

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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References

1. Alberg AJ, Forgy JG, Samet JM. Epidemiology of lung cancer. *Chest*. 2007;132:S29-55.

2. Yeh KY, Chang J WC, Hsueh S, Chang TG, Lin MC. Ovarian metastasis originating from bronchioloalveolar carcinoma: a rare presentation of lung cancer. *Jpn J Clin Oncol*. 2003;33:404-7.
3. Fujiwara K, Ohishi Y, Koike H, Sawada S, Moriya T, Kohno I. Clinical implications of metastases to the ovary. *Gynecol Oncol*. 1995;59:124-8.
4. Young RH, Scully RE. Ovarian metastases from cancer of the lung: problems in interpretation – A report of seven cases. *Gynecol Oncol*. 1985;21:337-50.
5. Mazur MT, Hsueh S, Gersell DJ. Metastases to the female genital tract. Analysis of 325 cases. *Cancer*. 1984;53:1978-84.
6. Spector M, Pollak JS. Management of malignant pleural effusions. *Semin Respir Crit Care Med*. 2008;29:405-13.

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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.

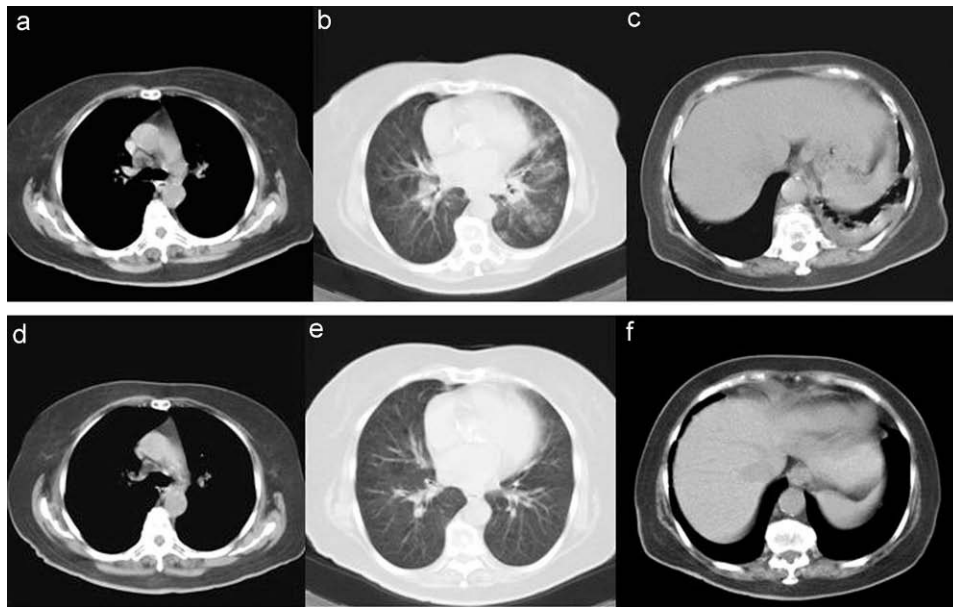


Figure. Pretreatment computed tomography scans of the chest without contrast enhancement. A. Chest CT with mediastinal window settings reveals a right paratracheal lymph node measuring 2 cm at the level of the aortic arch. B. Chest CT with pulmonary window settings shows atypical infiltrates and micronodular ground-glass opacities in the basal segments of the lower lobe and lingula of the left lung. C. Chest CT with mediastinal window settings shows left pleural effusion in the lower segments. After 1 month of follow-up. D. Chest CT scans reveal smaller mediastinal lymph nodes. E. No areas of lung infiltrate are observed. F. Pleural effusion has resolved spontaneously.

References

1. Ellis SJ, Cleverley JR, Müller NL. Drug-induced lung disease, high-resolution CT findings. *AJR Am J Roentgenol.* 2000;175:1019-24.
2. Graham JR, Suby HI, LeCompte PR, Sadowsky NL. Fibrotic disorders associated with methysergide therapy for headache. *N Engl J Med.* 1966;274:359-68.
3. Pfitzenmeyer P, Foucher P, Dennewald G, Chevalon B, Debieuvre D, Bensa P, et al. Pleuropulmonary changes induced by ergoline drugs. *Eur Respir J.* 1996;9:1013-9.
4. Colao A, Lombardi G, Annunziato L. Cabergoline. *Expert Opin Pharmacother.* 2000;1:555-74.
5. Gupta S, Promnitz AD. Pleural effusion and thickening due to cabergoline use in a patient with Parkinson's disease. *Eur J Intern Med.* 2005;16:129-31.

6. Villavicencio C, Ramírez-Sarmiento A, Gayete A, Grau S, Orozco-Levi M. Early pleuropulmonary toxicity associated with cabergoline, an antiparkinsonian drug. *Arch Bronconeumol.* 2007;43:519-22.

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Reduction in tobacco consumption: an emerging topic within the smoking debate

Reducción del consumo de tabaco: una subárea temática emergente dentro del tabaquismo

To the Editor:

Finding articles on the reduction of tobacco consumption (RTC) is normal in the recent literature on smoking, some articles discuss the reduction of damage; others discuss reducing until no longer smoking (RNS), and others discuss epidemiology. Therefore, and as it is an emerging topic in smoking, we want to know exactly which are the topics that the RTC deals with and their repercussions. The Science Citation Index Expanded (SCI-Expanded) was used to carry out a bibliographic search for the 2002-2007 period, using descriptors previously characterised and described.¹ After a manual review of the records by 2 researchers of our group, we found a total of 100 documents, from 272 authors, with a total of 372 signatures and, therefore with an index of signatures per study of 3.72, from a total of 119 different institutions. The average citation per study for the total number of documents was 5.34 (interval: 0-32). From the total number of articles, 53% were about damage reduction, 29% were

about RNS, 14% were about epidemiology and 4% were included in the "others" section. When analysing the average number of citations per study by topic, epidemiology reached 6.57 (interval: 0-30), RNS 6.17 (interval: 0-32) and damage reduction 4.96 (interval: 0-31).

The RTC is a current topic concerning smoking, as it presents, when deeply analysed, two topics that make it very interesting and controversial at the same time. The first concerns if there is a safety threshold in consumption and on the reversibility in the damaging effects of cigarettes, which seems to not exist,² as even with a low rate of consumption of cigarettes per day, damage is produced. The other topic is that there are many smokers that could try to reduce their consumption, without actually wanting to stop smoking, and it has been shown that this would lead to a greater number of people trying to stop smoking as well as an increased abstinence after reduction.³ As we have been able to confirm, these are the topics with the greater number of documents that have been produced, but it is interesting that they are not those that have had the greatest repercussions, therefore, as we have shown, the average of citations per study is greater in studies on epidemiology. Smoking, as we have previously stated, presents a high average repercussion, which could be explained by its multidisciplinary nature, as it is found to be included in all of those scientific areas that have increased its production, visibility and importance. The repercussion of the RTC is