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Opinion/Editorial

The New ACCP Lung Cancer Guidelines (3rd edition): Impact on Interventional Pulmonology/Bronchology

The new American College of Chest Physicians (ACCP) guidelines for the diagnosis and management of lung cancer was recently published in May 2013, which comprehensively addresses screening, diagnostic and treatment for lung cancer. There are several changes that should be noted as Interventional Pulmonologists and bronchoscopists. For invasive staging of the mediastinum, endobronchial ultrasound guided transbronchial needle aspiration (EBUS-TBNA) was first introduced as one of the staging modalities in the 2nd edition in 2007. The minimally invasive endoscopic modalities including EBUS-TBNA, endoscopic ultrasound guided fine needle aspiration (EUS-FNA) or combined EBUS and EUS approach have now been proven to be as effective as surgical staging.

Although invasive staging is not recommended in patients with extensive mediastinal infiltration of tumor and no distant metastases, invasive staging of the mediastinum is recommended over staging by imaging alone in patients with discrete mediastinal lymph node enlargement and or PET positive mediastinal lymph nodes. In these patients, a needle technique (EBUS-TBNA, EUS-FNA or combined EBUS/EUS approach) is now suggested over surgical staging as a best first test for invasive staging. However it should be noted that this recommendation is based on the availability of these technologies and the appropriate experience and skill of the operator. The thoroughness of the staging procedure is probably more important than which test is used. There are limitations in needle biopsies and therefore negative needle results should be confirmed by surgical staging if the clinical suspicion is still high. As a bronchoscopist, we will need to make sure that we can achieve similar high yields as referenced in the guideline. Although EBUS is now available in most major Interventional Pulmonology and Thoracic Surgery centres around the world, it is still not readily available in all centres assessing patients with lung cancer. It may not be considered the "gold standard" until the majority of centres have access to these technologies.

For the first time, CT screening is now recommended for those at high risk for lung cancer. This will possibly result in pulmonologists/thoracic surgeons to be asked to deal with more small indeterminate pulmonary nodules. It will be our responsibility to establish a diagnosis accordingly. The use of the radial probe EBUS is recommended as an adjunct imaging modality to increase the diagnostic yield over conventional bronchoscopy for peripheral nodules. In patients with peripheral lung lesions difficult to reach with conventional bronchoscopy, electromagnetic navigation guidance is recommended if the equipment and the expertise are available. Similar to invasive staging with endoscopic approach, expertise is of importance which raises the challenges of standard training for these procedures.

Finally, we are now in the era of personalized therapy for lung cancer. As a bronchoscopist, we will be asked to provide sufficient tissue for histological differentiation as well as mutation analysis. Obtaining enough tissues for these tests will require expertise in the procedure as well as proper knowledge of handling of specimens. Collaboration with pathologist and cytologists will be mandatory and I cannot stress enough the importance of multidisciplinary approach to management of patients with lung cancer.

Editor in Chief
Kazuhiro Yasufuku

News of Humanitarian Activities

The World Bronchology Foundation (WBF) is the philanthropic arm of the WABIP. The foundation was initiated in 2004 by Dr. Pablo Diaz Jimenez (Barcelona, Spain). Its officers were Pablo Diaz (president), Silvia Quadrelli, Ramon Rami-Porta and Patrick Barron (vice-presidents), Marie-Therese Argemi (secretary-treasurer), and Henri Colt (coordinator of operations). The mission of the foundation is to increase access to instruments and techniques needed to diagnose and treat patients with pulmonary diseases in countries in need.

Since its inception, the WBF has collaborated with organizations such as the Spanish Association for Respiratory Endoscopy, the Argentine Association for Bronchology, the America College of Chest Physicians, and transnational groups of bronchoscopy educators. Project funding has been from grants, individual donations, fund-raising events, and society sponsorships.

Thanks to the Foundation's efforts, and with help from companies providing donations of equipment and instruments, thousands of patients have gained access to procedures such as flexible bronchoscopy, rigid bronchoscopy and mediastinoscopy. With projects in countries such as Mozambique, Mauritania, Argentina, Bolivia, Ecuador and Vietnam, the Foundation helped establish pulmonary procedural services in many government and public hospitals. Equipment donations are always accompanied by week-long, on-site training programs and sustained follow-up in order to assure continuity of care and inclusion of individual physicians in our world community.

