Electromagnetic navigation bronchoscopy for the diagnosis of Aspergillus infection

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Abstract
Electromagnetic navigation bronchoscopy (ENB) is a new diagnostic tool for the evaluation of pulmonary lesions inaccessible by conventional bronchoscopy. Most often, ENB is used for the diagnosis of lung cancer, but can be used to evaluate fungal conditions and other diseases. We present the case of a 44-year-old woman who was diagnosed with Aspergillus via ENB.

Introduction
Chronic necrotising aspergillosis (CNA) is an indolent, cavitary and infectious process of the lung parenchyma secondary to local invasion by Aspergillus species usually Aspergillus fumigatus [1]. CNA usually affects middle-aged and elderly patients with altered local defenses, associated with underlying chronic lung diseases, such as chronic obstructive pulmonary disease, previous pulmonary tuberculosis, pneumoconiosis and cystic fibrosis [1]. Other documented risk factors are those mildly immunocompromised due to diabetes mellitus, chronic liver disease, low-dose corticosteroid therapy and connective tissue diseases, such as rheumatoid arthritis [1]. Patients with CNA may present with fever, chest pain, dyspnea, cough and hemoptysis, but these symptoms are not universal. Diagnosis is based on serology, culture and histology. In this paper, we present a case of pulmonary Aspergillus infection diagnosed by electromagnetic navigation bronchoscopy (ENB) in a patient with chronic obstructive pulmonary disease.

Case Report
A 44-year-old woman was referred with 4 months of productive cough, dyspnea (Medical Research Council Class III), 10 kg weight loss, and diaphoresis. Chest radiograph showed a right upper lobe mass and a chest computed tomography (CT) (Fig. 1A) confirmed a 5 cm × 4 cm mass surrounded by bullous emphysema. Past medical history included chronic obstructive pulmonary disease and hypertension. She had quit smoking 4 years earlier with a 65-pack year exposure. Physical examination revealed 52 kg weight and chest hyperinflation only. Respiratory function tests showed mild airflow obstruction (FEV1 2.27 L, 77% predicted; VC 4.23 L, 111% predicted; FEV1/FVC ratio 54%) and moderate gas transfer impairment (DLCO 14.25 mL min−1 mmHg−1, 54% predicted; KCO 2.36 mL min−1 mmHg−1 L−1, 45% predicted).

Laboratory investigations revealed peripheral blood eosinophilia (20% – 2.84 × 109/L; normal range <5% – <0.60 × 109/L), elevated C-reactive protein (172 mg L−1,
normal range <5 mg L\(^{-1}\)), and erythrocyte sedimentation rate (90 m h\(^{-1}\), normal range <20 mm h\(^{-1}\)). Sputum microscopy and culture were negative for bacteria, acid-fast bacilli, and fungi; cytology was unremarkable. The mass showed mild to moderate fludeoxyglucose avidity on CT positron emission tomography, suspicious of localized malignancy.

CT transthoracic needle aspirate (CT-TTNA) was considered high risk for pneumothorax due to bullous emphysema; initial bronchoscopy using an endobronchial ultrasound radial probe (EBUS-RP) failed to localize the lesion. A second bronchoscopy using electromagnetic navigation (InReach system, superDimension Ltd, Minneapolis, MN, USA) was performed under general anesthesia through a laryngeal mask airway. Navigation was possible within 19 mm of the target center; the procedure was free from complications. Transbronchial biopsies and cytology brush samples were collected; rapid on-site cytological evaluation confirmed diagnostic material. Histological analysis showed fibrinoid necrosis but no evidence of malignancy. Silver stain demonstrated multiple fungal elements with branching septated hyphae (Fig. 1B and C), consistent with *Aspergillus* infection. Serology was also consistent, with two lines positive for *Aspergillus* IgG precipitins.

The patient commenced voriconazole (Pfizer, Sydney, Australia; 400 mg twice daily for 1 day, then 200 mg twice daily for 4 weeks, then 200 mg daily for 2 months). CT imaging 5 months post-bronchoscopy demonstrated a reduction in lesion size to 3.6 cm \(\times\) 2.8 cm, and cavitation (Fig. 1D). Inflammatory markers normalized, exercise tolerance improved, and her weight increased to 56 kg. However, 14 weeks following cessation of voriconazole, her symptoms returned and the radiographic appearances regressed. Repeat ENB confirmed fungal hyphae in bronchial washing samples and no evidence of malignancy on biopsy. Serum and bronchial washing samples had non-significant levels of aspergillus galactomannan antigen (enzyme immunoassay optical density index 0.32 and 0.39, respectively; cut-point for detection \(\geq 0.50\)). The patient recommenced voriconazole.

Figure 1. A 44-year-old woman presenting with weight loss and cough. (A) Chest CT scan at time of presentation. A 5 cm \(\times\) 4 cm mass in the right upper lobe (white arrow) is demonstrated surrounded by severe emphysematous changes. (B) Transbronchial lung biopsy photomicrograph \(\times\)200 magnification – H&E stain demonstrating necrotic debris containing septate (arrows), irregularly branching fungal hyphae. (C) Transbronchial lung biopsy photomicrograph \(\times\)200 magnification – Grocott’s methenamine silver stain demonstrating argentaffin reaction of fungal elements (arrows). (D) Chest CT scan 5 months after diagnosis and following 3 months of voriconazole therapy indicating a reduction in size of the mass and cavitation (arrow).
Discussion

ENB is a new bronchoscopic tool, which combines CT-generated virtual bronchoscopy with electromagnetic tracking to enable passage of a steerable probe beyond the third generation of airways. This allows biopsy of peripheral lesions that are not accessible by conventional bronchoscopy [2, 3]. The system couples a “location board” situated underneath the patient’s chest which emits low-frequency electromagnetic waves, with a “locatable probe” containing sensors that allow precise tracking of position and orientation through the electromagnetic field [2, 3]. The probe’s position is superimposed on a virtual bronchoscopy image allowing precise navigation.

Prior to the advent of ENB, CT-TTNA was the preferred modality for biopsy of peripheral lesions; however, risk of pneumothorax is 15%, with a significant increased risk in patients with emphysema [4]. Although EBUS-RP allows the bronchoscopist to confirm their position within a lesion, it is not steerable; thus, ENB is advantageous as it is steerable and has a reported pneumothorax rate of less than 10% [2, 3]. However, with all emerging technologies, high capital and consumable costs limit availability, and the learning curve is steep. Although a combined approach of EBUS-RP and ENB has yielded significantly better yields than either modality alone, no studies have directly compared ENB to CT-TTNA diagnostic yield for peripheral lung lesions [2, 3].

In summary, this case highlights the utility of ENB as a safe and accurate diagnostic tool in the evaluation of pulmonary lesions that are not easily accessible by conventional techniques, or where the risk of pneumothorax from CT-TTNA is high. To our knowledge, this is the first reported case of Aspergillus infection diagnosed by ENB.

Disclosure Statements

No conflict of interest declared.

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

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