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Diagnosis based on electromagnetic navigational bronchoscopy-guided biopsied peripheral lung lesions in a 10-year-old girl: A case report

Meng FZ *et al*. ENB, peripheral lesion, child

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Abstract

BACKGROUND

Electromagnetic navigational bronchoscopy (ENB) is an emerging diagnostic tool that enables practitioners to biopsy peripheral lung tissues that were previously only accessible under computed tomography (CT) guidance. However, few studies have investigated ENB use in children. Here, we report a case of a 10-year-old girl with peripheral lung lesions who complained of a 7-day persistent fever. She was diagnosed with *Streptococcus parasanguinis* infection based on findings obtained using ENB-guided transbronchial lung biopsy (TBLB).

CASE SUMMARY

A 10-year-old girl presented with constitutional symptoms of cough and fever of 7 days' duration. Chest CT scans detected peripheral lung lesions and no endobronchial lesions. TBLB performed under the guidance of an ENB Lungpro navigation system was safe, well-tolerated, and effective for biopsying peripheral lung lesions. Examination of biopsied samples indicated the patient had a pulmonary *Streptococcus parasanguinis* infection, which was treated with antibiotics instead of more invasive treatment interventions. The patient's symptoms resolved after she received a 3-wk

course of oral linezolid. Comparisons of pre-treatment and post-treatment CT scans revealed absorption of some lung lesions within 7 mo of hospital discharge.

CONCLUSION
ENB-guided TBLB biopsying of peripheral lung lesions in this child is a safe, well-tolerated, and effective alternative to conventional interventions.

Key Words: Electromagnetic navigational bronchoscopy; Lungpro; Transbronchial lung biopsy; Child; Diagnosis; Case report

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Core Tip: Electromagnetic navigational bronchoscopy-guided transbronchial lung biopsy is used to diagnose and treat pulmonary disorders in adults worldwide, but very few were reported in children. Moreover, diagnosing patients with peripheral lung lesions is still challenging, due to difficulties related to existing biopsy procedures. Here we present a case study conducted in China that demonstrated that electromagnetic navigational bronchoscopy-guided transbronchial lung biopsy is safe and effective when used to diagnose pediatric patients afflicted with peripheral pulmonary lesion-inducing disorders. Ultimately, clinicians adopting this procedure will be able to diagnose pulmonary disease cases without subjecting patients to invasive and risky surgical interventions.

INTRODUCTION
With the development of auxiliary navigation equipment, such as the Lungpro navigation system, electromagnetic navigational bronchoscopy (ENB) has been increasingly applied in pulmonary clinical practice. Importantly, ENB can be used to

guide transbronchial lung biopsying (TBLB) of peripheral lung tissues that were previously only accessible by computed tomography (CT)-guided conventional bronchoscopy. To perform this function, ENB systems are used to virtually plan the lung bronchoscopic path in advance and to navigationally guide the bronchoscope in real time to ensure accurate localization of the disease focus during the biopsy. Although ENB has been shown to improve success rates of TBLB in adults with pulmonary diseases[1], this technology has been infrequently used to diagnose pediatric pulmonary diseases. In fact, a search of medical literature[2,3] revealed only one report of a Chinese pediatric patient with pulmonary lesions who was successfully diagnosed using ENB-guided TBLB, which permitted physicians to safely obtain biopsied tissues to distinguish between lung infection and lung tumor metastasis when diagnosing the patient[3].Here, we report the clinical application of ENB for diagnosing a second Chinese pediatric patient with pulmonary lesions.

CASE PRESENTATION

Chief complaints

A 7-d history of fever and cough.

History of present illness

A ten-year old girl presented to our hospital with a fever and cough of 7 days' duration. Her temperature peaked at 39.2℃. She had been initially admitted to a local hospital, where she was diagnosed with community-acquired pneumonia and treated with intravenous antibiotics that did not resolve her fever and cough. Due to lingering symptoms, she sought further treatment at our hospital.

