Adenocarcinoma of the lung masquerading as miliary mottling: a rare presentation

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Bronchogenic carcinoma usually presents as a mass lesion associated with variable degrees of lung collapse and associated effusion. Although primaries from other sites such as thyroid, choriocarcinoma, and sarcomas may present as miliary mottling, bronchogenic carcinoma presenting this way is uncommon. We present here the case of a 62-year-old housewife, who presented with bilateral miliary shadows on chest radiography and was treated for pulmonary tuberculosis on the basis of history and radiological findings. As the disease advanced, the diagnosis of primary adenocarcinoma of the lung was made.

Keywords:
adenocarcinoma lung, bronchogenic carcinoma, miliary mottling

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Introduction

The differential diagnosis of miliary pattern on chest radiography includes miliary tuberculosis, histoplasmosis,sarcoidosis,pneumoconiosis,pulmonary siderosis, and hematogenous metastases from primary cancers of the thyroid, kidney, trophoblast, and some of the other sarcomas [1]. The erstwhile disease entity of bronchoalveolar carcinoma (now, minimally invasive carcinoma) has been described rarely to present as miliary mottling. Primary bronchogenic carcinoma of the lung presenting as this radiographic sign is exceedingly rare [2] and would not be thought of as a primary diagnosis by most. It is always tempting to treat these patients for tuberculosis, as was the case in our patient. This led to a delay in diagnosis and an unfavorable outcome ensued for the patient. It is prudent, hence to obtain a tissue diagnosis in these patients before the start appropriate therapy.

Case report

A 62-year-old housewife, previously healthy, nonsmoker, presented with a history of dyspnea, dry cough, loss of appetite, and lethargy since 2–3 months. She was referred to a local health facility, where a chest radiography revealed bilateral miliary shadows. Sputum was checked for acid-fast bacilli (AFB) and was found to be negative for the same. The patient was started on first-line antituberculosis therapy comprising of isoniazid, rifampicin, pyrazinamide, and ethambutol. as the clinical condition worsened and the patient developed irritability, a chest radiography was repeated after 15 days. This showed an increase in left-sided pleural fluid. This was attributed to be an immune response and antituberculosis therapy was continued. As the symptoms progressively worsened, a therapeutic pleural tap was performed and around 1.5 l of hemorrhagic-appearing fluid was removed. Laboratory analysis of the fluid revealed an exudative lymphocytic fluid. Neither evaluation of pleural fluid adenosine deaminase levels nor AFB staining of the pleural fluid was carried out. Exact pleural fluid reports were not available. Because of irritability and off and on altered behavior, a diagnosis of isoniazid-induced psychosis was made, and isoniazid was discontinued and replaced with streptomycin.

The patient was subsequently referred to our center as a presumed case of drug-resistant tuberculosis and isoniazid-induced psychosis. On examination, the patient was in distress, with a pulse of 110/min, blood pressure of 130/80 mmHg, and respiratory rate of 30/min. General physical examination was unremarkable except for the presence of pallor and a low BMI (16 kg/m^2). Respiratory system examination revealed absent breath sounds in the left lower hemithorax with bilateral crackles. Laboratory examination revealed a hemoglobin of 7 g/dl, total leukocyte count of 9300/mm^3, with normal differential counts. Liver and renal function tests were within normal limits. The Mantoux test was negative. Erythrocyte sedimentation rate by the westergren method was 20 mm/h. Sputum samples were stained with ZN stain and were negative for AFB (3 samples). HIV by enzyme-linked immunosorbent assay was nonreactive. A chest radiography taken at our

center showed ill-defined heterogeneous opacities on the right side with left-sided massive pleural effusion with underlying collapsed lung and mediastinum shifted to the right side along with cardiomegaly. Contrast-enhanced computer tomography scan revealed multiple, randomly distributed nodules involving all lobes of the right lung and left-sided massive pleural effusion with underlying collapsed lung with right-sided mediastinal shift. There was no mediastinal lymphadenopathy. Pleural fluid analysis revealed an exudative lymphocytic effusion: protein, 4.5 g/dl; lactate dehydrogenase, 450; total leukocyte count, 100; differential leukocyte count – 90% lymphocytes and 10% neutrophils; adenosine deaminase, 7.4 IU/l. Gram and AFB stains and GeneXpert tests of the pleural fluid were negative. Pleural fluid cytospin was positive for malignant cells (Fig. 1). The patient then underwent medical thoracoscopy, which showed dense adhesions between the parietal and visceral pleura and partial collapse of the underlying lung. The pleural biopsy was suggestive of metastatic carcinoma/mesothelioma on histopathological examination.

