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An analysis of etiology, causal pathogens, imaging patterns, and treatment of Japanese patients with bronchiectasis

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ABSTRACT

Background: Bronchiectasis (BE), a syndrome that presents with persistent or recurrent bronchial sepsis related to irreversibly damaged and dilated bronchi, has not been well-characterized in Asians. This study aims to review the etiology, causal pathogens, imaging patterns, and treatment of BE and to define the prognostic factors for acute exacerbation in a Japanese population.

Methods: We performed a retrospective cohort study of 147 patients (104 women; median age, 73 years; range, 30–95 years) with BE at our institution using high-resolution computed tomography to identify imaging patterns and the area of pulmonary involvement.

Results: Common BE etiologies were idiopathic ($N=50$ [34%]), sinobronchial syndrome ($N=37$ [25%]), non-tuberculous mycobacteriosis (NTM; $N=26$ [18%]), and previous respiratory infection ($N=21$[14%]). *Pseudomonas aeruginosa* was the most common causal pathogen (24%). Common imaging patterns were cylindrical (66%) and mixed including cylindrical pattern (47%). The median number of involved lobes was 2; 49% of the patients had ≥ 3 involved lobes, and 49% had middle lobe and left lingula dominant BE. Patients with predominantly lower lobe BE comprised 4% of the NTM group and 48% of the non-NTM group ($P<0.001$). In multivariate analysis, cystic BE was a predictor for frequent exacerbations in non-NTM patients (OR=7.947; $P=0.004$) which led to increased hospital admissions ($OR=4.691$; $P=0.004$).

Conclusions: Idiopathic and sinobronchial syndrome were common causes of BE. Etiology did not contribute to imaging pattern or predictors of exacerbations. Cystic BE was a predictor for frequent exacerbations in the non-NTM BE patients.

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1. Introduction

Bronchiectasis (BE) is defined as a syndrome that shows symptoms of persistent or recurrent bronchial sepsis related to irreversibly damaged and dilated bronchi, and can be caused by multiple genetic, anatomic, and systemic factors [1–5]. The etiology of BE in adults has been reported in some studies; however, the patient populations were within Europe or the United States [2–6]. McShane et al. recently reported the etiology of BE in a diverse US population [7]; however, their study included only 3 Asian Americans (2.7%), which is an insufficient sample size to characterize the etiologies of BE in the Asian population. The Japanese population shows some characteristic features in BE etiology: cystic fibrosis is very rare [8] and sinobronchial syndromes (SBSs), such as diffuse panbronchiolitis (DPB), are common [9]. However, little is known about the frequencies of the different causes of BE in Japan.

The average frequency of exacerbations in patients who were receiving standard care for their BE is reported to be up to 2 exacerbations per year [6,10]. Hospitalization for an acute exacerbation of BE was associated with significant in-hospital and one-year mortality [11]. Factors associated with more frequent exacerbations include sinusitis, gastroesophageal reflux, low forced expiratory volume in one second, multiple bacteria cultured from the sputum, the presence of *Pseudomonas aeruginosa* and *Staphylococcus aureus* in the sputum culture [11], and primary ciliary dyskinesia, immunodeficiency, and chronic obstructive pulmonary disease as etiologies of BE [6]. However, there is little information about the association between the radiographic type of BE and exacerbations.

We reviewed the records of all the patients diagnosed with BE and currently followed as outpatients at the National Hospital Organization Matsue Medical Center. The aim of the study was to review the etiology, causal pathogens, imaging patterns, and treatment of BE and to elucidate the prognostic factors of acute exacerbation of BE.

2. Patients and methods

A retrospective review of data from patients at the National Hospital Organization Matsue Medical Center from 2008 to 2012 with a diagnosis of BE was carried out. We obtained a nearly full data of patients with BE in our hospital. The Ethics Committee of the hospital approved access to patient records (Approval date: May 30, 2013; Approved #: 53).

2.1. Etiology of BE

SBS was defined as a condition characterized by chronic paranasal sinusitis and simultaneous nonspecific chronic neutrophilic inflammation of the lower airways, presenting with expectoration (e.g., chronic bronchitis, diffuse bronchiectasis, and DPB) [12]. The presence of sinusitis was defined as an abnormal sinus detected by a computed tomography (CT) scan and/or suggestive symptoms such as postnasal drip, chronic (purulent) discharge from the nose, or symptoms of pain or tenderness over one of the sinuses [6]. Post-infectious BE was diagnosed when the patient reported a history of severe infection such as pneumonia, whooping cough, or tuberculosis. Patients with a history of childhood pneumonia, who then experienced a prolonged period without respiratory symptoms, were not classified as having post-infectious BE [4]. BE caused by aspiration of gastrointestinal contents was diagnosed if the patient had repeated aspiration pneumonia followed by the formation of BE, often seen in the lower lungs. BE associated with inflammatory bowel disease was diagnosed when patients presented with ulcerative colitis, Crohn's disease, or celiac disease and also developed BE [4], and patients who had underlying connective tissue diseases (CTDs) without other conditions causing BE were classified as showing CTD-associated BE. Allergic bronchopulmonary aspergillosis was diagnosed on the basis of established criteria [13]. Patients who had been diagnosed with Kartagener syndrome [1] were included in the primary ciliary dyskinesia group. Non-tuberculous mycobacteriosis (NTM) was diagnosed according to the American Thoracic Society criteria [14]. Finally, cases that did not fulfill the definition of SBS or post-infectious BE and showed normal or negative results in investigations into the cause of BE were classified as idiopathic [4].

2.2. Radiology and microbiology

All patients underwent a high-resolution computed tomography (HRCT) scan. HRCTs were performed on either a 4- or 64-channel multidetector CT machine (Aquilion Super 4 or Aquilion CXL Edition; Toshiba Medical Systems, Otawara, Japan). We used HRCT scanning to detect the airway abnormalities of BE, which include bronchi more than 1.5 times as wide as a nearby vessel and a lack of bronchial tapering on sequential slices [15]. We classified BE patterns into 3 types according to the traditional radiographic descriptions: cylindrical, varicose, and cystic [16]. We also counted the number of BE-positive lobes.

All sputum culture results were reviewed, and bacteria found since the diagnosis of BE were registered. All patients had at least two samples of sputum examined, and were considered colonized with a species if it had been cultured on two or more occasions in a 1-year period. Sputum samples were not obtained during acute antimicrobial treatment. When sputum was not spontaneously expectorated, induction was performed using nebulized hypertonic (7%) saline [7]. Sputum samples were sent for bacterial culture and sensitivity testing.

2.3. Acute exacerbation of non-NTM BE

Based on a previous study [10], an exacerbation was defined as including 4 of the following 9 symptoms: change in sputum production; increased dyspnea; increased cough; fever (>38 °C); increased wheezing; malaise, fatigue, lethargy,

Abbreviations: BE, bronchiectasis; CAM, clarithromycin; CTD, connective tissue diseases; DPB, diffuse panbronchiolitis; EM, erythromycin; HRCT, high-resolution computed tomography; NTM, non-tuberculous mycobacteriosis; RXM, roxithromycin; SBS, sinobronchial syndrome