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Endobronchial Ultrasound: New Insight for the Diagnosis of Sarcoidosis

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Running head: EBUS-TBNA in the diagnosis of Sarcoidosis

Abstract

Study Objective: Diagnosis of sarcoidosis should be substantiated by pathological means in order well to exclude other diseases. The role of real-time endobronchial ultrasound guided transbronchial needle aspiration (EBUS-TBNA) in diagnosis of sarcoidosis has not been reported. The purpose of this study is to evaluate the diagnostic yield of EBUS-TBNA in demonstrating the pathological feature of sarcoidosis.

Materials and methods: Sixty-five patients with suspected sarcoidosis with enlarged hilar or mediastinal lymph nodes on computed tomography were included. Patients with suspected or known malignancy or previously established diagnosis of sarcoidosis were excluded. The convex probe endobronchial ultrasound integrated with a separate working channel was used for EBUS-TBNA. Surgical methods were performed in whom no granulomas were assessed. Patients were followed up clinically.

Results: EBUS-TBNA was performed on a total of 77 lymph node stations in 65 patients from. The final diagnosis of sarcoidosis was given to 61 patients (93.8%). The remaining 4 patients were diagnosed as Wegener's granulomatosis (n=1) or indefinite (n=3). In patients with final diagnosis of

sarcoidosis, EBUS-TBNA demonstrated noncaseating epithelioid cell granulomas in 56 patients (91.8%). No complication was reported.

Conclusion: EBUS-TBNA proved to be a safe procedure with a high yield for the diagnoses of sarcoidosis.

Word count: 196 words

Keywords

Bronchoscopy

Hilar lymphadenopathy

Mediastinum

Sarcoidosis

Transbronchial needle aspiration

Ultrasound

Abbreviations

CP-EBUS: Convex probe endobronchial ultrasonography

CT: computed tomography

EBUS: endobronchial ultrasonography

EBUS-TBNA: real-time endobronchial ultrasound guided transbronchial needle aspiration

EUS: endoscopic ultrasound

EUS-FNA: endoscopic ultrasound with fine needle aspiration

TBLB: Transbronchial lung biopsy

TBNA: transbronchial needle aspiration

US: ultrasonography

VATS: video assisted thoracoscopic surgery

Introduction

Sarcoidosis is a multisystem disorder of unknown etiology characterized by noncaseating epithelioid cell granulomas. Minority of patients may progress to multiorgan failure. About one fourth of patients with chronic sarcoidosis die of respiratory failure. Incidence of sarcoidosis has been increasing possibly explained by greater awareness and recognition [1]. Diagnosis of sarcoidosis can be greatly substantiated by excluding other disease possibilities with compatible clinicoradiological, cytological or histological tissue examinations; especially when treatment with systemic steroids is contemplated. Cutaneous involvement occurs only in about 25% of all patients. Erythema nodosum, the hallmark of acute sarcoidosis, is rare in Japanese [2]. Biopsy of these lesions will not show granulomas [2]. On the contrary, up to 90 percent of patients have radiological evidence of thoracic hilar lymph node enlargement and presented with acute or insidious respiratory symptoms [3]. Transbronchial lung biopsy (TBLB) is the recommended procedure in most cases. The diagnostic yield however depends largely on the experience of the operator and number of biopsies [2]. Furthermore, TBLB is a procedure which has a risk of pneumothorax and haemoptysis [4].

Mediastinoscopy has been the method of choice when TBLB is futile [2, 5]. It is however invasive, carried out under general anesthesia, costly, requires inpatient care and has a complication rate of 2-3% [6]. This realization has led to the quest of a less invasive tool with high diagnostic yield and minimal complication.

We have evaluated the convex probe endobronchial ultrasound (CP-EBUS, XBF-UC260F-OL8, Olympus, Tokyo, Japan). Preliminary study using CP-EBUS has been performed on surgically resected specimens and its feasibility to perform real-time endobronchial ultrasound guided transbronchial needle aspiration (EBUS-TBNA) prior to its clinical use has been determined [7]. EBUS-TBNA was first proved to be useful clinically in evaluation of mediastinal and hilar lymph nodes under local anesthesia and conscious sedation [8]. It also had a significant role in the diagnosis and staging of lung cancer with hilar and mediastinal lymph node involvement [9, 10]. To our knowledge, the role of EBUS-TBNA in the diagnosis of sarcoidosis has not been established. The current trial therefore evaluates the diagnostic yield of EBUS-TBNA in demonstrating the granulomas in patients with sarcoidosis.

