Editorial

Bronchiectasis Management in China, What We Can Learn from European Respiratory Society Guidelines

Ning Wang[1], Jie-Ming Qu[2], Jin-Fu Xu[1]

[1]Department of Respiratory and Critical Care Medicine, Shanghai Pulmonary Hospital, Tongji University School of Medicine, Shanghai 200433, China
[2]Department of Respiratory and Critical Care Medicine, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai 200025, China

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Introduction

Non-cystic fibrosis (CF) bronchiectasis (bronchiectasis) is characterized as permanent airway dilatation, cough, sputum overproduction, and repeat pulmonary infections. It was thought as an orphan disease, and has gained much attention recently. The recent European Respiratory Society (ERS) guidelines for the management of adult bronchiectasis focused on nine key questions,[1] which will shed light on a better management of bronchiectasis. However, despite its fine evidence-based suggestions, there remains some questions when it is being used in China population due to different causes, diseases heterogeneity, geographic distribution, and lacking related studies in China.

The prevalence of bronchiectasis remains unclear. A report from Zhou *et al*.[2] showed that it was about 1.2% in people more than 40 years old in seven cities of China, which may be severely underestimated. The 2012 Expert Consensus is the only version available for diagnosis and treatment of adult bronchiectasis in China, of which, most suggestions are of low quality of evidences. Here, we summarize three utmost questions with considerations of the situation and the challenges faced in Chinese bronchiectasis patients.

Pay More Attention to Identifying of Etiological Causes and Comorbidities

Standardization of diagnostic criteria can help to elucidate the poor understanding of etiology of bronchiectasis. Given the disease complexity, some comorbidities largely affect its prognostics and disease severity; hence, it is also vital to screen on its comorbidities. The ERS guidelines suggest that differential blood count, serum immunoglobulins (total IgG, IgA, and IgM), could be tested for allergic bronchopulmonary aspergillosis in all adults with a new diagnosis of bronchiectasis. Other tests, such as CF, primary ciliary dyskinesia (PCD), and connective tissue disease could be considered in specific circumstances. While to present understanding of China situation on bronchiectasis, CF and PCD are rare in China. The etiology data of bronchiectasis in Guangzhou and Shandong Provinces both showed that idiopathic, postinfectious (including measles, pertussis, tuberculosis, and childhood or adulthood pneumonia), and immunodeficiency constitute major bronchiectasis etiologies.[3,4] Notably, more investigation of bronchiectasis is needed to find out the underlying causes in clinical practice, not just simply labeled as idiopathic bronchiectasis.[5,6] Furthermore, it is worth mentioning that posttuberculosis bronchiectasis takes up a large proportion in our country, which may present poorer lung function, comparing to other varying etiologies. Non-tuberculous mycobacterial lung disease also presents higher percentages than Western countries (nearly 5%); 24 h gastroesophageal pH monitoring would benefit patients with gastroesophageal reflux-related bronchiectasis.[3,7,8] Studies have shown that rheumatoid arthritis, chronic obstructive pulmonary disease, asthma, and chronic rhinosinusitis are associated with bronchiectasis.[9-12] Thus, attention should be paid to these factors to detect bronchiectasis

Address for correspondence: Prof. Jin-Fu Xu,
Department of Respiratory and Critical Care Medicine,
Shanghai Pulmonary Hospital, Tongji University School of Medicine,
Shanghai 200433, China
E-Mail: jfxucn@gmail.com

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in its initial stages and utilize optimization of patient care in China.

Optimize the Eradication Antibiotic Treatment in China is Needed

Infecting organisms may trigger bronchiectasis exacerbations, which has great impact on patients' disease progression.[6] It is well acknowledged that *Pseudomonas aeruginosa* is one of the most common pathogens isolated from the sputum or bronchoalveolar lavage fluid and plays an important role in bronchiectasis.[13] Our study reports that *P. aeruginos*a isolation in patients with non-CF bronchiectasis is a significant prognostic indicator, indicating higher rates of exacerbations.[14] Adults with bronchiectasis with a new isolation of *P. aeruginosa* are suggested to start eradication antibiotic treatment in ERS guidelines. The ERS eradication treatment suggestions presented as follows [Figure 1]. While eradication antibiotic treatment is not suggested to new isolation of pathogens other than *P. aeruginosa*. We agree with the principles of eradication of *P. aeruginosa* in the guidelines; however, more items need to be considered in China. We lack strong evidences for the safety and efficacy of the suggested drugs' doses and durations in China. It is hard to confirm that the therapy course like 3 months is proper or not for Chinese patients due to patients' tolerance and expense issues, regardless of the limitation that inhaled antibiotics have not been approved. Well-designed research is needed to customize proper recommendations for Chinese patients.