A new era is dawning for the Foundation. This year, new officers are being selected, and a search has begun to establish an active advisory council that will build connections with industry and philanthropists to solicit equipment donations. These are the life blood of the foundation's work. If you are interested in joining the advisory council or helping the WBF in other ways, including donating equipment, fundraising, or submitting ideas for projects in countries of need, please write us at : contact@wabip.com.

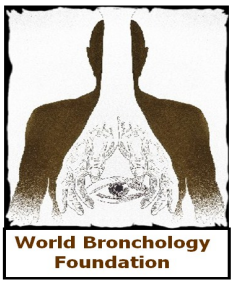


Figure 1: Logo of the World Bronchology Foundation (original sculpture designed by Italian artist Lorenzo Quinn).

Technology Corner

Technology corner: Radial Probe Endobronchial Ultrasound (RP-EBUS)

Introduction: Radial (RP-EBUS) and convex (CP-EBUS) probe endobronchial ultrasound are two commercially available ultrasound-based bronchoscopic imaging modalities. Each has different depth of penetration, image resolution and distinct clinical applications. This section will summarize the physics principles of RP-EBUS and its clinical applications.

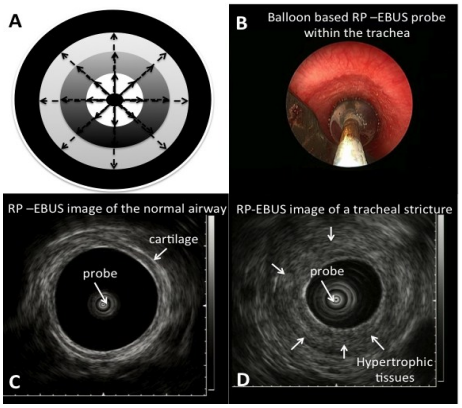
Background: EBUS visualizes structures within and surrounding the tracheobronchial tree using flexible bronchoscopes and probes with built-in specific ultrasound transducers. Transducers serve as source and sensor of the acoustic signal as they convert electrical signals to ultrasound waves, transmit them, capture reflected waves and convert them back into electrical signals. The radial mechanical transducer provides a scanning plane that is perpendicular to the probe (RP-EBUS), thus generating a radial image of the tracheobronchial wall and adjacent structures (Figure 1A). The RP-EBUS probes currently in use are 20 MHz or 30 MHz transducers protected within plastic sheaths. A water-filled balloon is used for certain probes to enhance 360 degree coupling with the airway, improving the transducer-tissue interface, as is the case when RP-EBUS is applied in the large airways (Figure 1B). A miniprobe with 1.7 mm diameter does not have a balloon and is applied in a direct contact mode to visualize peripheral pulmonary lesions (Figure 2C).

RP-EBUS probes do not allow real-time imaging during biopsy. Once the target area is located by RP-EBUS, the probe is removed and replaced with the appropriate biopsy instrument. These probes can be inserted through the working channel of a flexible bronchoscope (2.8 mm) or during rigid bronchoscopy (Figure 1B). Resolution is less than 1 mm and maximum penetration depth approximately 3 cm. Attention to anatomical orientation is necessary because the EBUS image must be rotated to match normal anatomical relationships. Accurate images of airway wall layers require that the probe be kept at the center of the balloon, so that the ultrasound beam will be perpendicular to the airway wall. The 1st layer should appear as a thick hyperechoic layer but the image of the mucosa and submucosa can be occasionally compressed and mixed with a balloon echo. The cartilage layer, however, is always visualized and could be used as a reference to evaluate the rest of the airway wall structure (Figure 1C).

Clinical applications:

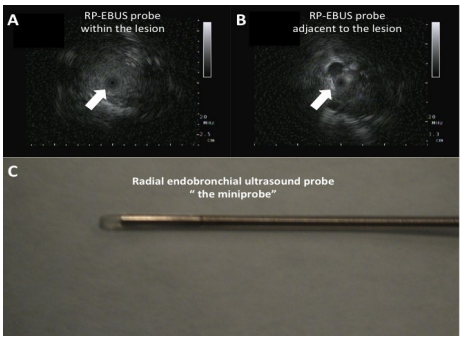
Airway Cancer: RP-EBUS is useful for T- factor staging. Lesions that invade through the cartilage are treated with surgery or external radiotherapy while those that don't, can potentially be treated bronchoscopically using modalities such as photodynamic therapy. The question of whether pure compression (clinical T2a–T3) or invasion (clinical T4) is present, can also be addressed using RP-EBUS. Studies comparing RP-EBUS images with histopathologic findings showed that the penetration depth was the same in 93-98% of cases. RP-EBUS was superior to CT scanning for this purpose.