Methods

Patients

The study was conducted in both Germany (Thoraxklinik University of Heidelberg and Japan (Chiba University) from June 2003 to October 2005. All patients with clinical and radiological features suggestive of sarcoidosis were considered if computed tomography (CT) revealed hilar or mediastinal lymph node enlargement (short axis >1cm). Patients with suspected or known malignancy or previous established diagnosis of sarcoidosis were excluded. Written informed consent was obtained from all patients recruited in this study which was approved by the respective local ethical committee. All patients were managed as outpatient basis unless for those who were already admitted to the hospital for other reasons. Conventional flexible bronchoscopy (model BF-240 bronchovideoscope; Olympus; Tokyo, Japan) was first performed in a standard fashion followed by EBUS-TBNA using the ultrasound bronchoscope (XBF-UC260F-OL8, Olympus, Tokyo, Japan) in the same bronchoscopy setting. Both bronchoscopic procedures were performed under local anesthesia and conscious sedation with midazolam in both study centers. From our previous study, EBUS-TBNA of mediastinal and hilar lymph nodes has

been shown to be safe and has a good diagnostic yield [8]. The decision on proceeding to transbronchial lung biopsy, which may give rise to pneumothorax or hemorrhage, would be left to the discretion of the operators. Diagnosis of sarcoidosis was made if clinicoradiological findings were supported by pathological tissue demonstrating noncaseating granulomas without necrosis and a result of negative culture obtained from EBUS-TBNA; or other surgical methods such as mediastinoscopy or thoracotomy. Other granulomatous diseases were excluded by reviewing patients' history and microbiological results. Cases would be classified as "indefinite" if no diagnosis could be made. All patients were followed up clinically and radiologically after the procedures for 18 months.

Procedure

The CP-EBUS was integrated with a convex transducer with a frequency of 7.5 MHz at the tip of a flexible bronchoscope. The outer diameter of the insertion tube of the flexible bronchoscope is 6.7 mm, and that of the tip is 6.9 mm. The angle of view is 90°, and the direction of view is 30° forward oblique. This CP-EBUS is a linear curved-array transducer that scans parallel to the

insertion direction of the bronchoscope. Images can be obtained by directly contacting the probe or by attaching an inflated balloon filled with saline to the tip which keeps the probe in contact while sampling the lymph node. The ultrasound image was processed in a dedicated ultrasound scanner (model EU-C2000; Olympus) and was visualized along with the conventional bronchoscopy image on the same monitor simultaneously. This system has an integrated color Doppler mode which allows blood vessels to be identified and inadvertent puncturing avoided. The inner diameter of the working channel is 2.0 mm. A dedicated 22-gauge needle was developed to perform transbronchial needle aspiration. The inner diameter of this needle is nearly equal to that of a conventional 21-gauge needle, which allows the sampling of histological cores in some cases.

Bronchoscopy procedures were performed orally. The station of lymph nodes was identified according to the International Staging System (Mountain classification). The designated lymph node was punctured under direct EBUS guidance. The aspirated material was smeared onto glass slides. Smears were air-dried as well as fixed in 95% alcohol. Dried smears were evaluated by an on-site cytopathologist to ensure cell material obtained was of adequate quality. Adequate cell material was defined as a specific diagnosis such as presence of

noncaseating granulomas without necrosis or the presence of lymphocytes on the specimen. If adequate tissue was not identified by on-site cytology after five passes, the procedure was terminated. Furthermore, Papanicolaou staining and light microscopy was carried out by an independent cytopathologist who was blinded to the details of the cases. Histological specimens obtained were fixed in formalin before being sent to the pathology department. Aspirated material was also sent for microbiological examination including special staining for fungi and acid-fast bacilli as were cultures for tuberculosis (TB) and fungi. All patients underwent a chest radiograph after the procedure to ensure that there was no pneumothorax.

