Coincidental Lung Presentation of Two Synchronous Non-Pulmonary Tumors

Daniel Starobin MD[1], Miriam Katz MD[2], Monica Huszar MD[3] and Zev Shtoeger MD[4]

[1]Pulmonary Institute, and Departments of [2]Imaging, [3]Pathology and [4]Internal Medicine B, Kaplan Medical Center, Rehovot, Israel and Hebrew University Medical School, Jerusalem, Israel

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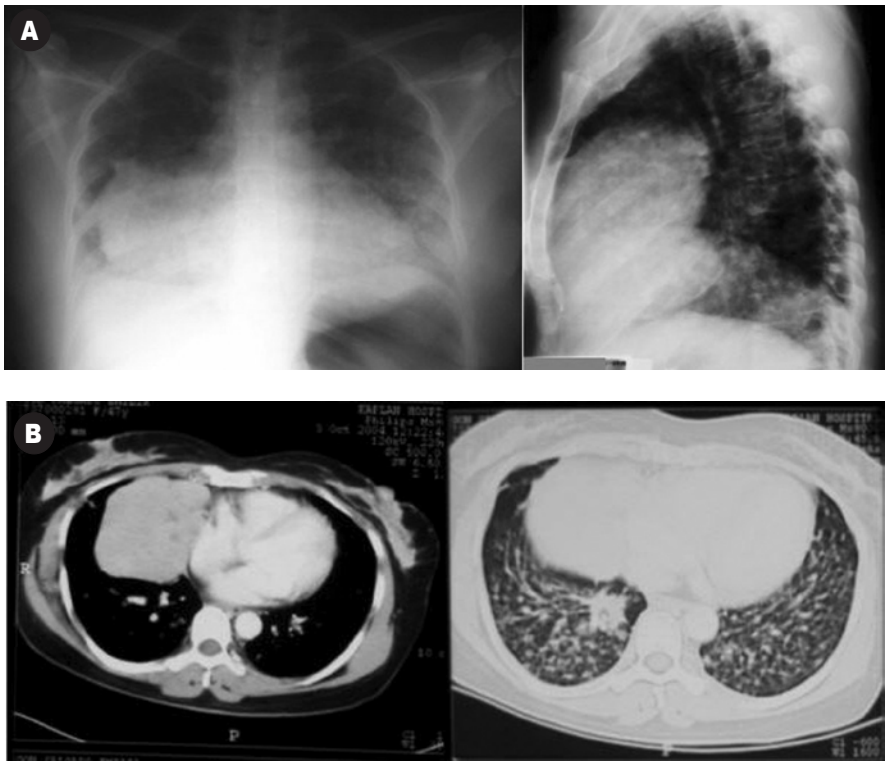
Synchronous and metachronous lung tumors are well-established topics. Intrapulmonary thymoma is much less common than mediastinal thymoma. Yet a review discussing eight cases of intrapulmonary thymoma showed no differences of immunohistochemical markers or prognosis compared with "classical" mediastinal thymoma [1]. Widespread metastatic disease is a well-known presentation of thyroid carcinoma [2,3]. Only three cases in which these tumors were found at the same time have been described in the literature [4,5].

The coincidence of both pathologies in our case – a middle-aged woman without known risk factors to develop malignancies (such as smoking, professional activity, familial history) – was either rare or unpredictable. This case presented challenging diagnostic issues.



[A] Posterior-anterior [left panel] and lateral [right panel] chest X-rays show multiple pulmonary opacities as well as a lesion at the lower right lung field obscuring the right cardiac silhouette. **[B]** Axial post-intravenous contrast chest CT scan at the lower part of the thorax demonstrates: a well-defined homogeneous soft tissue mass adjacent to the heart on the mediastinal window setting [left panel], and multiple bilateral pulmonary nodules on the lung window setting [right panel].

Patient Description

A 47 year old Filipina was admitted to a regional medical center with a 3 month history of dry cough. No other complaints were present on admission. She had five children. She had come to Israel from the Philippines approximately 5 years before onset of the coughing, and was employed by an elderly woman as a maid.

The patient had never smoked, used drugs or taken medications. She reported no fever, chills, weight loss or excessive sweating. She had not had any contact with dangerous materials or gases, or close contact in the past with persons with diagnosed pulmonary tuberculosis. The patient denied chronic rhinitis, heartburn or attacks of shortness of breath with or without wheezing. Symptomatic therapy with cough-relieving syrup, as well as a 7 day trial of amoxycillin did not cause any alleviation of the cough.

A chest radiograph was performed [Figure A], showing multiple bilateral small nodular opacities without specific predilection. A large homogeneous well-defined opacity adjacent to the right heart border, partially obscuring the lower part of the right lung, was also noted. The X-ray differential diagnosis included miliary tuberculosis, sarcoidosis and spread of malignancy. The large opacity in the lower part of the right lung was suspected for lung tumor, mediastinal mass or enlargement of the cardiac silhouette.