History of past illness

Her medical history was unremarkable.

Personal and family history

The patient had no relevant personal or family history.

Physical examination

At admission, the patient's weight was 34.0 kg and her vital signs were as follows: Body temperature, 37.0°C; blood pressure, 90/62 mmHg; heart rate, 130 beats/min; respiratory rate, 20 breaths/min; oxygen saturation, 98% in room air. At the time of admission, moderate and fine moist rales were heard in both lungs with no wheezing observed.

Laboratory examinations

Infection index white blood cell count, 17.52 × 10⁹/L; platelet count, 256 × 10⁹/L; erythrocyte sedimentation rate, 30 mm/h; C-reactive protein, 60.65 mg/L (0.00-5.00 mg/L) (December 16, 2021). Immune function was normal. Liver function: Alanine aminotransferase, 29U/L (0-40U/L); aspartate aminotransferase, 33U/L (0-40U/L). A positive culture result for *Streptococcus parasanguinis*was obtained, with no fungal growth detected.

Imaging examinations

During her first stay at our hospital, the patient underwent electronic lung bronchoscopy, which detected endobronchial inflammation in the left upper lobe proper segment and left lower lobe basal segment (Figure 1A). Results of CT retesting obtained 7 d later (Figure 1B) revealed growing, dense masses within lung tissues, as evidenced by darker shadows on the scan coinciding with the position of the outer basal segment of the lower lobe of the left lung that indicated the presence of multiple cystic translucent lesions. Moreover, various lesions of different sizes, multilocular thin-walled air-filled cavities, and patchy and highly dense shadows were observed that lacked clear boundaries and had approximate dimensions of 72 mm × 60 mm × 42 mm. The child was subsequently discharged with oral amoxicillin clavulanate potassium and advised to undergo an enhanced pulmonary CT scan 2 wk after discharge. The CT

results revealed that the previously noted multiple cystic lesions within the lower left lung lobe and the dense mass within the basal segment outside that lobe remained unchanged in appearance. In contrast, the inflammatory lesions within the middle and lower lobes of the right lung were larger than before (Figure 1C). Due to the fact that the pathological nature of the peripheral lung lesion could not be determined from these findings, the patient underwent a TBLB procedure to ensure that appropriate treatment would be administered to treat the disorder.

The entire procedure was conducted using the following steps. Prior to TBLB, inspiratory and expiratory CT images were uploaded to the Lungpro system (Lungpoint VBN, version 3,4, Broncus Medical Inc, CA, United States), which was used to construct a virtual airway leading to the above-mentioned peripheral lesions. Next, picture archiving and communication system-based integration was conducted to build a virtual three-dimensional image of the patient's lungs. Then, a bronchial centerline was used as a frame of reference to help the bronchoscope operator plan a path to the airway wall puncture point or focus point.

After the patient was prepared for the procedure, she was administered local anesthesia and intravenous midazolam, a mild sedative. Endobronchial occlusion was then performed using a bronchoscope (BF-P260, Olympus Ltd.). The patient was placed in the supine position and was administered oxygen through a nasal catheter. Using a nasal point of entry, the optimal navigational path to pulmonary lesions was selected, and the reconstructed 3D image was superimposed onto the image as viewed under the bronchoscope. During real-time navigation, the position of the bronchoscope and the distance from the pleura and the focus were displayed.

Finally, Lungpro-guided TBLB was performed using a bronchoscope with a working channel diameter of 2.8 mm (Figure 2, Figure 3A). Biopsy samples taken from the posterior basal segment of the left lower lobe were sent to the hospital pathology department for microscopic examination (Figure 3B). The patient experienced no complications after the procedure.

FINAL DIAGNOSIS

Streptococcus parasanguinis infection of the lung.

TREATMENT

During the patient's first stay at our hospital, her fever decreased after intravenous antibiotic therapy (intravenous amoxicillin clavulanate potassium, oral azithromycin) and anti-inflammatory therapy (intravenous methylprednisolone). Results of ENB-guided TBLB performance (which utilized the Lungpro navigation system) indicated lung infection with *Streptococcus parasanguinis*. Based on this finding, the patient was treated with a 3-wk course of oral linezolid.