Results

Sixty-five patients (35 men) of mean age 45 years (range 19-81) met the inclusion criteria. Forty two German patients and 23 Japanese patients were included in the study population. Seventy four percent of population had radiological stage I diseases, while the rest had stage II diseases. Among all the lymph nodes with shortest diameter equal to or longer than 1cm detected by CT scan, sixty eight hilar lymph nodes and 134 mediastinal lymph nodes were found which match to the typical description of sarcoidosis with bilateral hilar lymphadenopathy. EBUS was able to detect the enlarged lymph nodes in all recruited patients and EBUS-TBNA (Figure 1) was successfully performed in all the cases. Balloon was used in all cases in order to keep good visualization during the aspiration of lymph nodes. Granulomas or benign lymphoid cells were detected in the aspirated materials in 62 patients. For all the 65 patients with suspected sarcoidosis, final diagnosis of sarcoidosis was made in 61 patients (94%). A total of 77 lymph nodes were recorded and aspirated, thus giving an average of 1.2 lymph nodes sampled per patient. This small number of aspiration can be explained by the virtue ofrapid on-site cytopathologic evaluation (ROSE) - once an adequate sample was obtained, the operator would stop further puncturing other lymph nodes (Table 1). The mean size of

the enlarged lymph nodes as measured by EBUS was 20.5 mm (range 7-37mm) (Table 1). Sixty-seven (87%) enlarged lymph nodes were located in the mediastinal region and the remaining 10 lymph nodes (13%) were located around the hilum or interlobar area. The most common sampled lymph node station was subcarinal, station 7 (29/77, 38%), where the mean size was 22.4mm (range 16-31mm).More than half of the number (45 out of 77, 58%) of the enlarged lymph nodes were found in the subcarinal or the right lower paratracheal area which were located in the close proximity of the carina. The largest lymph node (37mm) was found in the right sided hilar area.

Inadequate specimens were obtained from three patients: one of them had video-assisted thoracoscopic surgery (VATS) done which showed Wegener's granulomatosis; another one had undergone mediastinoscopy which confirmed sarcoidosis; while the last one had no further invasive investigation done as the patient's condition had been improving (Figure 2). Two patients had adequate specimens sampled which showed nonspecific reactive changes only. These three patients with indefinite diagnosis had been followed up for at least 18 months and there was no clinical and radiological deterioration. No patient diagnosed with sarcoidosis in this trial required

amendment of final diagnosis during follow up. Microbiology evaluations for TB or fungal infection were all negative.

Among the patients with final diagnosis of sarcoidosis, EBUS-TBNA was diagnostic in 56 out of 64 patients (87.5%), assuming that the three “indefinite” patients were also sarcoidosis. TBLB was performed in 51 patients (78%) and eleven of them who had negative TBLB results were found positive with EBUS-TBNA; whereas only two patients had positive TBLB results but negative EBUS-TBNA. The remaining five patients were confirmed as having sarcoidosis by mediastinoscopy. There were no complications from pneumothorax, pneumomediastinum or excessive bleeding. Patients were followed up clinically and radiologically over this period.

Discussion

Pathological specimens are crucial in substantiating the diagnosis of sarcoidosis and to exclude other diagnosis such as tuberculosis, Hodgkin's lymphoma and malignancy, particularly when systemic steroids are contemplated [3]. TBLB is the recommended procedure in most cases [2]. However, it is a procedure with suboptimal yield with mean diagnostic rate of 65% (range 40-90%) [11, 12] and also associated with appreciable complication rate - up to 10% and 5.4% of patients had pneumothorax and pulmonary haemorrhage, respectively [4]. Added to this, the realistic diagnostic yield is somewhat lower than reported as the recommended number of biopsy is often not achieved. In the present study, we showed that the diagnostic yield of EBUS-TBNA achieved 87.5% with no complication noted. This figure had already taken into account that the three patients classified as "indefinite diagnosis" turned out to be sarcoidosis ultimately (i.e. false negative). The commonest mode of presentation of sarcoidosis is hilar and mediastinal lymphadenopathy and up to 90% of patients have evidence of hilar node enlargement on chest radiograph [3]. Tissue diagnosis of these areas is therefore reasonable and a likely target to confirm the diagnosis, especially when TBLB rendered 30% of patients with suspected sarcoidosis undiagnosed

[13]. The diagnostic yield of TBLB depends on the skill, number of biopsies taken, and degree of interstitial involvement at the time of biopsy [14, 15, 16]. The optimal results can only be achieved if up to 10 biopsies are taken for stage I disease and 4-5 biopsies are taken for stage II disease [11, 17]. The risk of complication increases, proportionally with the increased number of biopsy needed to be taken.

