Clinical Case Report

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Combined transbronchoscopic needle aspiration (TBNA) and rapid on-site cytological evaluation (ROSE) for diagnosis of tuberculous mediastinal lymphadenitis

A case report

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Abstract

Introduction: The diagnosis of tuberculous mediastinal lymphadenitis remains a challenge, and the use of transbronchoscopic needle aspiration (TBNA) combined with rapid on-site cytological evaluation (ROSE) is still unclear. A case of tuberculous mediastinal lymphadenitis was illustrated to show the diagnostic value of TBNA and ROSE.

Case presentation: In this case report, we presented a typical case of a 44-year-old male who underwent obvious odynophagia and mild symptom of dyspnea. One isolated mass positioned on posterior mediastinum was examined as positive discovery. Finally, he was diagnosed with tuberculous mediastinal lymphadenitis by using TBNA combined with ROSE and treated with anti-TB.

Conclusions: TBNA is an efficacious and safe approach, which is worth popularizing for the clinical diagnosis of mediastinal masses. Meanwhile, ROSE is useful to reduce the numbers of needle passes during TBNA. We aimed to emphasize 2 key points in this case report. Firstly, a rare symptom of Tuberculosis in adults was supported by the patient. Secondly, TBNA combined with ROSE is useful for the diagnosis of tuberculous mediastinal lymphadenitis.

Abbreviations: ATS = American Thoracic Society, CT = computed tomography, EUBS-TBNA = endobronchial ultrasound-guided transbronchial needle aspirate, IASLC = the International Association for the Study of Lung Cancer, IGRA = interferon-gamma release assay, MRI = magnetic resonance imaging, PET-CT = positron-emission tomography, ROSE = rapid on-site cytological evaluation, SUV = standardized uptake value, TB = tuberculosis, TBNA = transbronchoscopic needle aspiration, TNM = tumor-node-metastasis.

Keywords: mediastinal mass, ROSE, TB, TBNA, tuberculous mediastinal lymphadenitis

1. Introduction

The World Health Assembly officially reported that the incidence of tuberculosis (TB) is still a very serious problem and remains a global healthy crisis affecting on more than 9.0 million people worldwide, and it is the most common and major cause of infectious disease.[1,2] TB is caused by mycobacterium tuberculosis, which affects respiratory system and draining lymph nodes. Moreover, TB also can be observed in extra-pulmonary sites like urinary system or digestive system, about 25% patients of TB cases were diagnosed as extra-pulmonary tuberculosis.[3] Due to the vagueness and complexity of clinical symptoms, extra-pulmonary TB increase the difficulty in clinical diagnosis and therapy.

Tuberculous mediastinal lymphadenitis is one kind of extra-pulmonary TB, which happens rarely in adults. Generally, tuberculous mediastinal lymphadenitis is shown as an isolated and asymptomatic mediastinal mass on chest computed tomography (CT) images and discovered occasionally. Here we described a case of a 44-year-old male who was subsequently diagnosed as tuberculous mediastinal lymphadenitis, and presented the typical characters and preferred diagnose method of this disease.

2. Case presentation

A 44-year-old Asian man had undergone odynophagia and mild symptoms of dyspnea for 1 month without clear inducement. He had no cough, sputum, fever, hemoptysis, drenching night sweats, fatigue, poor appetite or obvious weight loss, with no history of diabetes, hypertension, chronic obstructive pulmonary diseases or coronary heart disease. He had more than 20 year history of tobacco use, about 4 branches per day. On examination, it was found that his blood pressure was 129/74 mm Hg, pulse rates were 82 beats per minute, respiratory rates were 15 breaths per minute, body temperature was 37.1°C, and oxygen saturation was 98% on room air at rest. Comprehensive

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physical examination was unremarkable. Interferon-gamma release assay (IGRA) in serum specimens was positive. It was shown that one isolated mass was positioned on posterior mediastinum in his first chest CT scanning images (Fig. 1A). Contrast-enhanced chest CT subsequently revealed an ill-defined soft tissue with heterogeneous density and enlargement on posterior mediastinum (Fig. 1B). Moreover, the intense accumulation of ^{18}fluorodeoxyglucose was observed in his positron-emission tomography (PET)-CT scanning, which confirmed lesions of malignancy (Fig. 1C).

