Bronchiectasis and Macrolides

To the Editor: We read the article by Máiz-Carro,[1] on long-term treatment with azithromycin in bronchiectasis, with particular interest and consider this relatively unexplored area of drug therapy of potentially great benefit to patients. As additional reflection on the subject, we present the case of a man with bronchiectasis who responded favorably to long-term treatment with macrolides. We also broach other issues for debate, such as use of antipseudomonal antibiotics and macrolides in such cases.[2]

Chronic colonization by *Pseudomonas aeruginosa* is common in panbronchiolitis, cystic fibrosis, and bronchiectases in general. Mucoid *P aeruginosa* produces alginate, which forms a biofilm that inhibits eradication of the microbe in spite of appropriate antibiotic treatment. The film behaves as an antigen, inducing an antigenic-antibody reaction on the surface of the airway, thereby causing an immune response and secondary tissue damage. By acting upon the alginate layer, macrolides enable antibiotic effectiveness.[3,4] Moreover, in vitro studies have shown that the ciprofloxacin—azithromycin combination increases *P aeruginosa* eradication over ciprofloxacin alone. This evidence strengthens the hypothesis that macrolides enhance the antibacterial action of antipseudomonal therapy.[2] Some studies have underscored the anti-inflammatory and immunomodulator effects of 14-to-15-atom macrolides in patients with chronic respiratory diseases.[5] However, there are few studies on the usefulness of inhaled antibiotics and macrolides for bronchiectasis without cystic fibrosis.

Following, we present the case of a patient with chronic obstructive pulmonary disease (COPD) and bronchiectasis who was colonized with *P aeruginosa*. He responded favorably to treatment with a combination of inhaled antibiotics and macrolides.

The patient was a 64-year-old man, an ex-smoker of 40 cigarettes per day until 1997 with no known adverse drug reactions. Fifteen years earlier, clinical and spirometric assessment had led to a diagnosis of COPD and he had been receiving bronchodilator treatment since then. In 2000 he was evaluated for increased cough and expectoration with episodes of hemoptysis. Computed tomography revealed signs of central lobe emphysema, and bronchiectasis in the middle lobe, lingula, and both inferior lobes. Bronchoscopy showed no endobronchial lesions but did show abundant mucopurulent secretions apparently related to inflammation. Cytology of the aspirated bronchial wash fluid was negative for malignant cells and suggested an inflammatory process. Abundant colonies of *P aeruginosa* sensitive to ciprofloxacin, aminoglycosides, colimycin, ceftazidime, piperacillin, and imipenem were isolated in cultures. Analysis of arterial blood gases while the patient was breathing room air indicated a PaO_2 of 50 mm Hg and a $PaCO_2$ of 31 mm Hg; pH was 7.45 and arterial oxygen saturation was 87%. Spirometry showed a severe, mixed, predominantly obstructive pattern: forced vital capacity (FVC) was 2.82 L (59%), forced expiratory volume in 1 second (FEV_1) was 1.52 L (43%), FEV_1/FVC was 54%, and maximal midexpiratory flow rate was 0.73 L/s (24%). Treatment started with a 3-week period of injections of 2 combined antipseudomonal antibiotics. At the fourth week oral antibiotic treatment continued and inhaled β_2-agonists, anticholinergics, and corticosteroids were prescribed. Although the patient's clinical picture improved, his quality of life deteriorated markedly with frequent respiratory reinfections by *P aeruginosa* and frequent hospitalizations. The decision was made to begin continuous treatment with inhaled colimycin and tobramycin, as the isolates were susceptible to both in the antibiograms. Clinical improvement was noted, although purulent sputum and repeated isolation of mucoid *P aeruginosa* persisted and hospitalization for exacerbation was necessary every 2 months. Clarithromycin (500 mg/12 h) was added to the treatment for a year. During this period the patient required no hospitalization and his quality of life improved. At the end of the year the clarithromycin was withdrawn and was only re-administered for 2-week cycles when increased production of purulent sputum was observed. For 2 years after initiating treatment with clarithromycin the patient has required no hospitalization due to recurrence of the respiratory disease and no *P aeruginosa* isolates have been detected in his sputum cultures.

Following our first experience in which a macrolide antibiotic seemed to have acted as a coadjutant to inhaled antipseudomonal drugs, we prescribed similar treatment in other cases using either clarithromycin or azithromycin with good results.

Given the lack of studies on inhaled antibiotic therapy for bronchiectasis without cystic fibrosis and with chronic infection by *P aeruginosa*, and the possible usefulness of macrolide antibiotics owing to their dual antiinflammatory and coadjutant effects in antipseudomonal treatment, we consider that further studies should be carried out to assess the real benefits of such treatment.

M. Vila-Justribo,[a] J. Dorca-Sargatal,[b] and S. Bello-Dronda[c]
[a]Hospital Arnau de Vilanova, Lleida, Spain.
[b]Hospital de Bellvitge, L'Hospitalet del Llobregat, Barcelona, Spain.
[c]Hospital Miguel Servet, Zaragoza, Spain.

1. Máiz Carro L. Tratamiento con azitromicina a largo plazo en un paciente con bronquiectasias idiopáticas. Arch Bronconeumol. 2005;41:295-6.
2. Jaffe A, Bush A. Anti-inflammatory effects of macrolides in lung disease. Pediatr Pulmonol. 2001;31:464-73.
3. Oligaki N. Bacterial biofilm in chronic airway infection. Kasenshogaku Zasshi. 1994;68:138-51.
4. Amsden GW. Anti-inflammatory effects of macrolides—an underappreciated benefit in the treatment of community-acquired respiratory tract infections and chronic inflammatory pulmonary conditions? J Antimicrob Chemother. 2005;55:10-21.
5. Rubin BK, Henke MO. Immunomodulatory activity and effectiveness of macrolides in chronic airway disease. Chest. 2004;125: 70-8.
6. Scheinberg P, Shore E, on behalf of the PC-TNDS-008 Study Group. A pilot study of the safety and efficacy of tobramycin solution for inhalation in patients with severe bronchiectasis. Chest. 2005;127: 1420-6.