signet ring cell carcinoma is a histologic subtype of gastric adenocarcinoma. This pathologic subtype of stomach tumor is an independent risk factor for a more severe prognosis. Signet ring cell carcinoma is prone to infiltrate the peritoneum and lymph nodes [14].

Owing to the gradual deterioration in the general condition of our patient, further imaging could not be carried out for the investigation of distant organ metastasis, and he was transferred to the oncology clinic in order to receive chemotherapy.

In conclusion, in the presence of chronic cough, progressive dyspnea, and lesions similar to interstitial lung disease in a patient previously diagnosed with cancer, a diagnosis of PLC should be considered among the preliminary diagnoses. We should still consider a diagnosis of PLC even though the patient is young. In these cases, it should be kept in mind that respiratory complaints and findings can be seen first rather than symptoms of the primary tumor. Diagnosis can be made clinically and radiologically if a biopsy cannot be performed via bronchoscopy because of the general condition of the disorder.

Informed Consent: Written informed consent was obtained from patient who participated in this case.

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