Due to the difficulty of diagnosis, the specimens of the isolated mass were collected by transbronchoscopic needle aspiration (TBNA) with a 22-gauge needle (Olympus, Olympus Corporation, Japan, Tokyo). Then the specimens were stained with standard hematoxylin-eosin staining for rapid on-site cytological evaluation (ROSE), and caseation was identified by cytological analysis. Therefore, he was consistent with the diagnosis of tuberculous mediastinal lymphadenitis (Fig. 2A–C). After 2 months of anti-TB treatment, his clinical symptoms were remarkably improved. The improvements of chest CT scanning were observed as well (Fig. 2D). The Medical Ethics Committee of Affiliated Hospital of Southwest Medical University approved this clinical experiments and informed consent was obtained from this patient.

3. Discussion

3.1. Mediastinal masses

The incidence rates of mediastinal mass in the anterior mediastinum, middle mediastinum, and posterior mediastinum are 42.86%, 11.43%, and 8.57%, respectively. However,

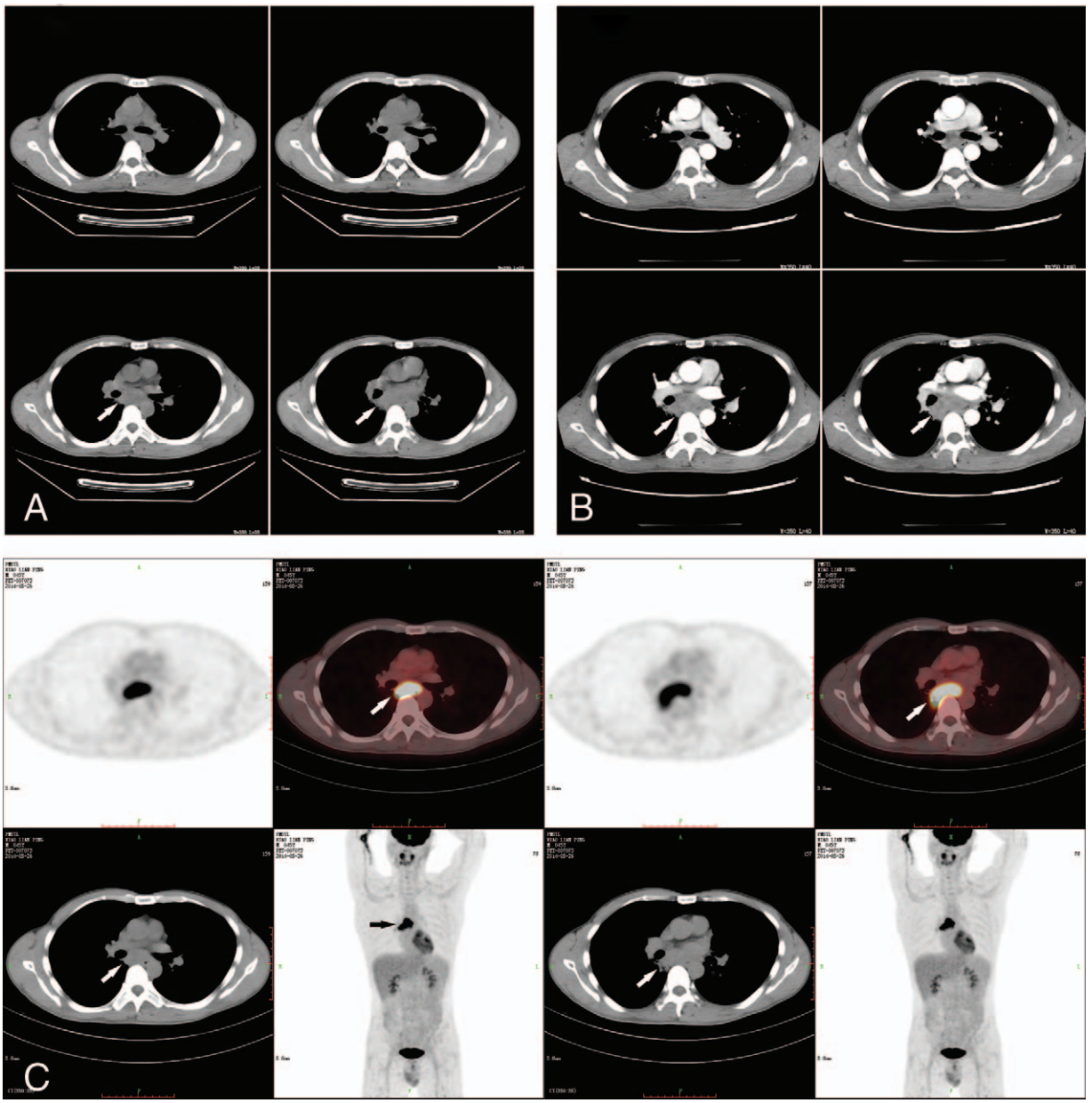

Figure 1. (A, B) Chest CT scan and contrast-enhanced scan showing subcarinal mediastinal masses. (C) PET-CT images showing intense ^{18}fluorodeoxyglucose accumulation in mediastinal masses. White arrows indicate the nidus. CT = computed tomography, PET-CT = positron-emission tomography.

