Microscopic Pulmonary Tumor Embolism in Adenocarcinoma of the Stomach

Tamar Shalev MD[1], Larisa Guranda MD[2], Ora Shovman MD[1] and Leonid Michael MD[1]

[1] Department of Medicine B and Center for Autoimmune Diseases, and [2]Department of Radiology, Sheba Medical Center, Tel Hashomer, Israel
Affiliated to Sackler Faculty of Medicine, Tel Aviv University, Ramat Aviv, Israel

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Microscopic pulmonary tumor embolism is the presence of multiple aggregates of tumor cells in the small pulmonary arteries, arterioles and septal capillaries. This entity can be expressed as cor pulmonale, which has been described in patients with various malignancies including carcinoma of the breast, stomach, pancreas, liver and prostate [1]. Adenocarcinoma and trophoblastic neoplasms are the most frequently reported etiologies. The majority of reported cases occurred in association with breast, lung and gastric carcinoma [2]. Among the various pulmonary findings of cancer, lymphangiosis carcinomatosa and paraneoplastic thromboembolism are the most frequent conditions leading to respiratory distress. Less attention is paid to tumor-related lesions of pulmonary blood vessels [3]. The incidence of pulmonary tumor emboli was estimated postmortem to be 2–26% in patients with solid tumors and was thought to have contributed to death in 8% of the cases [2].

We describe a patient with an unsuspected microscopic pulmonary tumor embolus that eventuated as a sub-acute cor pulmonale and resulted in death. This case illustrates the characteristic findings of this entity, including imaging modalities.

Patient Description

A 43 year old man was admitted for dyspnea; 1 month earlier he complained of dyspnea on exertion and dry cough without fever. One week prior to his admission he noted an exacerbation of dyspnea followed by general distress and a computed tomography scan of the chest was performed. Three years previously he was diagnosed with gastric adenocarcinoma without any evidence of metastases, and he underwent partial gastrectomy followed by chemotherapy. Abdominal CT a few weeks before his admission revealed retroperitoneal metastases.

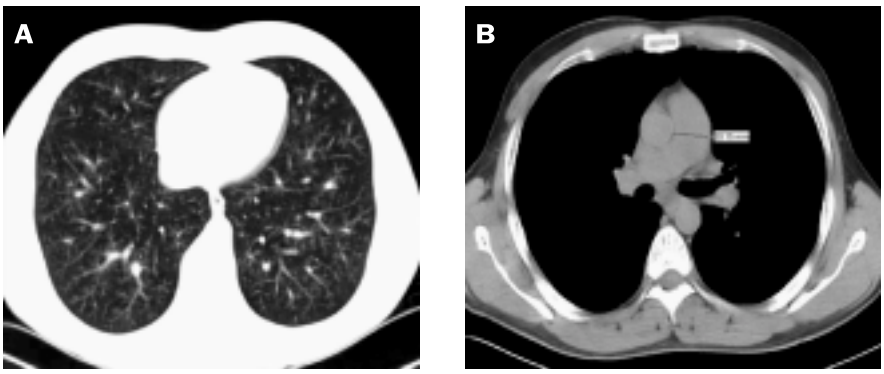
Physical examination showed a malnourished pallid patient with tachypnea (26 breaths/min), tachycardia (100 beats/min), normal blood pressure (120/70 mmHg) and oxygen saturation 93% with supplemental oxygen (room air 88%). Cardiovascular examination demonstrated elevated jugular venous pressure but no murmur or gallop. Accentuation of the second heart sound was not noted. The lungs were clear on auscultation. The remainder of the physical examination was interpreted as normal. Arterial blood gas measurements showed: pO_2 60 mmHg, pCO_2 32 mmHg, pH 7.44 (the patient breathing room air). Further laboratory analyses disclosed hemoglobin 11 g/dl, platelet count 120,000/mm^3, d-dimer 1,600 nl/L (Latex), normal liver function and normal renal biochemistry results. The electrocardiogram depicted sinus tachycardia.

CT scan of the chest showed branching linear opacities and small centrilobular nodules in both lungs. The main pulmonary trunk (30 mm) and the paratracheal lymph nodes were enlarged (22 mm). A ventilation-perfusion scan showed multiple sub-segmental peripheral perfusion defects without ventilatory abnormalities, and a low probability for pulmonary embolism [Figure A].