OUTCOME AND FOLLOW-UP

The patient's symptoms disappeared after a 3-wk oral linezolid treatment, after which the patient's health status was monitored through regular follow-up visits. A second chest CT scan obtained at seven months post-treatment revealed increased transparency of the basal segment of the left lower lobe, multiple lesions of unequal size, and multilocular thin-walled air-filled cavities. A comparison of the first and second chest CT scans suggested that some lesions were absorbed before the 7-mo follow-up visit (Figure 3C).

DISCUSSION

Modern imaging techniques have led to increased detection of peripheral lung lesions, of which the vast majority often require tissue biopsies for diagnosis. Barber *et al*[4] retrospectively analyzed etiologies of 88 pediatric cases with pulmonary nodules. They found that most nodules were caused by infections, while etiologies of the others included autoimmune diseases, hematologic diseases, vasculitis, and Crohn's disease. Nevertheless, diagnosing patients with peripheral lung lesions is still challenging due to difficulties related to existing biopsy procedures. The child described in this case report presented with cough and fever symptoms and rales. Chest high-resolution computed

tomography (HRCT) imaging revealed a dense mass, as evidenced by a dark area on the HRCT scan after the child had received regular antibiotic therapy. However, the lesion was located within the anterior segment of the left lower lobe in an area close to the anterior artery and thus would be inaccessible by conventional electronic bronchoscopy and require CT-guided percutaneous lung puncture treatment. As a major disadvantage, this procedure can lead to severe lung tissue damage, increasing the risk of intraoperative and postoperative bleeding and pneumothorax and leaving local skin wounds. To avoid these issues, we performed ENB-guided TBLB to obtain an accurate diagnosis for our patient.

Several bronchoscopic approaches are currently adopted to biopsy tissues in order to obtain diagnostic tissue samples, with pros and cons associated with each approach. Importantly, Bronchoscopy-guided modalities are increasingly being used to biopsy peripheral lung lesions, due to greater safety and superior diagnostic results obtained using these methods over results obtained using alternative biopsy techniques, such as percutaneous lung puncture, radial endobronchial ultrasound (EBUS), CT-guide flexible bronchoscopy, and combinations of these techniques[5,6]. In fact, a review of papers related to this topic suggests that diagnostic yields of peripheral lung nodule biopsies performed using conventional bronchoscopy range from43% to 65%, while diagnostic yields of procedures used to biopsy smaller peripheral lung lesions are lower, from 14% to 31%[7]. Although bronchoscopy with navigation provides the lowest overall diagnostic yield of the three procedures (70%), this procedure has the best safety profile, as evidenced by its low rate of pneumothorax requiring a chest tube (1%)[8].

CT is currently considered the gold standard imaging technique for guiding bronchoscopic biopsies of pulmonary lesions, due to its effectiveness as a diagnostic tool and ability to target a bronchoscope to a selected cytologic sampling site accurately. Nevertheless, CT-guided transthoracic biopsy has several disadvantages, such as exposure to ionizing radiation, the need to move the patient to a radiology unit, and prolonged execution time. Moreover, this modality requires an accessible path for

biopsy needle insertion and is associated with increased risks of pneumothorax, significant hemorrhaging, and respiratory failure.

Alternatively, radial EBUS is a current method to precisely locate peripheral lung lesions that are not visible by fluoroscopy, while it also provides clues regarding their internal structures. However, the effective use of this method requires careful patient selection, since the ultrasound wave does not easily penetrate aerated pulmonary parenchyma. Therefore, EBUS is used to locate peripheral pulmonary nodules that are not separated by areas of aerated pulmonary parenchyma, which would induce excessive acoustic impedance that would reflect the ultrasound wave. In addition, ultrasound is technically applicable for imaging peripheral pulmonary nodules that adhere to visceral pleura, detecting direct pleural infiltration, and detecting atelectasis involving subpleural lung parenchyma. Nonetheless, EBUS cannot target specific types of peripheral lesions that may be targeted using a navigational system.