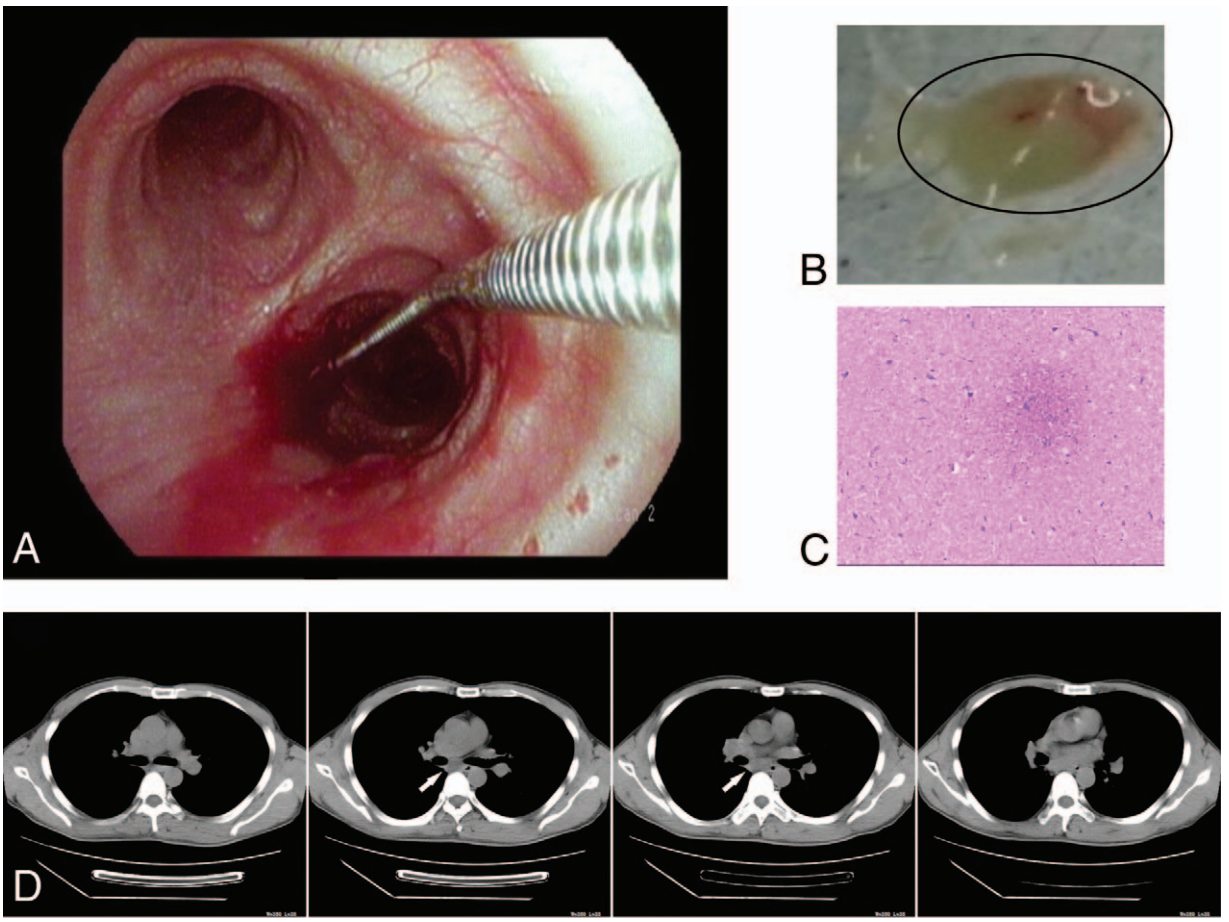

Figure 2. (A) Images of TBNA process. (B, C) Images of specimens collected by TBNA and then treated with ROSE. (D) Chest CT scan images after 2 months of anti-TB therapy. CT = computed tomography, ROSE = rapid on-site cytological evaluation, TB = tuberculosis, TBNA = transbronchoscopic needle aspiration.

