A Novel Approach to Extensive Clarithromycin-Resistant Mycobacterium avium Complex Pulmonary Disease

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Introduction

Resectional surgery achieves favorable treatment outcomes for patients with Mycobacterium avium complex pulmonary disease (MAC-PD).1) Patients without sufficient pulmonary reserve for tolerating the complete removal of extensive lesions, however, are not eligible for surgical treatment. A new approach that reduces the lesions sufficiently so that they can be removed by a less extensive resection is needed for these patients. We herein report a case for whom the combination treatment of preoperative intravenous/inhaled amikacin plus bronchial occlusion by Endobronchial Watanabe Spigots (EWSs) allowed preservation of the left upper division. This novel approach might be promising for patients with Mycobacterium avium complex lung disease whose pulmonary reserve will not allow an extensive parenchymal resection.

Keywords: amikacin, bronchial occlusion, clarithromycin-resistant, Endobronchial Watanabe Spigot, Mycobacterium avium complex

Case Report

A 48-year-old woman with extensive clarithromycin-resistant Mycobacterium avium complex pulmonary disease (MAC-PD) was successfully treated by left lower lobectomy and linguectomy following combination treatment of intravenous/inhaled amikacin plus bronchial occlusion by Endobronchial Watanabe Spigots (EWSs). A left pneumonectomy was initially indicated for removing all the lesions, but the procedure would have been barely tolerated by the patient. However, her preoperative combination treatment sufficiently reduced the lesions requiring resection to allow surgical preservation of the left upper division. This novel approach might be promising for patients with Mycobacterium avium complex lung disease whose pulmonary reserve will not allow an extensive parenchymal resection.
Fig. 1  Radiological findings at the time of referral to our institution (A, B), after intravenous/inhaled amikacin (C, D), and just before the surgery (E, F)
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The lesions with sufficient margins. The patient’s body surface area was 1.56 m² and forced expiratory volume in 1 second (FEV₁) was 1840 mL. Quantitative pulmonary perfusion scintigraphy showed a 29% blood flow to the left lung. The predicted postpneumonectomy FEV₁ per body surface area was 837 mL/m², which indicated that the patient could barely tolerate a left pneumonectomy. Her chemotherapy regimen was changed to daily intravenous amikacin (600 mg) plus the following oral antibiotics: ethambutol 500 mg, sitafloxacin 100 mg, and isoniazid 200 mg. Since the lesions did not improve, daily inhaled amikacin (700 mg) was added. Therapeutic drug monitoring showed serum amikacin trough and peak levels of <0.8 µg/mL and 35.8–38.9 µg/mL, respectively. Despite the administration of intravenous and inhaled amikacin, the surrounding consolidation was more extended to the left upper division although the size of cavity was changed little (44 × 43 × 54 mm) (Fig. 1C and 1D). Therefore, we performed a different therapeutic approach. With the patient under general anesthesia, we placed a total of 6 EWSs into the left B4, B5, and B8, which were the main bronchi draining the cavitary lesion (Fig. 2). These treatments were conducted after obtaining the approval of our ethics committee and informed consent from the patient. Following 3 months of hospitalization, the patient continued to receive thrice-weekly intravenous amikacin and oral antibiotics as an outpatient, and the inhaled amikacin was discontinued. The cavitary lesion was reduced to 30 × 34 × 46 mm with its wall becoming thinner, the surrounding consolidation that had spread to the left upper division was disappeared (Fig. 1E and 1F), and her sputum culture became negative. No adverse effects of amikacin were observed. The patient was readmitted to our hospital 5 months after initiation of the combined treatment and underwent combined resection of the left lower lobe and lingula. During her hospitalization, she again received inhaled amikacin. Her postoperative course was uneventful, and the patient was discharged 1 month postoperatively. Thrice-weekly administration of intravenous amikacin was continued for 4 months postoperatively, and the patient has continued on her oral antibiotic regimen. Her postoperative FEV₁ per body surface area at 5 months postoperatively was 1040 mL/m². Her sputum cultures remained negative after the surgery, and oral antibiotics could be discontinued 22 months postoperatively.

Discussion

Clarithromycin-resistant MAC-PD is difficult to treat, and the combination of aminoglycosides and resectional surgery might be the only predictably curative therapy for patients with this treatment-resistant disease. Surgery for our patient was not initially feasible because of her inadequate pulmonary reserve to tolerate pneumonectomy that was needed to remove all the lesions. The lesions targeted for resection required reduction. Especially, the surrounding consolidation spreading to the left upper division should be improved to preserve the left upper division. Since the pathogen was amikacin-sensitive, we introduced intravenous amikacin. Although no reports are available on the combination of intravenous amikacin and inhaled amikacin for nontuberculous mycobacterial PD (NTM-PD), we subsequently added inhaled amikacin to intravenous amikacin to attempt enhancement of the efficacy of treatment. We performed therapeutic drug monitoring of amikacin because the total dose of administered amikacin was high. Optimal serum amikacin levels were maintained, and no adverse effects of amikacin were observed.

Bronchial occlusion of the responsible lesions by EWSs has been used to control hemoptysis in a MAC-PD patient. Therefore, we speculate that occluding the drainage bronchi of the cavitary lesion by EWSs might...
be useful for limiting spillage of infectious material to other lung parenchyma, which could help not only improve the surrounding consolidation but also lead to negative conversion. Achieving a “nadir” in the mycobacterial counts in sputum before surgery is thought to help minimize perioperative complications in mycobacterial surgery. Preoperative microbiological control in sputum is crucial to preventing bronchopleural fistula. Furthermore, bronchial occlusion by EWSs might have some effect on reducing the size of a cavity by limiting air flow to the cavitary lesion. Endobronchial valve (EBV) placement has been reported as a lobar collapse therapy in patients with cavitary tuberculosis or NTM-PD to induce atelectasis and reduce the size of the cavity. An EWS could be less effective in collapsing cavitary lesions than an EBV because an EWS does not have a one-way valve. Nonetheless, a bronchial occlusion due to an EWS might have some effect on reducing the size of a cavity by limiting air flow to the cavitary lesion, which made it easier to divide the intersegmental plane between the left upper division and lingula by staplers.

A possible disadvantage of the combination of bronchial occlusion and inhaled amikacin could be that implanted EWSs inhibit the deposition of inhaled amikacin into peripheral lesions. Low concentrations of amikacin have been observed in lung segments of animal models of confluent and purulent bronchopneumonia treated by inhaled amikacin. The concomitant administration of intravenous amikacin for our patient was intended to overcome this disadvantage. The reduced size of the lesions and the negative conversion of sputum cultures were achieved after this combined treatment, which resulted in preservation of the left upper division during surgery.

**Conclusion**

The combination of intravenous/inhaled amikacin plus bronchial occlusion by EWSs sufficiently reduced clarithromycin-resistant MAC-PD lesions so that they could be removed by a less extensive resection. Our novel treatment approach might be promising for patients with pulmonary reserve insufficient for tolerating extensive parenchymal resection for MAC-PD.

**Disclosure Statement**

The authors declare no relevant conflict of interest.

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