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Primary Lung Adenocarcinoma With Ovarian Metastasis: A Rare Presentation of Bronchogenic Carcinoma

Adenocarcinoma de origen pulmonar con enfermedad metastásica en ovario: una forma rara de presentación de carcinoma broncogénico

To the Editor:

Around 40% of patients with bronchogenic carcinoma have metastasis when diagnosed.¹ Although metastasis can occur in practically any organ, those most commonly affected are the bones, the liver, the adrenal glands, the brain, and the skin.¹ We describe the case of a woman with non-small cell lung cancer with metastasis to the ovary.

The patient was a 54-year-old woman with no significant medical history or history of substance abuse. She consulted the gynecology department in regard to irregular menstrual bleeding and anemia. Pelvic and transvaginal ultrasound revealed an enlarged uterus and multiple images of intramymetrial, subserous, and pedunculated nodules; 1 nodule near the abdominal cavity measured 12 cm and reached the suprapancreatic level. Given our suspicion of neoplasm, the radiology study was complemented with a computed tomography scan of the thorax, abdomen, and pelvis. This revealed massive right pleural effusion with pleural thickening and focal contrast-enhanced areas, enlarged prevascular retrocaval and paraaortic lymph nodes, and multiple blastic lesions in the dorsolumbar spine, the sacrum, and both ilea. The clinical and radiological characteristics combined to suggest an initial diagnosis of uterine tumor with extensive metastasis. A blind pleural biopsy revealed infiltration as a consequence of epithelial neoplasm, suggestive of adenocarcinoma. Following uterine dilatation to rule out malignancy, the patient underwent a full hysterectomy and double adnexectomy. The uterine tumors were leiomyomas that showed no histologic signs of malignancy. In the right ovary, immunohistochemistry revealed 1 nodular lesion with a positive thyroid transcription factor-1 (TTF-1) profile—findings consistent with metastasis from a pulmonary adenocarcinoma (Figure). The same technique applied to the pleural biopsy samples revealed tumor cells with positive TTF-1 expression. The study was concluded with a fiberoptic bronchoscopy that revealed, in the basal pyramid, an edematous mucosa with no folding causing a stenosis of the entry to the basal bronchi. The result of the bronchial biopsies was adenocarcinoma originating in the lung.

The incidence of bronchogenic carcinoma is steadily on the rise, ranking as the leading cause of tumor-related deaths in developed countries. Adenocarcinoma, which is the histologic type of cancer most frequent in women, has been showing a clear growing trend in recent years. The main factor influencing prognosis is surgical treatment, although diagnosis is usually made at advanced stages of the disease.¹ The literature contains very few cases of bronchogenic carcinoma with metastasis to the ovary, which can occur with both small cell and non-small cell carcinomas.²⁻⁵ In the case described, the form of presentation pointed to gynecological neoplastic disease with pleural metastasis as a first diagnostic possibility. Malignant pleural effusion is a frequent complication of advanced neoplastic

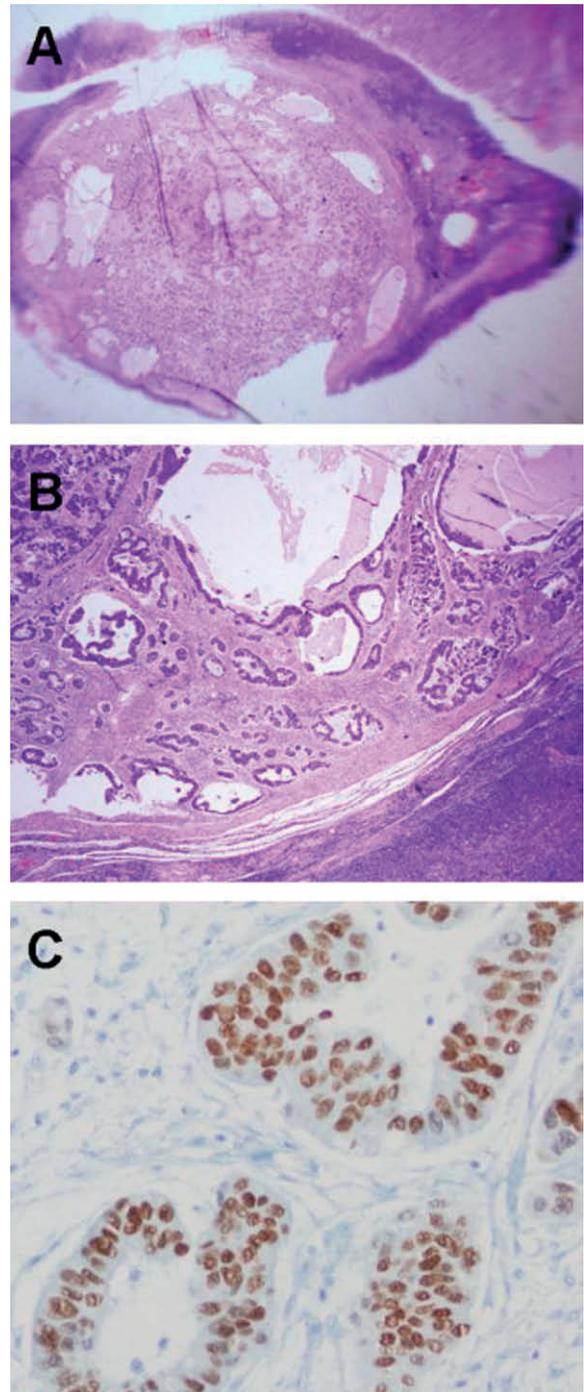


Figure. A. Macromicroscopy image of the ovarian nodule. B. Microscopy image of the ovarian tumor, clearly delimited with respect to the parenchyma of the other ovary, and with evident tubular-glandular differentiation. C. Positive nuclear immunohistochemical staining for thyroid transcription factor-1, showing a profile that was positive for keratin 7, negative for keratin 20, and negative for chromogranin.

