

Bronchoscopic diagnosis of sarcoidosis

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Bronchoscopic diagnosis of sarcoidosis. C. Leonard, V.J. Tormey, C. O'Keane, C.M. Burke. ©ERS Journals Ltd 1997.

ABSTRACT: Transbronchial lung biopsy (TBLB), transbronchial needle aspiration (TBNA) of mediastinal lymph nodes and bronchoalveolar lavage (BAL) are routinely performed at fiberoptic bronchoscopy. Up to the present time, no data have been available on the efficacy of performing all three of these procedures simultaneously in the bronchoscopic work-up of sarcoidosis. A prospective study was undertaken to compare the diagnostic yield from TBLB, TBNA and BAL in patients presenting with clinical and radiological features typical of sarcoidosis.

Thirteen consecutive patients with clinical and radiological features consistent with stage I and II sarcoidosis underwent bronchoscopy with TBLB, TBNA and BAL.

Noncaseating granulomata (stain and culture negative for tuberculosis bacilli and fungi) were found in seven of the 13 patients by TBLB, and in six of the 13 patients by TBNA (of which four patients had negative TBLB). Eight of the 13 patients had classical "sarcoid" BAL findings, *i.e.* >12% lymphocytes, and high CD4+:CD8+ lymphocyte ratio. Combining TBLB, TBNA and BAL gave a diagnostic sensitivity of 100% (12 out of 12 patients) for sarcoidosis. The remaining patient had nondiagnostic bronchoscopic studies and mediastinoscopy biopsy showed a non-Hodgkin's lymphoma.

Our data suggest that performing simultaneous transbronchial lung biopsy, transbronchial needle aspiration and bronchoalveolar lavage produces optimal results in the diagnosis of sarcoidosis.

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Sarcoidosis is a multisystem granulomatous disease of unknown aetiology, with an incidence of 15–40 per 100,000 of the population per year [1]. The commonest mode of presentation is hilar and mediastinal lymphadenopathy on a chest radiograph [2]. A tissue diagnosis is desirable both to exclude other conditions, which may mimic sarcoidosis [1, 3–7], and as a basis for management decisions, in particular the use of oral corticosteroids.

Transbronchial lung biopsy (TBLB), *via* a fiberoptic bronchoscope (FOB), is the usual method of obtaining a tissue diagnosis [1, 7, 8]. The presence of noncaseating granuloma in the biopsy specimen is considered diagnostic of sarcoidosis if the tissue is stain- and culture-negative for tuberculosis bacilli and fungi [1]. However, TBLB carries significant complications; in particular, there is a risk of pneumothorax (1–10%), and moderate (>25 mL) to severe (>100 mL) haemorrhage occurs in 5.4–0.6% of cases [8], although it is rarely life-threatening [1, 8]. Furthermore, the diagnostic yield with TBLB in sarcoidosis ranges 40–90%, depending on the skill of the bronchoscopist, the number of biopsies taken, and degree of interstitial involvement at the time of biopsy [1, 9, 10]. Because of this variable yield from TBLB, alternative diagnostic modalities, such as mediastinoscopy or open lung biopsy, may be required to obtain a tissue diagnosis, with the associated risks and costs of a procedure requiring hospital admission and general anaesthesia.

Bronchoalveolar lavage (BAL) is helpful in the diagnosis of sarcoidosis [11–14], but even the European Society

of Pneumology Task Group on BAL note that no single feature in BAL is diagnostic of sarcoidosis, and state rather conservatively that the combination of a lymphocytosis with a CD4+:CD8+ ratio >3.5 would be consistent with sarcoidosis in an appropriate clinical setting [15]. Other work has shown that whilst a CD4+:CD8+ ratio of 5:1 on BAL has a positive predictive value of 94% in distinguishing sarcoid from other interstitial lung disease, the sensitivity is only 59% [12], confirming that BAL alone is not sensitive enough for use as the sole diagnostic tool in the diagnosis of sarcoidosis.

