



## EDITORIAL

## Endobronchial ultrasound in sarcoidosis: Time to rethink the diagnostic strategy?



### Ecoendoscopia brônquica na sarcoidose: é tempo de repensar a estratégia de diagnóstico?

Currently the diagnosis of pulmonary sarcoidosis is shifting from conventional bronchoscopy procedures to other minimally invasive techniques, which are safer and more effective. In this issue of the Portuguese Journal of Pulmonology, Ribeiro C and co-authors prospectively evaluated 39 patients with suspected sarcoidosis (stages I or II) and obtained 94% diagnostic yield based on EBUS-TBNA findings, without complications.<sup>1</sup> These results are in line with current international literature and certainly reflect the value of the technique in experienced hands.

Sarcoidosis is the most prevalent interstitial lung disease in Europe and in the United States and is characterized by accumulation of non-caseating granulomas in tissue. Though it may involve virtually every organ, it affects the lungs and intrathoracic lymph nodes in 90% of cases. Diagnosis is usually initially based on clinical and radiological suspicion but tissue confirmation is strongly recommended in order to exclude diseases of similar presentation, such as tuberculosis, fungal infections, lymphoma and even lung cancer. In clinical practice, the vast majority of patients referred for the evaluation of pulmonary sarcoidosis present stages I or II. In the absence of easily accessible biopsy sites (skin or superficial lymph nodes) for the current diagnostic work-up, conventional flexible bronchoscopy endobronchial biopsy (EBB) and transbronchial lung biopsy (TBLB) are recommended, however, their sensitivity in detecting granulomas is moderate even when they are combined. Moreover TBLB may be associated with serious adverse events such as pneumothorax and hemoptysis. In cases of enlarged mediastinal or hilar lymph nodes an additionally "semi-blind" transbronchial needle aspiration (TBNA), guided by previous CT scans, is able to increase diagnostic yield, especially if puncture is performed in subcarinal and right paratracheal stations, but this technique is highly operator-dependent. Bronchoalveolar lavage (BAL) findings such as lymphocytosis in combination with a CD4+/CD8+ ratio >3.5 are considered helpful for the final diagnosis but are very variable. If the

diagnosis of sarcoidosis is not confirmed by bronchoscopy findings, more invasive and expensive surgical procedures such as mediastinoscopy (MS) or video assisted thoracic surgery (VATS) lung biopsy may be required.

In the XXI century, tissue proof of non-caseating granulomas can instead be obtained by sampling intrathoracic lymph nodes under real-time ultrasound guidance. Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) and transesophageal ultrasound-guided fine-needle aspiration (EUS-FNA) are complimentary techniques regarding their diagnostic reach in combination. Virtually they can reach all hilar, interlobar and mediastinal lymph nodes including paratracheal, subcarinal and paraoesophageal stations. The decision to perform either EUS or EBUS is usually left to the local endoscopist and may depend on availability of equipment, CT findings or the preference of either physician or patient. In 2009, a randomized controlled trial<sup>2</sup> showed that EBUS-TBNA improved the diagnostic sensitivity by 22% compared to conventional TBNA and in 2013 a frequently cited study proved that the diagnostic yield of EBUS/EUS (80%) was better than bronchoscopy (53%).<sup>3</sup> These results agree with a meta-analysis that revealed a pooled accuracy of EBUS-TBNA of 80% in sarcoidosis (range 54–93%).<sup>4</sup>

Therefore, head-to-head comparisons between conventional techniques and EBUS-TBNA/EUS-FNA in sarcoidosis have proved that endosonography is superior and it is expected that in the near future it will become the primary diagnostic tool in patients suspected of stage I/II sarcoidosis. With the growing experience of pathologists the demonstration of non-caseating epithelioid granulomas based on cytological material is feasible and reliable. Some authors have pointed out the need to obtain histological core tissue biopsies with a 19-gauge needle because histological evaluation is more reliable in excluding lymphoproliferative disorders and tuberculosis (at present 19-gauge needles are available only for conventional TBNA and EUS).

One may wonder if every bronchoscopy unit all over the world should invest in echoendoscopes and if conventional procedures have already become redundant in the diagnosis of sarcoidosis. Flexible bronchoscopy still seems to have some advantages because it is a widely available diagnostic tool. A single scope can be used for the entire procedure enabling several sampling techniques. It is quite easy to learn to use and is also maneuverable with optimal endobronchial image for the majority of bronchoscopists. Finally, standard flexible video bronchoscopes are less expensive as well as more robust compared to the echoendoscopes. In addition, some of the published endosonography trials have design problems such as, patient selection bias; the majority of lymph nodes were sampled in bulky stations 4R and 7 that are easily sampled by "semi-blind" TBNA with comparable yield; and others have been criticized due to the exclusion of conventional TBNA in the bronchoscopy group.<sup>3</sup> Two recent studies have confirmed the importance of conventional procedures in the diagnosis of sarcoidosis. Firstly, a systematic review and meta-analysis<sup>5</sup> has shown that conventional TBNA has a pooled efficacy of 62% in sarcoidosis, without any major complications, and when TBNA and TBLB are combined the diagnostic yield increases to 83%, similar to EBUS/EUS-FNA. And secondly, a well-designed randomized controlled trial<sup>6</sup> has demonstrated that individually EBUS-TBNA has the highest diagnostic yield (74.5%) and this is even better when combined with TBLB (90.9%) but the diagnostic yield of "semi-blind" TBNA plus EBB and TBLB allows comparable results (85.5%,  $p > 0.05$ ).

In conclusion, those who do not have EBUS/EUS or cannot refer the patient to a center with this equipment still have a good chance to diagnose sarcoidosis by optimizing and combining conventional techniques.

So, is EBUS-TBNA the best tool available to diagnose pulmonary sarcoidosis? Yes, it is. Is it the only tool? No, of course not!

## References

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