diseases. The most common causes are bronchogenic carcinoma and breast cancer, although any tumor may cause the metastasis, including ovarian and uterine carcinoma.⁵

Differentiation between metastatic adenocarcinoma and primary ovarian tumor is crucial, as management and prognosis for these 2 cancers is very different. For this reason, advances in immunohistochemical techniques are essential to clinical practice.

Given the increase in incidence of bronchogenic carcinoma in women, the ovaries should not be excluded as a possible location for metastasis originating in the lung.

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Pulmonary Toxicity Associated With Cabergoline

Toxicidad pulmonar por medicamentos inducida por cabergolina

To the Editor:

Pulmonary drug toxicity is increasingly being diagnosed as a cause of acute and chronic lung disease.¹ Many drugs have been reported to give rise to adverse respiratory reactions and pulmonary diseases. A distinctive pattern of pleuropulmonary changes was first described by Graham et al.² This syndrome developed during the use of methysergide, an ergoline derivative. Since then, other cases have been reported related to the use of methysergide as well as other ergolines, such as bromocriptine, cabergoline, and ergotamine.³

A 78-year-old woman presented to the pulmonary medicine department of our hospital with progressive dyspnea and dry cough. On examination the most notable sign was a reduction in vesicular sounds in the lower third of the left hemithorax, though no adventitious respiratory sounds were noted. Laboratory findings showed a moderately elevated neutrophil count and a raised erythrocyte sedimentation rate (55 mm/h). The patient had been diagnosed with Parkinson disease 15 years previously and had been receiving treatment with cabergoline for 2 months. She was referred to our center for a chest computed tomography (CT) study after clinical examination. CT scans were obtained without intravenous contrast enhancement using a spiral CT scanner and a section thickness of 8 mm. The chest CT scan with mediastinal window settings at the level of the aortic arch revealed a right paratracheal lymph node measuring 2 cm (Figure A). The chest CT scan obtained with pulmonary window settings showed alveolar infiltrates, micronodular ground-glass opacities in the apicoposterior segment of the upper lobe, lingula, and lower lobe of the left lung (Figure B). Pleural effusion was also observed in the left hemithorax (Figure C). The differential diagnosis included infection, malignancy, and drug toxicity. No specific etiology was identified, however, because neither the clinical nor laboratory findings suggested infection or tumor. We therefore considered the possibility of pulmonary drug toxicity. The antiparkinsonian drug cabergoline was stopped, and the patient was monitored without undergoing further treatment. A

CT scan performed at 1-month follow-up showed smaller mediastinal lymph nodes (Figure D) and spontaneous resolution of lung infiltrates and pleural effusion (Figure E and F), confirming our initial suspicion of pulmonary drug toxicity and the association between cabergoline and pulmonary disease.

High-resolution CT of drug-induced lung disease shows histologic findings similar to those seen in other conditions such as infection, pulmonary fibrosis, and disease recurrence.¹ Abnormalities most commonly overlooked on radiography include ground-glass opacities and slight fibrotic changes.¹ Interstitial pneumonitis and fibrosis result in ground-glass opacities, focal areas of consolidation, and irregular linear opacities that tend to involve the lower lung fields. Hypersensitivity reactions can give rise to a pattern that resembles hypersensitivity pneumonitis, with ground-glass opacities and poorly defined centrilobular nodules, and can also result in extensive bilateral air-space consolidation. Bronchiolitis obliterans with organizing pneumonia-like reactions commonly causes peribronchial or subpleural areas of consolidation. Pleural effusions, chronic pneumonitis, and fibrosis may also occur. Diffuse interstitial thickening, nodular areas of subpleural consolidation, and areas of dependent consolidation can also be seen on CT scans.¹

Cabergoline is a widely used, well-tolerated drug to which fibrotic side effects have recently been attributed.⁴ Currently, the main indication for this drug is as a treatment for hyperprolactinemia, although it can also be used to treat motor fluctuations associated with Parkinson disease, where it has proven effective when used as monotherapy in the initial phases.⁵ The most common adverse effects of cabergoline are nausea, vomiting, headache, dizziness, constipation, asthenia, abdominal pain, and vertigo.⁶

The case we report supports prior observations about the onset of pleuropulmonary disease during cabergoline administration. In conclusion, we believe health care professionals should remember that many drugs can cause pleuropulmonary diseases that may be confused with infections or tumors. This diagnosis should be suspected in patients receiving 1 or more drugs known to be potentially damaging to the lung, provided that there is radiologic evidence. The main value of CT is that it shows parenchymal abnormalities in symptomatic patients with normal or equivocal findings on chest radiography.