Problems Faced in Long-Term Antibiotic Treatment in China

Chronic or recurrent pulmonary infections takes an important part in the vicious cycle in bronchiectasis. Long-term antibiotic treatment is suggested for adults with bronchiectasis who have three or more exacerbations per year (conditional recommendation and moderate quality evidence) in the ERS guidelines. Inhaled antibiotics or oral macrolides as well as other specific optional antibiotics could be chosen considering *P. aeruginosa* infection. We reported that long-term inhaled antibiotic therapy enormously reduced the sputum bacterial density and increased the eradication of sputum *P. aeruginosa* in non-CF bronchiectasis according to systematic reviewing of the published data.[15] The problem is that there has not any access to inhaled antibiotics in China yet. In addition, the recent results of ciprofloxacin dry powder for inhalation (DPI) are out of expectations for some reasons,[16] while the latest trial of DPI of ciprofloxacin nanoplex shows better *ex vivo* mucus permeability and antibacterial efficacy[17] and may act as a promising therapy for bronchiectasis. Whether patients with two exacerbations per year but have severer symptoms or marked clinical deterioration should consider long-term antibiotic therapy or not, is also an issue worth debating. To determine the suited patient population, improvements of the inhaler devices and proper formula (twice or thrice daily vs. once daily) in our country perhaps are the next frontier.[18] Furthermore, to elucidate the question that, when administering oral or inhaled antibiotics,[19] which one is more effective in different patients' population, perhaps more data is needed.

As for the choice of macrolides, macrolides are reported to protect against *P. aeruginosa* infection through inhibition of NLRC4 and NLRP3 inflammasomes, reduce the frequency of exacerbations, and improve the quality of life for its anti-inflammatory, immunomodulatory, and antiviral properties.[20] However, cautions should be given for the associated increase in microbial resistance, bronchospasm as well as risk of cardiovascular death.[21] Thus, while identifying optimal patient population, its pros and cons should be well balanced. Since the relatively higher prevalence of nontuberculosis mycobacteria (NTM) infection in bronchiectasis in China,[7] which is related to worse clinical outcomes and an increased risk of macrolide

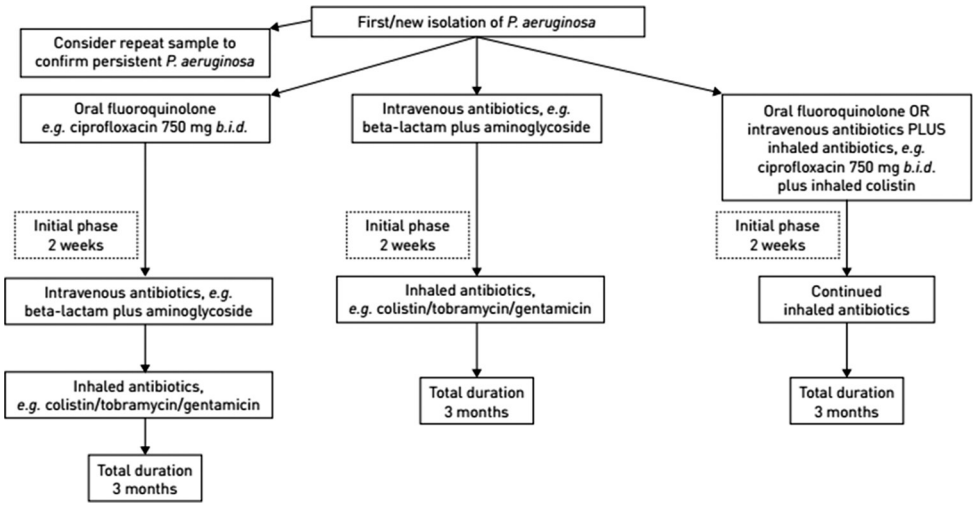

Figure 1: ERS eradication treatment suggestions (Quoted from European Respiratory Society guidelines for the management of adult bronchiectasis). ERS: European Respiratory Society.

resistance, active NTM infection should be cautioned before long-term treatment with macrolides. In conclusion, all therapy should be individualized, according to drug accessibility and patients' affordability, as well as a good response to the microbiological environment.

Prospects

After all, while learning from Western countries' experience, implementation of clinical practice guidelines in China is needed, which requires more data from our own country with regard to our specific national conditions and patients' characteristics. Still, many problems remain unsolved, nationwide epidemiological studies to find out the true burden of the bronchiectasis, further investigation of the underlying causes, stable stage management and health education, clinical significance of traditional Chinese medicine in bronchiectasis, and so on.[5,6,22] Clearly, further research and larger studies are required to set up strong evidence-based comprehensive managements, to break the vicious cycle, reduce exacerbations, alleviate symptoms, improve quality of life, and decrease the risk of future complications.

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