Transbronchial needle aspiration (TBNA), a technique first used in 1949 through a rigid bronchoscope [16], was modified more recently for use through the FOB and is used to sample hilar and mediastinal lymph nodes [17]. TBNA is a safe and effective method of obtaining cores of tissue for the histological diagnosis of benign and malignant disease in the mediastinal and hilar lymph nodes, and for staging malignant disease [9, 10, 17–24]. Some authorities suggest that TBNA may become the procedure of choice for the diagnosis of stage I and II sarcoidosis [17, 19]. In a series of 51 patients with suspected sarcoidosis, the diagnostic yield was 60% from TBLB and 53% from TBNA in stage I disease [10]. Combining TBLB and TBNA increased the diagnostic yield to 83%. In stage II disease, 76% had the diagnosis confirmed by TBLB and 48% by TBNA. Combining TBLB and TBNA increased the yield to 86%.

Up to the present time, there have been no data available on the simultaneous use of the three procedures of TBLB, BAL and TBNA. We therefore wished to investigate 13 consecutive patients with radiological features of stage I or II sarcoidosis in this way.

Materials and methods

Subjects

Thirteen consecutive subjects with clinical history, physical findings and chest radiograph consistent with stage I or II sarcoidosis were entered into the study. All patients had a chest radiograph, high-resolution computed tomography (HRCT) scan, full blood count (FBC), coagulation screen and serum calcium prior to entry into the study.

Bronchoscopy

Patients attended the day ward and were premedicated with 10 mg diazepam, and lignocaine local anaesthesia was used. An Olympus BF10 FOB (Tokyo, Japan) was then inserted nasally, with continuous monitoring of oxygen saturation and cardiograph tracing during the procedure.

Bronchoalveolar lavage

The bronchoscope was wedged in the right middle lobe bronchus, and three aliquots (180 mL) of sterile 0.9% saline instilled through the biopsy channel. After 10 s, the fluid was recovered under suction into a plastic container. The percentage of the lavage fluid recovered ranged 50–65%. The BAL fluid was analysed for total cell count, differential count and CD4+:CD8+ ratio (using fluorescence-labelled monoclonal antibodies and a flow cytometer).

Transbronchial needle aspiration

The needle used for TBNA was an MW-319 (Mill-Rose Laboratories Inc., Mentor, OH, USA), a 140 cm long flexible plastic catheter with a retractable 19-gauge metal needle at the distal end. Inside the 19-gauge needle was a 21-gauge needle which was also retractable.

The catheter was advanced through the FOB, with both needles retracted. When the metal hub appeared through the distal end of the FOB, both needles were fully advanced and the tracheal or bronchial wall was pierced. Lymph node tissue was sampled in a standard fashion [17] by advancing, partially withdrawing, and readvancing the needle several times under suction. The areas sampled were the right paratracheal, aortopulmonary window, and anterior and posterior carinal lymph node stations. CT scans were not used to map the areas to be sampled. Once obtained, the TBNA specimen was flushed into formalin for histological examination.

Transbronchial lung biopsy

Alligator forceps were used *via* the FOB to obtain four or five biopsies from the right lower lobe in a standard fashion [8].

Results

No complications were seen in the patients studied, and all were discharged home from the day ward within 4 h

Table 1. – Results of TBLB, TBNA, BAL and HRCT scan in the patients studied

Patient No.	TBLB	TBNA	BAL % lym	CD4+/ CD8+	HRCT scan ^{††}
1	-ve	+ve	4	1.5/1	Normal parenchyma
2	+ve	-ve	85	5.5/1	Normal parenchyma
3	-ve	-ve	84	8/1	Normal parenchyma
4	+ve	-ve	2	2/1	Early interstitial disease
5 [‡]	-ve	-ve	0.5	18/1	Normal parenchyma
6	-ve	+ve	<1	1.3/1	Interstitial disease
7	+ve	-ve	3	2.5/1	Interstitial disease
8	-ve	+ve	18	6/1	Interstitial disease
9	+ve	-ve	36	7.5/1	Normal parenchyma
10	+ve	+ve	25	20/1	Interstitial disease
11	-ve	+ve	76	17/1	Interstitial disease
12	+ve	+ve	36	9/1	Interstitial disease
13	+ve	-ve	41	6/1	Interstitial disease

A positive TBNA or TBLB required the finding of noncaseating granulomata on histological examination, with all tissue negative for tuberculosis and fungal stains. [‡]: patient No. 5 had negative TBLB, TBNA and BAL (mediastinoscopic lymph node biopsy confirmed non-Hodgkin's lymphoma); ^{††}: all patients had hilar and mediastinal lymphadenopathy as defined by entry criteria to study. -ve: negative, *i.e.* nondiagnostic; +ve: positive, *i.e.* diagnostic; TBLB: transbronchial lung biopsy; TBNA: transbronchial needle aspiration; BAL: bronchoalveolar lavage; lym: lymphocytes; HRCT: high-resolution computed tomography.

of the bronchoscopy. Postbronchoscopy chest radiographs showed no evidence of pneumothorax in any of the cases.