Benign central airway disorders: RP-EBUS (20 MHz, balloon-based probe) allows evaluation of airway wall structural abnormalities (cartilage edema, fragmentation, hypertrophic tissue) in benign processes including tracheal stenosis (Figure 1D) or tracheomalacia due to relapsing polychondritis, chronic tracheatis, tuberculosis or vascular compression (1). RP-EBUS quantitatively assesses bronchial wall structures in lung transplant recipients.



Asthma: Thickness and wall area of the bronchial wall as measured by RP-EBUS were found to be significantly greater in patients with asthma than in controls; findings which negatively correlated with FEV_1. PC_{20} negatively correlates with thickness of the 2nd layer visualized on RP-EBUS images. These data suggest the potential for using RP-EBUS to assess remodeling and possibly monitor treatment effectiveness in patients with asthma(2).

Peripheral Pulmonary Lesions: RP-EBUS can be used with or without fluoroscopy to visualize a peripheral pulmonary lesion (PPL) and to provide image guidance for transbronchial biopsy (TBB). Diagnostic yield may vary depending on lesion size, location in relation to the probe, air bronchus sign and distance from lesions to the hilum and pleura. While the diagnostic rate of CT-guided biopsy may be higher (especially for lesions < 2 cm in size), cost may be similar to that of RP-EBUS guided TBB, and pneumothorax rate higher, so clinical and radiologic factors must be considered in choosing a specific procedure strategy. Two meta-analyses showed the diagnostic yield of RP-EBUS guided bronchoscopy was 73% and 71%, respectively (3). The RP-EBUS detection yield is usually 10–20% higher than the diagnostic yield after TBB. The use of fluoroscopy, guide sheath and distance measurement were not responsible for differences between detection and diagnostic yield. The feature consistently associated with improved yield was the ability to locate the RP-EBUS probe within the pulmonary lesion, as compared to positioning in a bronchus adjacent to the lesion (Figure 2 A and B). Virtual bronchoscopy navigation systems or electromagnetic navigation (ENB) may further increase yield. In the combined group of one study, after ENB, the ultrasound probe was passed through an extended working channel to visualize the lesion (4). The diagnostic yield of the combined procedure was 88%, greater than RP- EBUS (69%) or ENB alone (59%).



Guidance of Bronchoscopic Interventions: RP-EBUS reveals airway wall structures, vessels and lung parenchyma beyond the tumor surface. RP-EBUS guided therapy in can be used to help adjust stent dimensions, stop tumor debridement when in proximity of vessels, and prompt referral for surgical interventions. During rigid bronchoscopic intervention, RP-EBUS was shown to reveal cartilage disruption and residual hypertrophic tissue, the evidence of which might contribute to stricture recurrence (5). RP- EBUS, with or without ENB, has been used to guide fiducial marker placement for stereotactic radiosurgery.

Conclusions: Balloon-based RP-EBUS is used for detecting intracartilaginous tumor invasion,and to reveal airway wall structure abnormalities and remodeling in malacia, stenosis and asthma. The miniprobe assists in localizing PPL prior to bronchoscopic sampling. RP-EBUS may help guide bronchoscopic interventions, fiducial marker and radiation seed placement.

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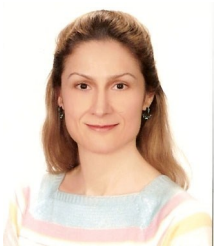
Tips from the Experts

Conventional Transbronchial Needle Aspiration



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Conventional transbronchial needle aspiration (TBNA) has a 64-year history and is considered a *"sine qua non"* of bronchoscopy. Its use, however, has been limited by many factors, some related to acquisition of technical skills (1). This section describes a few tips we have incorporated in our TBNA practice. These are based on our experience and readings of existing literature.