TBNA was shown to have diagnostic yield from 42% to 76% for sarcoidosis with higher yield in stage I disease [18,19,20]. However, it is performed with “blind” needle aspiration guided by prior CT imaging. TBNA is often underutilized although it is useful in diagnosing and staging of pulmonary malignancy. In United States, only 54% of pulmonologists used TBNA in year 2000 and the low percentage of usage was mainly attributed to the perceived difficulty of this technique [21]. This survey was further highlighted by another trial in which the successful yield of TBNA could only be increased from 21.4% to 47.6% after 3-year period of training [22]. On the contrary, accuracy of EBUS-TBNA in staging of mediastinum in lung cancer could be as high as 89% in doing the first 20 cases [23]. Information of TBNA in the setting of sarcoidosis is not even mentioned as a diagnostic tool in ATS statement on the disease [2].

Mediastinoscopy has a high diagnostic rate and therefore has been the procedure of choice when TBLB is futile [2, 5]. Nonetheless it is not without limitations; not all intrathoracic lymph nodes (e.g.peri-hilar lymph nodes which are the typical features of stage I and II sarcoidosis) are accessible. In the present study, the largest enlarged lymph node with mean 29mm (range 19-37mm) was located in the hilar region (Table 1) which may provide a better target for needle puncture and subsequent lower risk of complication. Although only 10 of 77 lymph nodes (13%) were located extra-mediastinally, in the absence of EBUS-TBNA, at least some of these patients might require surgical exploration. Furthermore, if repeated procedure is required, it is almost impossible to perform the procedure for the same patient again. Generally, sarcoidosis has a particular proclivity for adults under the age of 40 [3] and mediastinoscopy inevitably leaves scars over the neck in these young people.

The recent advancement of endoscopic sampling of mediastinal lymph nodes using EBUS-TBNA and EUS-FNA has been further developed for the diagnosis and staging of lung cancer or mediastinal lymphadenopathy [13, 23]. With a higher diagnostic yield and minimal complication, it has been used in diagnosis of mediastinal lymphadenopathy in benign disease. Recent trials of

EUS-FNA in sarcoidosis had a diagnostic value of 82% [13], sensitivity of 89-100% and specificity of 94-96% [24, 25]. Lymphadenopathies in sarcoidosis are typically hilar and involvement of right paratracheal and aortic-pulmonic window lymph nodes is common (70–76%) [26]. EBUS-TBNA is able to sample stations where it may be difficult to be reached by mediastinoscopy, such as hilar nodes and posterior carinal nodes. On the other hand, it has been shown that the right sided paratracheal and hilar lymph nodes (2R, 4R and 10R) are better reached by the transbronchial approach i.e. EBUS, than for the transesophageal approach i.e. EUS, which could be explained by the fact that the esophagus is commonly located more to the left of the trachea [27]. The preference of sampling the right sided paratracheal station more than the left sided station has been gauged from the experience of mediastinal lung cancer staging in which the left paratracheal approach is known to be associated with the worst yields and the major complications [28, 29]. Usually, EUS-FNA is incapable of reaching lymph nodes located in the anterior mediastinum and the rest of the thorax beyond the mediastinum. Previous report has shown that it was difficulty to assess the fibrotic lymph nodes in stage II disease by using EUS-FNA approach [13]. However, this problem was not encountered in the present study.

One further advantage of EBUS-TBNA over EUS-FNA lies in the fact that EBUS-TBNA can be performed with conventional bronchoscopy with BAL +/- TBLB so that peripheral parenchymal lesions, endobronchial and mediastinal lesions can be assessed at the same bronchoscopy setting without the need for further referral and hence saving time and cost.