The following diagnostic possibilities were considered: pulmonary embolism, pulmonary infection, and pulmonary parenchymal metastases. For these reasons treatment with supplemental oxygen, levofloxacin and low molecular weight heparin was instituted. On the third day of hospitalization the dyspnea worsened rapidly and the patient developed acute cardiorespiratory failure. His condition deteriorated rapidly and he expired. Permission for postmortem examination was not granted.

Comment

This patient had a sub-acute progressive dyspnea, which seemed to be the most



[A] Branching linear opacities and small centrilobular nodules, with "tree-in-bud" appearance.
[B] Dilated pulmonary artery (30x15 mm).

common initial clinical symptom of microscopic pulmonary tumor embolism. The clinical and radiologic presentations raised the possibility of microscopic pulmonary embolism. However, this diagnosis is relatively rare and difficult to be determined antemortem.

Other common findings in this entity are cough (8–47% of cases), pleuritic chest pain (18–28%) and hemoptysis (5–18%). Systemic symptoms such as fatigue and weight loss can also be present. Physical examination usually discloses signs of pulmonary hypertension in association with tachypnea, tachycardia, clear lungs on auscultation, elevated jugular venous pressure, and accentuated pulmonary valve component of the second heart sound [2]. Arterial blood gases evaluation typically shows hypoxemia in the setting of clear lung fields on chest X-ray, in contrast to the interstitial pattern of lymphangitic carcinomatosis. The most common electrocardiographic finding is sinus tachycardia. Echocardiography typically reveals elevated pulmonary and right ventricular pressures.

Imaging modalities may help to define the process. Ventilation-perfusion lung scan typically shows multiple peripheral sub-segmental perfusion defects without ventilatory abnormalities, a pattern called "segmental contour." Radiographic appearance of the microscopic tumor emboli resembles a "tree-in-bud" pattern [Figure B]. The tree-in-bud appearance on CT is characterized by small centrilobular nodules and branching linear opacities. This pattern is often seen in patients with small airways disease. Differential diagnostic considerations include: infection, bronchial disease, congenital and immunologic disorders. In these cases, the pattern of tree-in-bud is caused by dilatation and plugging of small airways by mucus. There is evidence in the literature that in some patients the tree-in-bud appearance may be caused by a vascular disorder [4]. A rare mechanism leads to malignant cells filling the small pulmonary vessels. Dilated arterioles are seen as a tree-in-bud pattern. Differential diagnosis of a tree-in-bud pattern entails small airways disease or small vessels diseases.

A sub-acute clinical presentation, in conjunction with a history of underlying cancer and characteristic imaging features should prompt the clinical diagnosis of microscopic pulmonary tumor emboli, as in the case described here. A definitive diagnosis can be reached either by open lung biopsy, transbronchial lung biopsy, or cytologic examination of the aspirate through a properly placed Swan-Ganz catheter. Possible mechanisms for sub-acute pulmonary emboli include endothelial dysfunction and hypercoagulable state induced by the microemboli, rather than a mechanical obstruction.

Tumor cell embolization to the lung does not necessarily mean parenchymal metastases, because many of the tumor cells are destroyed in the vessel lumen by a secondary thrombus formation and subsequent organization, and fewer than 20% of the tumor cells result in parenchymal metastases. Tumor cell microembolization is also accompanied by fibroblastic intimal hyperthrophy. If a significant amount of pulmonary microvasculature is occluded by tumor emboli before the development of metastases, acute or sub-acute cor pulmonale will ensue, depending on the extent and speed of embolization. Repeated emboli may explain how a relatively fulminant event was superimposed on the sub-acute clinical course, as seen in our patient.

There are two proposed routes of embolization; one is through the abdominal viscera (primary or metastatic) to the inferior vena cava, and the other is extension through the lymphatic spread into the thoracic duct and then to the superior vena cava [5]. In our case, lymphatic spread through the thoracic duct could not be ruled out since involvement of the regional lymph nodes was seen in the CT scan of the chest.

The present evidence favors surgical intervention for the treatment of tumor emboli, particularly when the source is renal cell carcinoma or myxoma. A few reports of chemotherapy treatment in microscopic pulmonary thromboembolism suggested favorable results in breast cancer and choriocarcinoma [2]. An antemortem diagnosis of microscopic pulmonary embolism may prevent unnecessary and potentially dangerous therapies such as anticoagulation or inferior vena cava ligation.

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Correspondence: Dr T. Shalev, Dept. of Internal Medicine B, Sheba Medical Center, Tel Hashomer 52621, Israel.
Phone: (972-3) 530-2661
Fax: (972-3) 530-2428, 535- 28-55
email: Michael_shalev@bezeqint.net