Case Report

Pleural Effusion and Pulmonary Hypertension in a Patient With Parkinson Disease Treated With Cabergoline

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ABSTRACT

Cabergoline is a synthetic dopamine agonist used to treat Parkinson disease. The drug occasionally induces pleuropulmonary adverse effects, which manifest as pleural thickening or effusion, interstitial pneumonitis, pulmonary infiltrates, or fibrosis. We report a rare case of pleural effusion and severe pulmonary hypertension in a 79-year-old man with Parkinson disease who had been treated with cabergoline for 1 year. The symptoms disappeared 10 months after the drug was discontinued.

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Derrame pleural e hipertensión pulmonar en un paciente con enfermedad de Parkinson en tratamiento con cabergolina

RESUMEN

La cabergolina es un fármaco sintético dopaminérgico, que se utiliza en el tratamiento de la enfermedad de Parkinson y que rara vez produce efectos adversos pleuropulmonares, los cuales se manifiestan como engrosamiento o derrame pleurales, neumonitis intersticial, infiltrados pulmonares o fibrosis. Presentamos un caso excepcional en un varón de 79 años con enfermedad de Parkinson, tratado con cabergolina durante un año, que presentó un derrame pleural y grave hipertensión pulmonar, que desaparecieron a los 10 meses de la retirada de este fármaco.

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Introduction

Parkinson disease is an insidious, progressive clinical entity of unknown origin that is characterized by tremor, muscle stiffness, slow movements, and abnormal gait or postural reflexes. It affects 1% to 5% of the population and has an annual incidence of approximately 20 cases per 100,000. The condition is the second most common neurodegenerative disease after Alzheimer disease, and lifelong medical treatment is required. The main drugs used to manage the condition are anticholinergic agents, amantadine, and levodopa or other dopamine agonists (including bromocriptine, pergolide, and cabergoline) used as first-line alternatives with a similar efficacy. The most common adverse effects are vomiting, nausea, and orthostatic hypotension, as well as dyskinesias, insomnia, hallucinations, confusion, and other neurologic disorders. Coronary vasospasm, heart valve involvement, pulmonary fibrosis, and pleural effusion are far more unusual and have never been diagnosed concurrently with
pulmonary hypertension, as occurred in the case we describe below.3,5

Case Description

The patient was a 79-year-old man with no history of substance abuse or allergies who had been previously diagnosed with Parkinson disease. He was receiving oral therapy with levodopa (250 mg/d), methylphenidate hydrochloride (20 mg/d), rasagiline (1 mg/d) and, for the past 12 months, cabergoline (2 mg/d). Thirty days before admission, he presented persistent cold symptoms with cough, sputum production, and progressively increasing dyspnea, but no chest pain, constitutional syndrome, or fever. There was no improvement after treatment with oral levofloxacin; radiographs showed a left pleural effusion with no loss of volume or condensation (Figure 1A). Physical examination ruled out symptoms of heart failure, venous thrombosis, or palpable enlarged lymph nodes. Auscultation of the heart detected a systolic murmur with no third heart sound or rhythm abnormalities; auscultation of the chest revealed symptoms of a left pleural effusion with no rales or signs of bronchospasm.

Discussion

Some of the drugs prescribed most often by neurologists, such as carbamazepine, hydantoin, and antidepressants, can cause...
pulmonary toxicity, particularly in the form of pneumonitis (with or without eosinophilia), noncardiogenic pulmonary edema, or hypersensitivity reactions.\textsuperscript{5,6} This possibility is less common in the ergoline group, which includes bromocriptine and cabergoline.\textsuperscript{7}

Cabergoline is a long-acting synthetic dopamine agonist used to treat Parkinson disease, hyperprolactinemia, and acromegalia; it rarely causes adverse pleuropulmonary effects.\textsuperscript{4,7,8} The pathogenesis of these adverse effects is unclear; they are known to be potentially reversible and to include pleural thickening and effusion, as well as possible interstitial pneumonitis and pulmonary infiltrates and fibrosis.\textsuperscript{9-11} Pleural involvement is more common than parenchymal involvement, and a literature search (MEDLINE, 1966-2007) did not reveal any cases with severe pulmonary hypertension attributable to cabergoline or other dopamine agonists in the same family used to treat Parkinson disease.

Most pleural effusions associated with dopamine antagonists are lymphocytic, and occasionally eosinophilic, exudates.\textsuperscript{12,13} In these patients, the agonist effect on serotonin receptors stimulates fibroblast activity and the subsequent fibrosis of affected organs or tissues, which reverts with discontinuation of the drug.\textsuperscript{12,14} In our patient, the echocardiography results, bilateral pleural involvement, and confirmation of transudate without pleural thickening did not suggest direct pleural involvement or valvular or ischemic heart disease, as reported in other patients.\textsuperscript{9,11} The mechanism by which cabergoline causes pulmonary hypertension is not clear; however, in some patients it is probably a similar mechanism to that of anorexigenic agents, such as fenfluramine, with complex cell biology effects that alter the production, release, and metabolism of serotonin or its metabolites.\textsuperscript{15} The progressive rise in pulmonary pressure increases hydrostatic pressures and reduces the reabsorption of pleural fluid, facilitating its accumulation in the form of transudate, with no direct pleural lesion.\textsuperscript{13,17}

Most of the adverse pleuropulmonary effects of cabergoline have a good prognosis and are reversible once the drug is discontinued, as occurred in our patient, although persistence or progression have been reported in cases with fibrosis.\textsuperscript{7,9,10} This possibility, along with increasing reports of pleuropulmonary adverse effects, makes it necessary to recommend follow-up of these patients, as well as to consider possible alternatives to cabergoline in those at higher risk of developing heart or lung disease.

References