Indications

Diagnostic indications for TBNA are hilar and mediastinal masses or lymphadenopathy, submucosal or peribronchial disease. TBNA can be performed in all peripheral pulmonary lesions with a positive bronchus sign on computed tomography (CT). Image guidance (radial EBUS, fluoroscopy) or navigational bronchoscopy is required for sampling peripheral lesions. Other indications for TBNA are to diagnose hemorrhagic or necrotic endobronchial masses, avoid crush artifacts in biopsies, inject drugs bronchoscopically, and aspirate mediastinal cysts (1-3).

Planning

CT scans should be reviewed to localize the lesion in relation to known reference points such as the main carina, and to identify the needle insertion site accurately. Familiarity with the airway and mediastinal anatomy as well as integration and correlation of radiologic and endoscopic anatomy (spatial orientation) are prerequisites (2, 3).

Sampling

Careful attention should be given to TBNA technique

* The needle should be secured within metal hub during insertion of catheter through scope
* During insertion, the scope should be kept straight and its distal tip should be in neutral position
* After the catheter's metal hub is visible beyond the scope tip, the needle is advanced and locked in place
* The catheter is retracted till only the needle tip is seen to splint the catheter and prevent kinking
* The scope is advanced to the target and the needle is anchored into the intercartilaginous space perpendicularly (at least 45^{o})
* Jabbing, piggyback, cough and/or hub-against-wall techniques are used to facilitate needle insertion
* After insertion, suction is usually applied by an assistant using a 20-30-ml syringe while the bronchoscopist agitates the catheter to and fro, keeping needle within lesion
* The needle is withdrawn smoothly after suction is released while the scope is kept in neutral position

Accurate identification of TBNA site, placing needle at a 45-90^{o} angle to the airway wall, ensuring complete penetration of needle up to the hub, using the scope channel to support the catheter, stopping aspiration before pulling the needle into the airway, proceeding with N3→N2→N1 at staging mediastinal lymph nodes, and working with a trained assistant are important points for increasing diagnostic yield and assuring equipment and operator safety.

The 22-gauge needle is usually sufficient in diagnosis and staging of lung cancer. The 19-gauge needle is recommended particularly for benign diseases and malignancies other than lung cancer. It increases the yield by 14-38% in lung cancer but can be used in all indications if preferred or if TBNA using a 22-gauge needle is non-diagnostic (1, 4).

Specimen acquisition

* Specimens should be smeared on slides and put in 95% alcohol immediately to prevent drying artifacts
* At least 2-3 adequate samples per station should be obtained (2 if 1 is core specimen)
* Smear method should be preferred for cytology
* All flush solution and cell block samples should be analyzed
* Adequate specimen has abundant lymphocytes and no epithelial contamination, or gives specific malignant/benign diagnosis (i.e. granulomas, anthracotic histiocytes) (4).

Rapid on-site evaluation (ROSE) increases sample adequacy and diagnostic yield insignificantly (2.7-18%). Its routine use does not appear to reduce procedure time or sedative use. Furthermore, it brings additional costs and may not be available in all hospitals However, ROSE enables avoidance of additional biopsy without loss in diagnostic yield and reduces the complication rate of bronchoscopy. It is also associated with fewer sites of puncture. Trained interventional pulmonologists or experienced cytotechnologists can perform ROSE to evaluate the adequacy of aspirates when cytopathologist cannot be available in bronchoscopy suite (5).

Diagnostic Efficacy and Quality Control

Efficacy and safety

TBNA has proven efficacy, safety and cost-effectiveness in diagnosing-staging and restaging lung cancer (accuracy: 60-90%, 71%, respectively) but also in diagnosing benign diseases such as tuberculous lymphadenitis (accuracy: 50-85%) and stage I-II sarcoidosis (accuracy: 54-65%). It decreases the rate of mediastinoscopies in lung cancer by 25-35% and thus spares costs. In peripheral pulmonary lesions, its yield is 62-77% and it is solely diagnostic in the lesions with "compressed and "narrowed-thickened" types of bronchus sign (1-3). The sensitivity and accuracy of TBNA depend on severity and prevalence of disease and study methods. It has high specificity with almost no false positives. The complications are usually minimal and related to self-limited bleeding. Damage to the flexible bronchoscope can occur only if TBNA is not performed properly (1, 2, 4).

