

INVASIVE PULMONARY FILAMENTOUS FUNGAL INFECTION IN A PATIENT RECEIVING INHALED CORTICOSTEROID THERAPY

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We report a case of invasive pulmonary filamentous fungal infection in a patient with chronic obstructive pulmonary disease (COPD) treated with a conventional dose of inhaled fluticasone in the absence of other causes of immunosuppression. A 63-year-old male smoker with COPD, hypertension, coronary artery disease, and normal pressure hydrocephalus treated with a ventriculo-peritoneal shunt, presented with an asymptomatic cavitating mass (3x3.5x4.5 cm) in the right upper lung. A computed tomography (CT) scan 5 months earlier showed a small right upper lobe nodular lesion measuring less than 1 cm in diameter, which was unchanged on the current CT scan. A fine needle aspiration showed non-diagnostic necrotic material. Histopathology of a wedge resection showed extensive necrosis with invasive hyphae morphologically consistent with an *Aspergillus* species. Though this case satisfies the criteria for invasive filamentous fungal infection, an alternative less likely scenario is that the patient had a sterile pulmonary infarction due to thromboembolism followed by secondary fungal infection of the necrotic regions. Therapy with oral itraconazole cyclodextrin formulation 400 mg daily was begun due to concern about residual microfoci of fungal infection. There has been no recurrence of infection since surgery 1 year ago. The patient had no history of unusual or recurrent infections. The patient had been treated with a conventional dose of inhaled Fluticasone (440 mg twice daily) for over 2 years, but had not received systemic corticosteroids during this period. Because of the rarity of invasive filamentous fungal infections in a normal host, we attempted to identify an underlying immune deficiency. Testing for human immunodeficiency virus was negative. The patient had normal circulating leukocytes and differential. The CD4 count (1307cells/ml), CD8 count (1858cells/ml), and NK cell count (349cells/ml) were normal. Lymphocyte proliferative responses to multiple antigens (tetanus, MMR, streptolysin O and *Candida albicans*) were normal. Neutrophil function assays including chemotaxis, NADPH oxidase activity, myeloperoxidase levels, and CD11b were normal. In view of the negative evaluation for a systemic immunodeficiency, we propose that the inhaled fluticasone predisposed to the development of invasive filamentous fungal infection. Invasive pulmonary aspergillosis in patients with COPD treated with systemic corticosteroids is well documented, though uncommon. However inhaled corticosteroids were not previously thought to increase the risk of systemic infections, though local mucosal infections are known. Leav et al. (1) reported a case of invasive pulmonary aspergillosis in a patient with asthma and adrenal insufficiency treated with high-dose inhaled fluticasone (1760mg daily). In contrast, our patient was treated with a standard dose of inhaled fluticasone (440 mg twice daily) commonly used in clinical practice. Given that the high potency inhaled fluorinated corticosteroids such as fluticasone are lipophilic, a slow dissolution/absorption rate from the lung and a greater local tissue dwell time would be expected, and this potential reduction in clearance of the drug may further depress local pulmonary alveolar macrophage and neutrophil function. Our case report and the report by Leav et al. (1) suggest a note of caution in the long term use of highly potent inhaled corticosteroids in patients with COPD vis a vis the risk of opportunistic respiratory fungal infections.