Limitations of this study follow the inherent nature of sarcoidosis. The high pretest probability of the disease in the current study population (94%) could therefore led to bias to this high diagnostic yield. The diagnosis of sarcoidosis could be difficult and considerably relies on other examinations to exclude other diseases. Tuberculosis is an epidemic disease in Japan whereas the spontaneous remission course of sarcoidosis poses further confusion as patient may “response” to empirical anti-tuberculosis treatment and so the diagnosis of sarcoidosis may be compounded. As this study was originally designed to evaluate patients with hilar and/or mediastinal lymph nodes enlargement, the results obtained here cannot be applied directly to stage III or IV sarcoidosis.

It is envisaged that this accurate, steerable yet safe technique may be able to serve as an indispensable diagnostic tool in patients suspected of sarcoidosis and obviates the need for invasive procedures with obvious cost-effectiveness implications

References:

1. Perng RP, Chen JH, Tsai TT, Hsieh WC. Sarcoidosis among Chinese in Taiwan. J *Formos Med Assoc*. 1997; 96: 697-9.

2. Statement on sarcoidosis. Joint Statement of the American Thoracic Society (ATS), the European Respiratory Society (ERS) and the World Association of Sarcoidosis and Other Granulomatous Disorders (WASOG) adopted by the ATS Board of Directors and by the ERS Executive Committee, February 1999. *Am J Respir Crit Care Med*. 1999; 160: 736-55. Review.

3. Newman LS, Rose CS, Maier LA. Sarcoidosis. *N Engl J Med* 1997; 336: 1224–34.

4. McDougall JC, Cortese DA. Bronchoscopic lung biopsy.*In*: Prakash UBS, ed. Bronchoscopy. New York, Raven Press, 1994; pp. 141–6.

5. Gossot D, Toledo L, Fritsch S, Celerier M. Mediastinoscopy vs thoracoscopy for mediastinal biopsy. Results of a prospective nonrandomized study. *Chest* 1996; 110: 1328–31.

6. Hammoud ZT, Anderson RC, Meyers BF,Guthrie TJ, Roper CL, Cooper JD, Patterson GA. The current role of mediastinoscopy in the evaluation of thoracic disease. *J Thorac Cardiovasc Surg* 1999; 118: 894–9.

7. Yasufuku K, Chhajed PN, Sekine Y, Nakajima T, Chiyo M, Iyoda A, Yoshida S, Otsuji M, Shibuya K, Iizasa T, Saitoh Y, Fujisawa T. Endobronchial ultrasound using a new convex probe: a preliminary study on surgically resected specimens. *Oncol Rep*. 2004; 11: 293-6.

8. Yasufuku K, Chiyo M, Sekine Y, Chhajed PN, Shibuya K, Iizasa T, Fujisawa T. Real-time endobronchial ultrasound-guided transbronchial needle aspiration of mediastinal and hilar lymph nodes. *Chest*. 2004; 126: 122-8.

9. Yasufuku K, Chiyo M, Koh E, Moriya Y, Iyoda A, Sekine Y, Shibuya K, Iizasa T, Fujisawa T. Endobronchial ultrasound guided transbronchial needle aspiration for staging of lung cancer. *Lung Cancer*. 2005; 50: 347-54.

10. Rintoul RC, Skwarski KM, Murchison JT, Hill A, Walker WS, Penman ID. Endoscopic and endobronchial ultrasound real-time fine-needle aspiration for staging of the mediastinum in lung cancer. *Chest*. 2004; 126: 2020-2.

11. Gilman MJ, Wang KP. Transbronchial lung biopsy in sarcoidosis. An approach to determine the optimal number of biopsies. *Am Rev Respir Dis* 1980; 122: 721–4.

12. Koonitz CH, Joyner LR, Nelson RA. Transbronchial lung biopsy via the fiberoptic bronchoscope in sarcoidosis. *Ann Intern Med* 1976; 85: 64–6.

13. Annema JT, Veselic M, Rabe KF. Endoscopic ultrasound-guided fine-needle aspiration for the diagnosis of sarcoidosis. *Eur Respir J*. 2005 ; 25: 405-9.