The results are presented in table 1. The TBLB was positive in seven patients (*i.e.* showed noncaseating granulomata, which were stain- and culture-negative for tuberculosis bacilli and fungi), five of whom also had a positive BAL [7] (lymphocytosis >12 % with a CD4+:CD8+ ratio >4:1). TBNA was positive in six patients, of whom two also had a positive TBLB and BAL and two had a positive BAL alone. Therefore, two patients were diagnosed solely by TBNA and two solely by TBLB.

Two patients had negative TBLB and TBNA. One of these had a typical "sarcoid" BAL (Subject No. 3 in table 1), with 84% lymphocytes and a CD4+:CD8+ ratio of 8:1, and a diagnosis of sarcoidosis was made on this basis. This patient did not receive any corticosteroid medication and the chest radiograph had returned to normal 3 months later.

The final patient (Subject No. 5) had negative TBNA and TBLB and normal BAL findings. A mediastinoscopic lymph node biopsy showed non-Hodgkin's lymphoma.

Therefore, simultaneous use of the three diagnostic modalities of TBLB, TBNA and BAL successfully diagnosed sarcoidosis in all of the 12 with this diagnosis and prevented the need for more invasive procedures.

Chest radiography and HRCT scan demonstrated lymphadenopathy in all cases, and showed evidence of interstitial disease in eight patients. Of these eight, only five had a positive TLB. Five patients had no evidence of interstitial disease on chest radiography or HRCT, but two of these had positive TBLB.

Discussion

Thirteen consecutive patients with clinical and radiological features consistent with stage I or II sarcoidosis

were studied. The data show that combining the modalities of TBLB, TBNA and BAL achieved significantly better results than either TBLB, TBNA or BAL alone. Furthermore, the significantly enhanced diagnostic yield from combining these three procedures at the same bronchoscopy sitting was not associated with any additional complications. TBLB was diagnostic in seven out of 12 patients with sarcoidosis (58%), five of whom had interstitial lung disease on HRCT scan. However, TBLB was positive in two patients in whom HRCT scan showed normal lung parenchyma. These data are consistent with previous reports, which show that HRCT scanning is not useful in predicting the diagnostic yield of TBLB [25, 26]. Although our yield of 58% from TBLB is comparable to previous reports, five of the 12 patients with sarcoidosis had negative TBLB, and in the absence of TBNA and BAL at least some of these patients might have required the significantly more risky and costly procedures of mediastinoscopy or open lung biopsy to confirm the diagnosis.

TBNA can successfully sample lymph glands in a variety of pathological states. There are few reports of complications following this procedure and only a single case report records a significant complication, namely bacterial pericarditis following TBNA [27]. In four of the present patients with a negative TBLB, TBNA confirmed the diagnosis of sarcoidosis and obviated the necessity for consideration of more invasive procedures in these patients, with obvious cost-benefit implications. The overall diagnostic yield from TBNA in patients with sarcoidosis was 50% (six out of 12 patients) and is consistent with previous reports. None of the patients had any complications from the TBNA procedure.

With regard to BAL, the present data are consistent with previous reports on the utility of BAL in the diagnosis of sarcoidosis; four of the 11 patients with positive biopsies had negative BAL, underlining the poor sensitivity of BAL in sarcoidosis. However, combining BAL, TBLB and TBNA gave a 100% diagnostic yield for those patients with sarcoidosis.

We are not aware of any existing information which addresses the usefulness of combining bronchoalveolar lavage, transbronchial needle aspiration and transbronchial lung biopsy at the same bronchoscopy sitting in the diagnosis of sarcoidosis. Our results suggest that the three procedures can be safely and effectively carried out at a single bronchoscopy sitting with enhanced diagnostic yield, little additional cost and no additional complications in patients with sarcoidosis.

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