Conventional TBNA vs image-guidance

For stations 7, 4R and lymph nodes larger than 20 mm, the yield of TBNA equals that of endobronchial ultrasound (EBUS)-guided TBNA. Imaging - usually EBUS and/or endoscopic ultrasound (EUS)- can be used to guide needle aspirations in sampling smaller (<1 cm) and difficult-to-reach or inaccessible mediastinal lymph nodes (e.g. 2R/L, 4L, 8R/L, 9R/L), when respiration-induced nodal mobility and varying distance between carina-nodal position cause procedural difficulty, and after failing conventional TBNA (1, 2).

Controlling and increasing quality

Videos of TBNA procedures can be reviewed after the procedure. There should be good communication with pathologists. Slides should be reviewed with an experienced cytopathologist for specimen adequacy. Hands-on courses, practicing with lung models, simulators and reviewing instruction videos can help improve cognitive and technical skills. Educational interventions for bronchoscopists and technical staff improve TBNA performance and yield progressively (from 21-33% to 48-81% in 36-42 months) (1, 4).

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Education and Training

Tokyo was the site of a recent Faculty Development Program (Train the Trainers) organized by Professor Hideo Saka and endorsed by the Japanese Society for Respiratory Endoscopy. Bronchoscopy educators came from China, Egypt, Japan, Saudi Arabia, Thailand and the United States to work two and half days with checklists, bronchoscopy assessment tools, structured lectures, patient-centered practical approach exercises and "instructor hands-off/learner hands-on" technical skills workshops in a program centered on Fundamentals of Bronchoscopy©. Much was shared and learned by participants who also helped teach a one day Introduction to Flexible Bronchoscopy program for a group of Japanese trainees.

The WABIP gratefully acknowledges Dr. Hideo Saka, the Terumo Corporation, Olympus Japan, and all the international participants for their participation in this educational endeavor! For more information about hosting similar programs, check out the education page on the new WABIP website!

Figure 1: Professor Quangfa Wang (China) using the Bronchoscopy Skills and Tasks Assessment tool (BSTAT) with colleagues during a technical skills workshop in Tokyo, Japan.

Figure 2: Dr Hideo Saka (center) with participants from Japan, Thailand, China, Saudi Arabia, Egypt and the United States in the Faculty Development Program held in Tokyo, Japan.

Research

Bronchoscopic Lung Volume Reduction
A Beacon Of Hope For Severe Emphysema Patients

Several clinical trials for Bronchoscopic Lung Volume Reduction (BLVR) are underway around the world. Some of these modalities are already approved for clinical use in Europe. However in the United States of America, these modalities are still undergoing clinical trials. Some of these modalities show promise in the management of not just heterogeneous but also homogenous emphysema carrying an enormous potential to impact a much larger segment of emphysema population. One such modality is thermal vapor ablation, which induces a controlled inflammatory airway parenchymal response leading to lung volume reduction (1).

Other novel approaches such as coils that contorts the airways to block downstream ventilation (2) and sealants or biological glue that polymerizes and blocks the airways after being injected in a liquid form in the airways (3) work unaffected by the collateral ventilation, which has been a major issue in the past in achieving satisfactory outcomes.

Endobronchial valves that block the airflow to the affected parts of the lungs (4) have been under investigation in the United States for the treatment of emphysema. Food and Drug Administration (FDA) rejected the earlier iteration of similar valves (Emphasys Valves) in the US due to the concerns of increased complications (5). However, they were accepted by the European FDA equivalents and are being currently used in many European countries..

Finally, after decades of limited application of surgical lung volume reduction, due to patient selection with heterogeneous emphysema only and associated morbidity, we are now able to not only offer our emphysema patients with another option, BLVR, but we can personalize it in regards to the presence or absence of heterogeneity, full fissures (6) and collateral ventilation (7). These modalities carry a real potential to substantially benefit millions of patients around the world who may not be candidates for surgical lung volume reduction or lung transplantation. BLVR also offers a bridge to lung transplant in patients with severe emphysema. Surgical lung volume reduction still remains a time tested and effective treatment of heterogeneous emphysema in well-selected patient population.

