Long-Term Treatment With Azithromycin in a Patient With Idiopathic Bronchiectasis

To the editor:

Patients with bronchiectasis present recurring episodes of obstruction, infection, and inflammation that progressively destroy the lung. Although various studies have demonstrated the efficacy and safety of long-term treatment with azithromycin in cystic fibrosis and diffuse panbronchiolitis, its efficacy in idiopathic bronchiectasis is unknown. The activity of macrolides in cystic fibrosis and diffuse panbronchiolitis can be attributed to the fact that they have an antiinflammatory effect, reduce the virulence of *Pseudomonas aeruginosa*, lower sputum viscosity, and improve mucociliary clearance. We describe the case of a patient with idiopathic bronchiectasis who was successfully treated with oral azithromycin for 2 years.

The patient, a 49-year-old woman, was a nonsmoker and had presented cough with expectoration and progressive dyspnea since childhood, along with frequent episodes of purulent expectoration and fever. There was no family history of congenital respiratory disease. The patient was admitted to hospital in January 1994 with fever and exacerbated cough, expectoration, and dyspnea. Blood and biochemical analyses showed a white cell count of 15 000 cells/µL (88% of which were neutrophils), a hemoglobin concentration of 12.3 g/dL, and a basal glucose concentration of 256 mg/dL. Bilateral basal bronchiectasis was observed in the chest radiograph. Arterial blood gas analysis on admission showed basal values of pH 7.31, PaO_2 38 mm Hg, and $PaCO_2$ of 56.2 mm Hg. Treatment was initiated with antibiotics (initially intravenous and then subsequently oral), oxygen therapy, and bronchodilators. Although respiratory failure persisted, the patient showed clinical improvement at 16 days. On discharge, oxygen, bronchodilators, and inhaled corticosteroids were prescribed, and it was recommended that the patient receive annual vaccination against influenza and treatment with antibiotics during respiratory exacerbations. From 1994 to July 2002, when treatment with azithromycin was initiated, the patient was readmitted to hospital on 14 occasions, each time for infectious exacerbations, accompanied on 3 occasions by life-threatening hemoptysis; in total, 234 days were spent in hospital (26 days per year). During this period, various sweat tests were performed along with analysis of immunoglobulins and α_1-antitrypsin; all results fell within the normal range. Allergic bronchopulmonary aspergillosis and nontuberculous mycobacterial infection were also ruled out. Clinical deterioration was much more pronounced in later years; the patient came to require a course of oral antibiotics each month and presented cor pulmonale, weight loss of 14 kg, and notable worsening of her quality of life. In sputum cultures, only *P aeruginosa* and *Candida albicans* were regularly isolated. Tobramycin aerosol treatment was attempted but had to be withdrawn due to intense bronchospasm. In July 2002—with a forced expiratory volume in the first second of 510 mL (20% of predicted)—, maintenance treatment was initiated with oral azithromycin (500 mg/48 hours). In 2 years of treatment with this drug the patient did not require oral or intravenous antibiotics and only required hospital admission (14 days) on one occasion, thereby reducing the average number of days spent in hospital (26 days per year prior to treatment with azithromycin compared with 7 days per year after initiation of the treatment). The treatment resulted in a weight gain of 14 kg and an improvement in the patient's quality of life. However, no spirometric or blood gas improvements were observed. No side effects of the treatment were observed during this period and the pattern of *P aeruginosa* colonization did not change.

Treatment of bronchiectasis essentially consists of respiratory physiotherapy and administration of antibiotics during exacerbations. Inhaled maintenance antibiotics are normally used in cystic fibrosis patients with *P aeruginosa* colonization.[1,2] The benefit of maintenance treatment with azithromycin and other macrolides containing 14 or 15 carbon atoms has only been described in vivo in cystic fibrosis[3] and diffuse panbronchiolitis. In both diseases, the majority of studies show a reduction in the number of pulmonary exacerbations and a slight improvement in lung function.[4] Only 2 reports have evaluated long-term treatment with macrolides in bronchiectasis not due to either cystic fibrosis or diffuse panbronchiolitis. In one of these, azithromycin reduced the incidence of respiratory exacerbations and lowered the volume of sputum.[5] However, it did not halt functional deterioration. In vitro studies have demonstrated the antiinflammatory activity of macrolides, in particular the reduction of proinflammatory cytokines and the modulation of neutrophil activity.[6] Thus, it has been observed that erythromycin inhibits the synthesis of tumor necrosis factor, while clarithromycin inhibits the production of interleukin 8. Other authors have demonstrated that erythromycin and flurithromycin inhibit the activity of neutrophil elastase and that azithromycin modulates neutrophil function and mediators of inflammation. Despite these in vitro results, the efficacy of azithromycin in reducing the production of proinflammatory cytokines has not been demonstrated in vivo.[4] In the case presented here, *P aeruginosa* was the only bacterium isolated from sputum either before or after treatment with azithromycin. Consequently, it is reasonable to suggest that the marked improvement in the patient was not due to the antibacterial activity of azithromycin against other species, but rather to its effects of reducing inflammation and/or the virulence of *P aeruginosa*. Although many questions about treatment of bronchiectasis with azithromycin remain to be addressed, the excellent response of our patient to this macrolide suggests a role for prolonged treatment with azithromycin in idiopathic bronchiectasis. Nevertheless, more extensive studies are required to evaluate the true effect of azithromycin in this disease.

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1. Máiz L, Baranda F, Coll R, Prados C, Vendrell M, Escribano A, et al. Normativa del diagnóstico y tratamiento de la afección respiratoria en la fibrosis quística. Arch Bronconeumol. 2001;37:316-24.

2. Cantón R, Girón R, Martínez-Martínez L, Oliver A, Solé A, Valdezate S, et al. Patógenos multirresistentes en la fibrosis quística. Arch Bronconeumol. 2002;38: 376-85.
3. Máiz Carro L, Cantón Moreno R. Tratamiento con azitromicina en la fibrosis quística. Med Clin (Barc). 2004;122:311-6.
4. Saiman L, Marshall BC, Mayer-Hamblett N, Burns JL, Quittner AL, Cibene DA, et al. Azithromycin in patients with cystic fibrosis chronically infected with *Pseudomonas aeruginosa*: a randomized controlled trial. JAMA. 2003;290:1749-56.
5. Kasahara K, Maeda K, Mikasa K, Uno K, Takahashi K, Konishi M, et al. Longterm azithromycin therapy for three patients with chronic lower respiratory tract infections. J Infect Chemother. 2004;10:42-4.
6. Nguyen T, Louie SG, Beringer PM, Gill MA. Potential role of macrolide antibiotics in the management of cystic fibrosis lung disease. Curr Opin Pulm Med. 2002;8:521.