14. Seaton A, Seaton D, Leitch AG. *In*: Crofton and Douglas's Respiratory Diseases. 4th Edn. Oxford, Blackwell Scientific Publications, 1989; pp. 630–59.

15. Pauli G, Pelletier A, Bohner C, Roeslin N, Warter A, Roegel E. Transbronchial needle aspiration in the diagnosis of sarcoidosis. *Chest* 1984; 85: 482–4.

16. Morales CF, Patefield AJ, Strollo PJ Jr, Schenk DA. Flexible transbronchial needle aspiration in the diagnosis of sarcoidosis. *Chest* 1994; 106: 709–11.

17. Roethe RA, Fuller PB, Byrd RB, Hafermann DR. Transbronchoscopic lung biopsy in sarcoidosis. Optimal number and sites for diagnosis. *Chest* 1980; 77: 400–2.

18. Bilaceroglu S, Perim K, Gunel O, Cagirici U, Buyuksirin M. Combining transbronchial aspiration with endobronchial and transbronchial biopsy in sarcoidosis. *Monaldi Arch Chest Dis*. 1999 Jun;54(3):217-23.

19. Trisolini R, Agli LL, Cancellieri A, Poletti V, Tinelli C, Baruzzi G, Patelli M. The value of flexible transbronchial needle aspiration in the diagnosis of stage I sarcoidosis. *Chest* 2003; 124: 2126-30.

20. Cetinkaya E, Yildiz P, Altin S, Yilmaz V. Diagnostic value of transbronchial needle aspiration by Wang 22-gauge cytology needle in intrathoracic lymphadenopathy. *Chest*. 2004 Feb;125(2):527-31.

21. Colt HG, Prakash UBS, Offord KP. Bronchoscopy in North America: survey by the American Association for Bronchology,1999. *J Bronchol* 2000; 7: 8–25.

22. Haponik EF, Cappellari JO, Chin R, Adair NE, Lykens M, Alford PT, Bowton DL. Education and experience improve transbronchial needle aspiration performance. *Am J Respir Crit Care Med* 1995; 151:1998–2002.

23. Rintoul RC, Skwarski KM, Murchison JT, Wallace WA, Walker WS, Penman ID. Endobronchial and endoscopic ultrasound-guided real-time fine-needle aspiration for mediastinal staging. *Eur Respir J*. 2005; 25: 416-21.

24. Wildi SM, Judson MA, Fraig M, Fickling WE, Schmulewitz N, Varadarajulu S, Roberts SS, Prasad P, Hawes RH, Wallace MB, Hoffman BJ. Is endosonography guided fine needle aspiration (EUS-FNA) for sarcoidosis as good as we think? *Thorax.* 2004 ; 59: 794-9.

25. Fritscher-Ravens A, Sriram PV, Topalidis T, Hauber HP, Meyer A, Soehendra N, Pforte A. Diagnosing sarcoidosis using endosonography-guided fine-needle aspiration. *Chest*. 2000; 118: 928-35.

26. Bein ME, Putman CE, McLoud TC, Mink JH. A reevaluation of intrathoracic lymphadenopathy sarcoidosis. *AJR* 1978; 131: 409–13.

27. Herth FJ, Lunn W, Eberhardt R, Becker HD, Ernst A. Transbronchial versus transesophageal ultrasound-guided aspiration of enlarged mediastinal lymph nodes. *Am J Respir Crit Care Med*. 2005 15; 171: 1164-7.

28. Agli LL, Trisolini R, Burzi M, Patelli M. Mediastinal hematoma following transbronchial needle aspiration. *Chest*. 2002; 122: 1106–7.

29. Kucera RF, Wolfe GK, Perry ME. Hemomediastinum after transbronchial needle aspiration [letter]. *Chest*. 1986; 90: 466.

Table 1: Lymph node characteristics as sampled by endobronchial ultrasound guided transbronchial needle aspiration.