Physical examination was normal; the general appearance of the patient was good and she appeared healthy. Blood tests including complete blood count, complete blood chemistry panel, C-reactive

protein and erythrocyte sedimentation rate were normal. A serology test for human immunodeficiency virus was negative. Blood level of angiotensin-converting enzyme was normal. Serology tests for collagen vascular diseases screening panel were negative. Purified protein derivative was 13 mm. Induced sputum and feces were negative for parasites. Mammography was normal. Ultrasound imaging tests of the abdomen, pelvic organs and neck were normal. Total body gallium scan showed non-specific enhanced uptake of gallium in the lumbar spine, skull and lower part of the right lung. A spine radiograph showed a few small lytic lesions in lumbar vertebrae. A computed tomography scan of the brain disclosed three small lesions in the brain, which were presumed to be metastatic spread.

Three induced sputum samples were obtained. Cultures for bacteria, fungi and viruses were negative. Smears for acid-fast bacilli were negative. The bacteriological laboratory reported early growth in a mycobacterial culture. Features of the bacteria were defined and classified as *Mycobacterium simiae* belonging to a non-tuberculous mycobacteria group.

Chest CT scan showed multiple small pulmonary nodules in both lungs [Figure B]. In addition, there was a large homogeneous pulmonary mass involving the right middle and lower lobes abutting the pleura. No lymphadenopathy or other mediastinal abnormalities were seen. A tru-cut biopsy of the right lung mass was performed under CT guidance. On pathological examination, it was identified as a thymoma according to specific microscopic features and positive keratin and TdT immunostains. No evidence of thymic carcinoma, lymphoma or small cell carcinoma was found.

The patient underwent fiberoptic bronchoscopy with transbronchial biopsy under fluoroscopic guidance without complications. No endobronchial pathology was found. Bronchoalveolar lavage was performed for cytological and bacteriological tests, which were negative. Microscopically, transbronchial biopsy samples were consistent with adenocarcinoma. Immunostaining was positive with surfactant, TTF-1 and thyroglobulin and negative with carcinoembryonic antigen. Finally, the transbronchial biopsy specimen was reported as thyroid adenocarcinoma.

Another ultrasound examination of the neck was performed, which detected a small nodule in the thyroid gland. Thus, two synchronous tumors were diagnosed in this patient: an ectopic intrapulmonary thymoma and thyroid adenocarcinoma metastasizing to the lung, brain and spine. Exertional dyspnea and weakness gradually developed. The patient was referred to the oncology department where brain radiation and chemotherapy was begun. The patient returned to the Phillipines after the initial oncological treatment and was lost to follow-up.

Comment

The rule of thumb for diagnostic investigation says: "Look for the common pathway to explain different signs or symptoms that exist." It is almost always correct in relatively young individuals, as in our patient. What type of disease can explain nodular lung disease and a large pulmonary mass? Metastatic spread of lung cancer or a tumor of mesenchymal origin (such as sarcoma or blastoma) and lymphoma may be realistic explanations. If nodular lung disease and the mass in the right lung were presentations of different diseases, in this case, sarcoidosis, tuberculosis and rheumatoid arthritis have to be considered in the differential diagnosis. Exotic infections, developing as indolent disease, such as the chronic form of melioidosis, paragonimiasis, hydatidosis and histoplasmosis, may also be considered, keeping in mind that our patient came from the Phillipines.

On the one hand, this patient presents a unique case of synchronously diagnosed ectopic intrapulmonary thymoma and metastatic thyroid carcinoma. On the other hand, the extremely common complaint of dry cough led us to a diagnosis that initially seemed an unlikely possibility. Overt radiological abnormalities on the chest radiograph and CT scan narrowed the differential diagnosis to lung-related pathologies. Sarcoidosis, tuberculosis and lymphoma were considered as more consistent with this clinical picture and more common before histological lung sampling was performed. A "false route" of non-tuberculous mycobacterium disease was avoided owing to the absence of clinical signs of infectious disease, no evidence of immunocompromise and very late growth in tuberculosis cultures, although the radiological picture could have been consistent with miliary tuberculosis.

Genetic aspects have been suggested as causes of metachronous and synchronous tumors in recent decades. However, we did not perform genetic analysis because of health insurance limitations. Our gut feeling about genetic proneness to multiple malignancies in this patient was not confirmed by genetic screening.

This case warns us that our common diagnostic algorithm of parsimony does not always work. Efforts to cluster all signs together under one label are sometimes not effective. Unusual cases like this one oblige the medical staff to look for a correct solution off the prevalent highways.

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Correspondence: Dr. D. Starobin, Pulmonary Institute, Kaplan Medical Center, Rehovot 76100, Israel.
Phone: (972-8) 944-1406
Fax: (972-8) 944-1063
email: daniel_s@clalit.org.il