TBLB, an important method used to clinically diagnose pulmonary lesion-associated disorders, offers advantages over conventional bronchoscopic biopsy methods that provide low diagnostic yields due to inaccurate targeting of lesions with biopsy forceps[9]. However, during TBLB operation, misalignments (offsets) between actual and virtual bronchoscopic images can occur when the bronchoscope is rotated as it advances to the target site, which can lead to lesion-targeting errors. Furthermore, rapid realignment of the virtual bronchoscopic image to actual bronchial branch points is not easily accomplished after the bronchoscope moves unexpectedly (*e.g.*, when the patient moves or coughs)[10]. To address these issues[10,11], the Lungpro system was recently developed to serve as a virtual navigation device that can display virtual bronchoscopic images adjacent to actual video images (Video 1), thus enabling the operator to overlay an electronic pathway onto the endoscopic image and maintain their alignment in real-time. In practice, the identified lesion shape is initially overlaid onto the airway wall near the target location (as indicated on the aligned actual and virtual bronchoscopic images) to provide further biopsy site localization guidance. Importantly, this method can be applied to quickly and accurately guide the

bronchoscope to the focus without puncturing blood vessels, thus making it possible to more effectively biopsy lung lesions present outside the airway[10,12]. Notably, when this procedure was used to biopsy our patient, no adverse events, such as pneumothorax or hemorrhage, occurred during or after the procedure.

Ultimately, the biopsy results obtained for our pediatric patient suggested that the child's lungs were infected with *S. parasanguinis*, a gram-positive, non-motile, catalase-negative organism belonging to the sanguinis group of viridans streptococci. Although this organism is not viewed as an important human pathogen, it has been isolated from human blood, urine, and throat samples[13], is a primary colonizer of teeth that supports biofilm formation on tooth surfaces[14], and is a common cause of native and prosthetic valve endocarditis. *S. parasanguinis*-induced endocarditis has been shown to begin with bacterial colonization on heart valve surfaces that is followed by biofilm formation that leads to colonization in valves with small surface aggregates of bacteria. These aggregates grow into rounded bacterial colonies that promote the deposition of a layer of fibrin and platelets on their surfaces that ultimately supports biofilm formation. This biofilm then shields the bacteria from antibiotics, thus making their eradication difficult despite the fact that the organisms are sensitive to vancomycin, linezolid, daptomycin, quinupristin–dalfopristin, clindamycin, and levofloxacin[15]. Notably, an analysis of 50 cancer patients with streptococcal infections revealed that 5 patients harbored *S. parasanguinis* with intermediate resistance to penicillin and azithromycin and susceptibility to vancomycin, linezolid, quinupristin–dalfopristin, and ceftriaxone[16]. These results were consistent with *S. parasanguinis* antibiotic responsiveness as observed in the current case study. In our patient, inflammatory lesions increased in size after treatment with amoxicillin clavulanate potassium and subsequently shrank significantly after 3 wk of oral linezolid treatment. Our results thus highlight the bacteriological and therapeutic challenges associated with pneumonia caused by *Streptococcus parasanguinis* infection.

CONCLUSION

Worldwide, ENB-guided TBLB is used to diagnose and treat pulmonary disorders in adults but has been infrequently performed in children as its effectiveness and safety in pediatric patients remains unknown. Meanwhile, ENB technology is expensive, and ENB systems are not available in all countries of regions. Here we present a case study conducted in China that demonstrated that ENB-guided transbronchial lung biopsy is safe and effective when used to diagnose pediatric patients afflicted with peripheral pulmonary lesion-inducing disorders. Ultimately, clinicians adopting this procedure may help diagnose pulmonary disease cases without subjecting patients to invasive and risky surgical interventions.

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