Lymph node Station	Size/mm	(mean, range)	Number
2R	20.5	(11-34)	11
2L	16.1	(11-21)	7
4R	15.8	(07-26)	16
4L	20.3	(17-26)	4
7	22.4	(16-34)	29
10R	29	(19-37)	2
10L	19.7	(16-23)	3
11R	13	(09-18)	4
11L	19	(19)	1
Regional Mediastinum			67
Hilar or lobar			10
Total	20.5	(07-37)	77

Figure legends

Figure 1. Chest CT scan (*top left, A*) showing enlargement of lymph nodes over right lower paratracheal and subaortic lymph nodes. EBUS scan (*top right, B*) showing the endobronchial ultrasound image of the right lower paratracheal lymph node sitting on top of the superior vena cava which was confirmed by color Doppler. EBUS scan (*lower right, C*) of the same view of B, showing the real-time endobronchial ultrasound guided TBNA and the needle within the lymph node. Histological specimen (*Lower left, D*) demonstrating a noncaseating granuloma without necrosis.

Figure 2. Patients suspected with sarcoidosis undergoing diagnostic algorithm Numbers refer to the number of patients. EBUS-TBNA: real-time endobronchial ultrasound guided transbronchial needle aspiration. VATS: Video assisted thoracoscopic surgery. Indefinite: Patients have been followed up and no specific diagnosis was made.