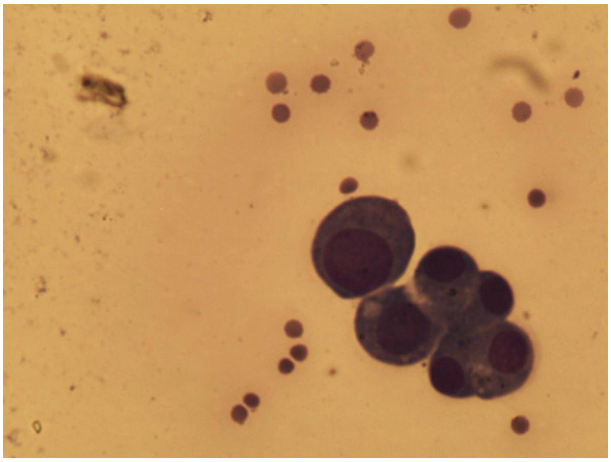
Despite pleural fluid drainage, the lung did not fully expand. To look for any intrabronchial mass lesion, fiberoptic bronchoscopy was performed, which showed narrowed and infiltrated left lower lobe bronchus. Endobronchial biopsy was taken from the left lower lobe. Rest of the airways were normal. Bronchial washings were negative for AFB stain, GeneXpert, and culture. Endobronchial biopsy showed dysplastic epithelium, and subepithelium showed infiltration by neoplastic cells. Findings were suggestive of non-small-cell carcinoma of the lung. To further typify the tumor, immunohistochemistry was carried out, which showed positivity for TTF1 and CK7 and negative for calretinin, WT 1, KI 67, and HBME1. Immunohistochemistry and morphology favored the diagnosis of primary adenocarcinoma of the lung (Fig. 2). On further evaluation the tumor tested negative for epidermal growth factor receptor and anaplastic lymphoma kinase, thus precluding any targeted therapy.

MRI of the brain was carried out in view of the neurological complaints. This revealed a ring-enhancing, T2 hypointense lesion in the periventricular white matter adjacent to the occipital horn of the right lateral ventricle suggestive of metastatic lesion in the brain. The patient underwent talc pleurodesis of the left pleural cavity. Stereotactic brain radio therapy was offered to the patient for brain metastasis, which was refused by the attendants. First cycle of chemotherapy with pemetrexed and cisplatin was given to the patient, along with 4 mg of zolendronic acid. The patient is under close follow-up.

Discussion

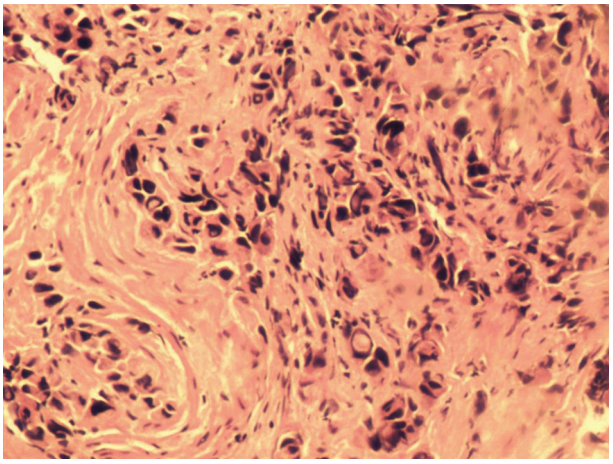
The literature contains a few, similar cases reported as miliary primary lung carcinoma [2]. The largest case series is from a Japanese worker, in which five such patients were described [3]. This group concluded that the prevalence of miliary phenotype might be ~1% in Japanese patients and that such a presentation is associated with a poor outcome. Adenocarcinoma is the most common histological variety of bronchogenic carcinoma seen in nonsmoker women. Timely identification of these tumors is important, as specific therapy in the form of tyrosine kinase inhibitors and anaplastic lymphoma kinase fusion inhibitors are available and may improve the overall survival in these patients [4,5]. This case reiterates the fact that tissue diagnosis is must before we subject our patients

Figure 1



Pleural fluid cytospin showing a cluster of malignant cells.

Figure 2



Histopathological examination confirming the diagnosis of adenocarcinoma of the lung.

to any form of therapy. With the armamentarium of modern investigation tools such as medical thoracoscopy, endobronchial ultrasound-guided transbronchial needle aspiration, cryotransbronchial lung biopsies, etc., we should not be tempted to treat all patients of miliary mottling on chest radiography for TB.

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Conflicts of interest
There are no conflicts of interest.

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