37.14% of the incidence rates of mediastinal masses are multiple compartments.[4] Mediastinal mass implies malignant cancer such as lymphoma or metastatic from lung cancer in a large extend. Actually, we were confused with benign and malignant mass at most of the time, which caused heavy diagnose barrier. Compartmental approach has been widely used to indicate the diagnosis of mediastinal masses and the surgical treatment for many years. Around 45.5% of mediastinal masses in the anterior mediastinum, 31.8% in the middle mediastinum, and 22.7% in the posterior mediastinum were indebtified as tumors by using compartmental approach.[5] Generally, the malignant rates of mediastinum mass are 36.4%, that means 63.6% of mediastinum masses are benign disease.[6] However, in Aroor's study, the incidence rates of tuberculous mediastinal lymphadenitis, lymphoma, and bronchogenic carcinoma in mediastinal masses are 18.5%, 44.44%, and 25.93%, respectively.[4]

Because of the highly asymptomatic cases rates, mediastinal mass is discovered incidentally during chest CT examination.[4] The most common symptoms of mediastinal mass are chest pain (20%), fever (13%), cough (10%), and dyspnea (10%), and other rare symptoms include chills, myasthenia gravis, superior vena caval syndrome, weight loss, and hoarseness of voice.[7] Of note is that, under the conception of "B-symptoms," unexplained fevers, drenching night sweats or greater than 10% unintentional weight loss in the first 6 months, combined with the absence of pulmonary nodules or calcification and abnormal uric acid level, are the symbol of mediastinal malignant tumor.[8]

CT, PET-CT and magnetic resonance imaging (MRI) are the common noninvasive approaches to evaluated mediastinal masses, but the radiological features could be under suspicion as lymphoma, distant metastases, neurogenic tumor, cyst or infectious mass which are all included in the differential diagnosis of tuberculous mediastinal lymphadenitis.[9] CT is superior to MRI because CT is more sensitive in both parenchymal disease and mediastinal lymphadenopathy.[9,10] CT scanning characters of tuberculous lesions include moderate intensity, well-defined outlines, and 2–6 mm in size. Moreover, mediastinal masses, which are smaller than 3 cm in diameter and remain unchanged size, are more inclined to benign disease.[11] Evaluation of the standardized uptake value (SUV) of PET-CT is another method to distinguish the quality of mediastinal masses. SUV of benign mediastinal masses is 1.80 ± 1.42, while malignant mediastinal masses is 4.20 ± 3.16.[12] However, SUV has a sizable overlap between benign and malignant lesions. Therefore, differentiation of tuberculous mediastinal lymphadenitis with lymphoma by PET-CT is difficult and inadvisable as well.[3,13]

3.2. Tuberculous mediastinal lymphadenitis

Tuberculous mediastinal lymphadenitis is rare in adults. The incidence rates of tuberculous mediastinal lymphadenitis are 5%

to 17.6% of total TB cases and decreased with the increasing of age.[14,15] Although, it is usually asymptomatic, the symptoms was reported that lymph nodes compresses upon adjacent structures.[4] The sensitivity of CT scanning on tuberculous lymphadenitis is 57% in total. The characteristics of CT scanning image of tuberculous lymphadenitis are: the Hounsfield unit (HU) value is usually >40; under 2 cm in diameter; with nodal calcification; central low attenuation with peripheral rim enhancement.[16,17] Notably, right paratracheal lymph node enlargement is common in tuberculosis.

3.3. Diagnostic value of TBNA and ROSE

Noninvasive approaches combined with invasive approaches are the best way to assess mediastinal masses. Compared with mediastinoscopy lymphonodus biopsy, TBNA, which has been widely accepted in clinical since 1968, is an alternative approach with less invasion. The International Association for the Study of Lung Cancer (IASLC) and Wang's nodal map are 2 well-documented intrathoracic lymph node guidelines for TBNA. IASLC map was revised based on the Naruke map and American Thoracic Society (ATS) map, and defined 14 stations and 5 groups of intrathoracic lymph node. It is more tending for tumor-node-metastasis (TNM) staging system instead of TBNA guiding. Compared with IASLC map, Wang's map is employed to facilitate the localization of biopsy sites for bronchoscopists during TBNA performance.[18] Wang's puncture needles are divided into MW-122, 322, 522, 319, and SW121. Among them, MW-319(dose equate to 19-G) is a dual core biopsy needle, which is used for acquisition of histopathology samples. MW-122, 322, 522 (22-G), and SW121 (21-G) are used for cytology samples acquisition. For malignancy, no difference is found between 21-G and 22-G TBNA needles in the evaluation of diagnostic utility (96.6% vs 95.3%), but 21-G needle is significantly better than 22-G needle on obtaining nonsmall cell lung cancer (88% vs 65%) and analyzing subgroup of benign tissue samples (83% vs. 60%).[19] With the rapid development of puncture needles, specimens by TBNA for comprehensive mRNA and miRNA expression analysis will more true.