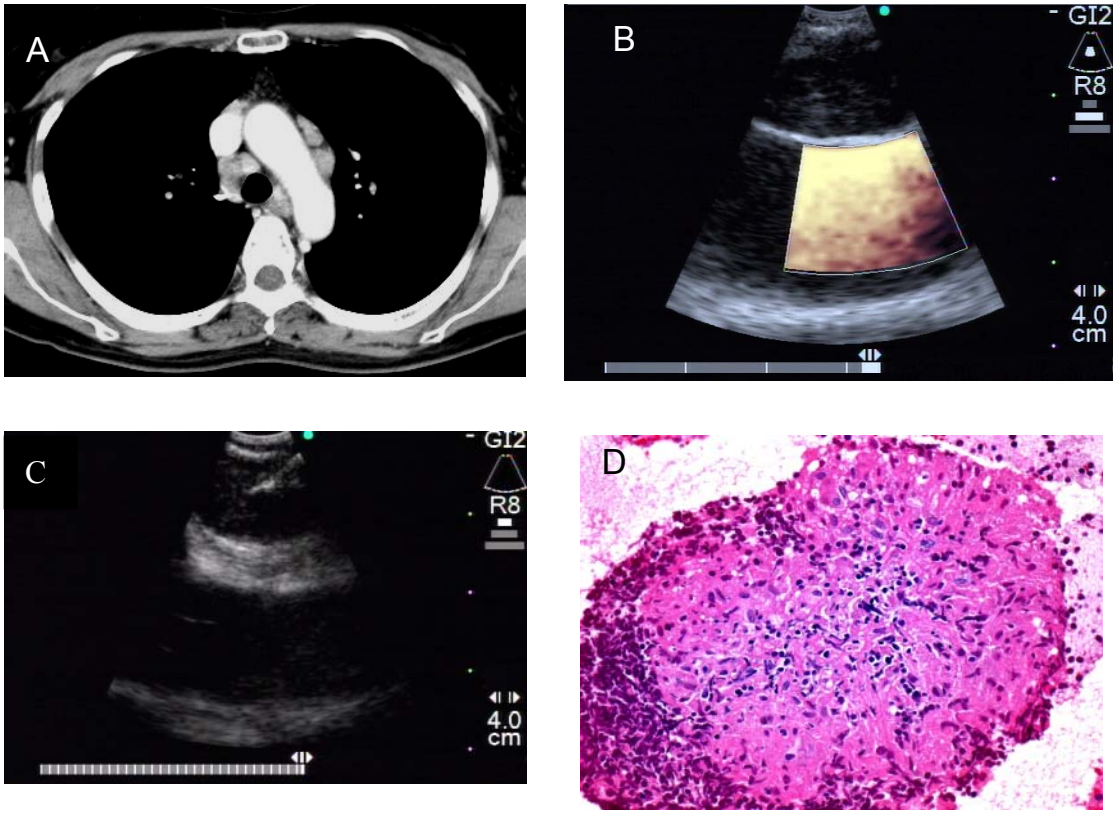
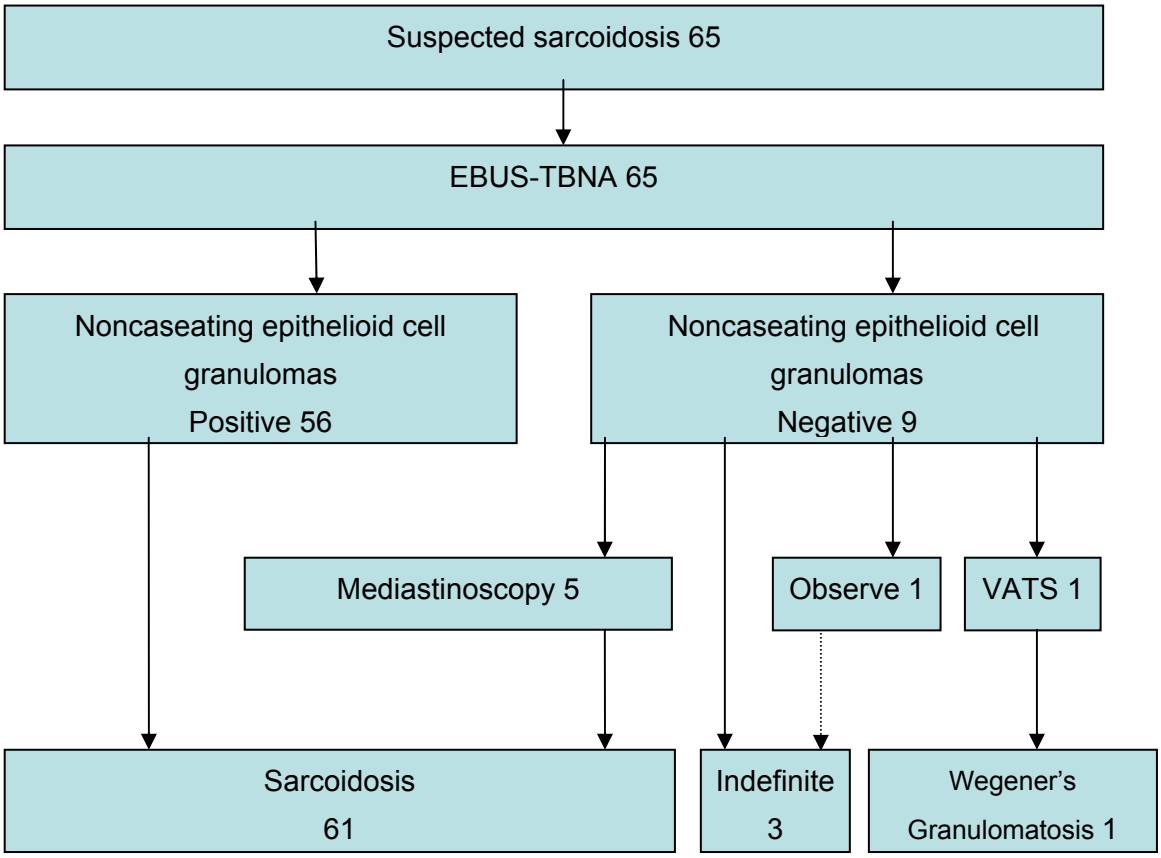


Figure 1: Chest CT scan (*top left, A*) showing enlargement of lymph nodes over right lower paratracheal and subaortic lymph nodes. EBUS scans (*top right, B*) showing the sonographic feature of the right lower paratracheal lymph node sitting on top of superior vena cava which was confirmed by colour Doppler signal. EBUS scan (*lower right, C*) of the same view of B, showing the real-time CP-EBUS-guided TBNA and the needle was seen within the lymph node. Histological specimen (*Lower left, D*) as obtained by CP-EBUS guided TBNA demonstrating a noncaseating granuloma without necrosis, as seen in sarcoidosis.



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Numbers refer to the number of patients. EBUS-TBNA: Real-time endobronchial ultrasound guided transbronchial needle aspiration. VATS: Video assisted thoracoscopic surgery. Indefinite: Patients have been followed up and no specific diagnosis was made finally.