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WABIP News

ITEM 1: The WABIP welcomes several new member societies representing health care providers from Egypt, Thailand, and The Group of French Speaking Pulmonologists (GELF). Thanks to membership interest and your wonderful response to our request for nominations, we have filled positions for the WABIP *Flag*, *Bylaws*, and *Awards* committees.

ITEM 2: The WABIP is proud to announce that in addition to the well known Killian Centenary Medal, our organization now has two new awards: Please see their descriptions below and at www.wabip.com!

The Gustav Killian Centenary Medal was originally designed in 1997 to celebrate the 100 year anniversary of the first bronchoscopy performed by Gustav Killian, German laryngologist and noted founder of bronchology. The Killian Medal recognizes accomplished senior bronchologists whose career achievements and clinical practices have made a significant impact on the art and science of bronchology. The Killian Medal is awarded only if a nominated candidate is deemed deserving of the medal, in which case the medal is awarded at the biennial World Congress for Bronchology and Interventional Pulmonology (WCBIP).

The WABIP-Dumon Award began as an award of the Japanese Society for Interventional Pulmonology. Since 2007, four individuals have received the award. In 2013, it was adopted by the WABIP and renamed the WABIP-Dumon Award to recognize those individuals who have generously devoted their careers to enhancing others' technical skills in rigid bronchoscopy and improving knowledge and understanding of central airway obstruction. The WABIP-Dumon Award is given at the biennial World Congress for Bronchology and Interventional Pulmonology.

The Heinrich Becker Young Investigator Awards for Research and Clinical Innovation are designed to recognize young researchers and clinicians whose work significantly contributes to bronchology-related patient care, research, or technological innovations. Three equal awards of $1,000 each are given at the biennial World Congress for Bronchology and Interventional Pulmonology. These funds are intended to help offset costs for attending the WCBIP.

ITEM 3: The WABIP continues to grow, venturing even into the darkest corners of the Amazon (see photo below). If you are interested in doing volunteer medical work in the Peruvian Amazon, please write our member services at contact@wabip.com.

Figure Legend: (from left to right): The WABIP flag held by Dr. Pedro Garcia Mantilla (President, Peruvian Association for Bronchology and interventional Pulmonology) and Mr. Hulber Paredes (guide) in a remote village near the confluence of the Amazon and Maranon rivers in Peru.

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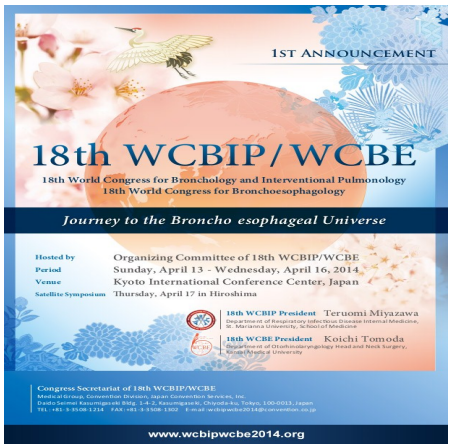

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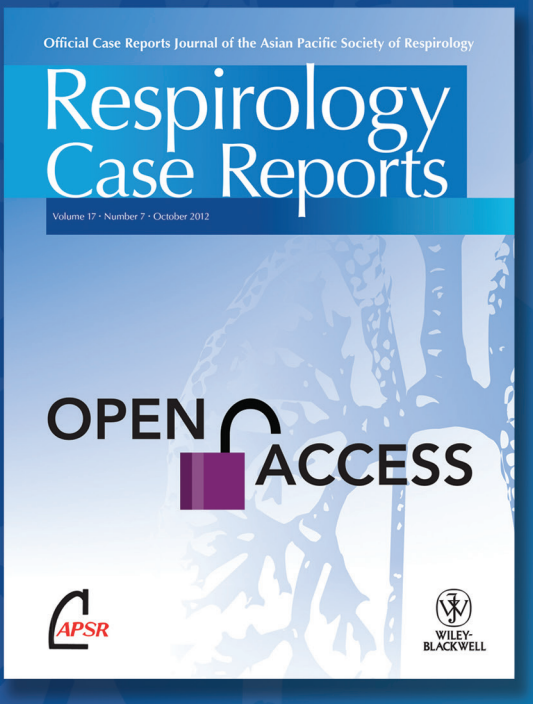

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