Available data showed that the sensitivities and specificities of CT scanning, TBNA and endobronchial ultrasound-guided transbronchial needle aspirate (EBUS-TBNA) are 55% and 51%, 78% and 100%, 89%, and 100%, respectively.[20] Compared with EBUS-TBNA, TBNA has more limitations. TBNA is a blind technique that impacts the accuracy of the result seriously, and the needle of TBNA is hard to control in absence of systemic training.[21] Moreover, the short axis of nodes match to TBNA is >10 mm, which makes it difficult to assess small lymph nodes. While the mean short axis of the lymph node biopsied by EBUS-TBNA is 6.9 ± 2.9 mm.[22] In total, EBUS-TBNA supply clear images of mediastinal anatomy and decreases the number of aspirates required for paratracheal lymph node sampling with increasing safety. TBNA is more suitable for wide spreading in primary hospitals because of the high sensitivity and specificity, simple operation as well as the low cost.

By using ROSE in TBNA, the sample adequacy for subsequent biopsy procedures is ensured. Meanwhile, the sensitivity, specificity, and diagnostic accuracy in the evaluation of mediastinal masses are increased as well. The sensitivity and specificity of ROSE in EBUS-TBNA are 98.4% and 100% respectively, which were verified on histopathological evaluation. By means of ROSE, the sensitivity and accuracy rates are increased to 98.6% and 97.3%, respectively. ROSE also significantly improves the diagnostic yield stratified by pathology, from 81.2% to 90.5%. Notably, the proficiency of the operator, tissue core size (≥2 cm), lymphocyte density (≥40cells/field), and microscopic pigment are significantly associated with the final results.

Here, we introduce 2 ROSE criteria for lymph node sample, Minnesota Criteria, and New York Criteria. Minnesota Criteria specifies a scoring standard to evaluate lymphocyte count in the most cellular area on a slide at ×40 magnification, score>1 (41–200 lymphocytes) is considered adequate.[23] While in New York Criteria, at least 5 low power fields (10×objective, ×100 magnification) on a slide are in needed to assess sample adequacy. When lymphocytes per field are ≥100 and groups of contaminating bronchial epithelial cells per field are <2, the sample is considered adequate.[24] Minnesota Criteria and New York Criteria have similar diagnostic categories. A systematic comparative analysis of these 2 ROSE criteria reported that there were no significant differences between Minnesota Criteria and New York Criteria.[25]

Author contributions

Conceived designed the study: Guo-Ping Li. Performed the operation: Xi Dai, Bin Niu, Xiao-Qiong Yang and Guo-Ping Li. Wrote the paper: Xi Dai and Guo-Ping Li. All authors read and approved the final manuscript.
Conceptualization: Guo-Ping Li.
Data curation: Bin Niu, Xiao-qiong Yang.
Project administration: Guo-Ping Li.
Writing – original draft: Xi Dai.
Writing – review & editing: Xi Dai, Guo-Ping Li.

References

[1] Nnadi CD, Anderson LF, Armstrong LR, et al. Mind the gap: TB trends in the USA and the UK, 2000–2011. Thorax 2016;71:356–63.
[2] Zumla A, George A, Sharma V, et al. The WHO 2014 global tuberculosis report—further to go. Lancet Glob Health 2015;3:e10–2.
[3] Wang Q, Chen E, Cai Y, et al. A case report: systemic lymph node tuberculosis mimicking lymphoma on 18F-FDG PET/CT. Medicine 2016;95:e2912.
[4] Aroor AR, Prakasha SR, Seshadri S, et al. A study of clinical characteristics of mediastinal mass. J Clin Diagn Res 2014;8:77–80.
[5] Thacker PG, Mahani MG, Heider A, et al. Imaging evaluation of mediastinal masses in children and adults: practical diagnostic approach based on a new classification system. J Thorac Imaging 2015;30:247–67.
[6] Davis RDJr, Oldham HNJr, Sabiston DCJr. Primary cysts and neoplasms of the mediastinum: recent changes in clinical presentation, methods of diagnosis, management, and results. Ann Thorac Surg 1987;44:229–37.
[7] Bastos P, Magalhaes A, Fernandes G, et al. Primary cysts and tumors of the mediastinum. Rev Port Pneumol 2007;13:659–73.
[8] Naeem F, Metzger ML, Arnold SR, et al. Distinguishing benign mediastinal masses from malignancy in a histoplasmosis-endemic region. J Pediatr 2015;167:409–15.
[9] Pirina P, Spada V, Santoru L, et al. Chest tuberculosis with mediastinal asymptomatic lymphadenitis without lung involvement in an immuno-competent patient. J Infect Dev Ctries 2013;7:280–5.
[10] Tomiyama N, Honda O, Tsubamoto M, et al. Anterior mediastinal tumors: diagnostic accuracy of CT and MRI. Eur J Radiol 2009;69:280–8.
[11] Henschke CI, Lee IJ, Wu N, et al. CT screening for lung cancer: prevalence and incidence of mediastinal masses. Radiology 2006;239:586–90.
[12] Gupta NC, Graeber GM, Bishop HA. Comparative efficacy of positron emission tomography with fluorodeoxyglucose in evaluation of small (<1 cm), intermediate (1 to 3 cm), and large (>3 cm) lymph node lesions. Chest 2000;117:773–8.
[13] Chen YK, Shen YY, Kao CH. Abnormal FDG PET imaging in tuberculosis appearing like lymphoma. Clin Nucl Med 2004;29:124.

[14] Iyengar KB, Kudru CU, Nagiri SK, et al. Tuberculous mediastinal lymphadenopathy in an adult. BMJ Case Rep 2014;2014: bcr2013200718.
[15] Kim D, Kim J, Lee D, et al. Multidrug-resistant tuberculous mediastinal lymphadenitis, with an esophagomediastinal fistula, mimicking an esophageal submucosal tumor. Clin Endosc 2016;49:564–9.
[16] Moon WK, Im JG, Yeon KM, et al. Mediastinal tuberculous lymphadenitis: CT findings of active and inactive disease. AJR Am J Roentgenol 1998;170:715–8.
[17] Toloza EM, Harpole L, McCrory DC. Noninvasive staging of non-small cell lung cancer: a review of the current evidence. Chest 2003;123:137s–46s.
[18] Xia Y, Ma Y, Arias S, et al. Utilization of the International Association for the Study of Lung Cancer and Wang's nodal map for the identification of mediastinum and hilar lymph nodes. Thorac Cancer 2015;6:464–8.
[19] Jeyabalan A, Shelley-Fraser G, Medford AR. Impact of needle gauge on characterization of endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) histology samples. Respirology (Carlton, Vic) 2014;19:735–9.
[20] VanderLaan PA, Wang HH, Majid A, et al. Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA): an overview and update for the cytopathologist. Cancer Cytopathol 2014;122:561–76.
[21] Xia Y, Wang KP. Transbronchial needle aspiration: where are we now? J Thorac Dis 2013;5:678–82.
[22] Yasufuku K, Pierre A, Darling G, et al. A prospective controlled trial of endobronchial ultrasound-guided transbronchial needle aspiration compared with mediastinoscopy for mediastinal lymph node staging of lung cancer. J Thorac Cardiovasc Surg 2011;142: 1393.e1-1400.e1.
[23] Alsharif M, Andrade RS, Groth SS, et al. Endobronchial ultrasound-guided transbronchial fine-needle aspiration: the University of Minnesota experience, with emphasis on usefulness, adequacy assessment, and diagnostic difficulties. Am J Clin Pathol 2008;130:434–43.
[24] Nayak A, Sugrue C, Koenig S, et al. Endobronchial ultrasound-guided transbronchial needle aspirate (EBUS-TBNA): a proposal for on-site adequacy criteria. Diagnostic Cytopathol 2012;40:128–37.
[25] Jeffus SK, Joiner AK, Siegel ER, et al. Rapid on-site evaluation of EBUS-TBNA specimens of lymph nodes: Comparative analysis and recommendations for standardization. Cancer Cytopathol 2015;123: 362–72.