EDITORIAL

Combined EBUS and EUS-B in sarcoidosis: time to understand "if" and "when" it can be useful

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RELATED ARTICLE

by Filarecka et al, see p. 582

The pathologic confirmation of the clinical suspect of sarcoidosis is a common indication for bronchoscopy.[1] As lymphadenopathy is, by far, the most common manifestation of the disease across all ethnic groups, endosonography (endobronchial ultrasound [EBUS]; endoscopic ultrasound [EUS]) has become the first-choice diagnostic technique in most centers worldwide.[2] Several groups have addressed the influence of technical aspects of endosonography on its diagnostic success in sarcoidosis, including the needle gauge, availability of rapid on-site cytological evaluation, number of needle passes, number of sampled lymph nodes, and endosonography route (airway or esophagus).[2] However, despite a considerable amount of clinical research, large individual studies[3,4] and systematic reviews / meta-analyses[5,6] have demonstrated that endosonography still fails to detect granulomas in approximately 20% of patients with sarcoidosis.

In this issue of the *Polish Archives of Internal Medicine* (*Pol Arch Intern Med*), Filarecka et al[7] report the results of a prospective multicenter effort to evaluate another technical aspect, that is, the added value of combined endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) and endoscopic ultrasound with bronchoscope with fine needle aspiration (EUS-B-FNA) in patients with suspected sarcoidosis, stage I and II. Of note, combined EBUS-TBNA and EUS / EUS-B performed in the same diagnostic session had never been assessed in sarcoidosis, but had been tested and had proved useful in the mediastinal staging of lung cancer.[8,9]

Over the study period, the authors enrolled 50 patients evenly distributed with regard to the disease stage, and submitted them to EBUS-TBNA (first) and to EUS-B-FNA in the same session. They sampled a large number of lymph node stations (at least 2 from the airways and 2 from the esophagus) and performed a large number of needle aspirations per lymph node (3 to 5), as per the study design. They also managed to prepare the material retrieved from lymphadenopathy as both smears and cell blocks in a systematic fashion.

The significant diagnostic advantage associated with sampling of the subcarinal lymph node station and with the combination of smears and cell block (as compared with the single cytological preparations) are interesting findings of the study. However, the performance characteristics of EBUS, EUS-B, and of the 2 methods combined represent the key outcome. While no differences in diagnostic success were noted between EBUS-TBNA and EUS-B-FNA, the combination of the 2 methods provided a significant advantage in terms of both sensitivity and granuloma detection rate as compared with the single methods. Interestingly, the only diagnostic failures occurred in stage II, as combined EBUS / EUS-B identified correctly all patients with stage I sarcoidosis. Based on these results and keeping in mind the potentially increased complication risk associated with a higher number of biopsies, the authors suggest that combined EBUS / EUS be reserved for patients with suspected stage II sarcoidosis.

Even in the presence of limitations such as a small sample size and very high prevalence of sarcoidosis in the study population, Filarecka et al[7] have designed and delivered a much needed study which raises several discussion points regarding the opportunity ("if") of using a combined EBUS / EUS approach in sarcoidosis, and the clinical scenario ("when") in which it can be most useful.

This study provides preliminary yet solid data suggesting that there is actually room for performing combined EBUS / EUS in sarcoidosis, based on 2 simple observations. First, the diagnostic success (granuloma detection rate and sensitivity) of EBUS-TBNA and EUS-B-FNA alone was below 80%, a finding which further confirms the limits of these procedures in sarcoidosis. Second, the combination of the 2 methods raised

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the overall diagnostic sensitivity up to a level of 91.7%.

It is certainly more difficult to set a scientifically, ethically, and practically sound perimeter in which the use of combined EBUS / EUS-B in sarcoidosis would be reasonable, that is "when" to use it. From an ethical standpoint, it is never useless to remember that the diagnosis of sarcoidosis is basically clinical. There are many cases (Lofgren syndrome, Heerfordt syndrome, asymptomatic symmetric hilar lymphadenopathy) in which an invasive confirmation may be waived and a clinical diagnosis associated with a careful follow-up may be appropriate.[1] That said, there certainly is a rationale for the proposal made by Filarecka et al[7] to reserve the use of combined EBUS / EUS-B for patients with stage II sarcoidosis. It is well known, in fact, that the diagnostic yield of endosonography is significantly higher in stage I than in stage II sarcoidosis.[2-4] This stage-specific diagnostic imbalance has been attributed mostly to a smaller size and an increased fibrotic content of lymph nodes in stage II sarcoidosis.[2-4] As for the lymph node fibrosis, in particular, several operators have noticed that lymph nodes of patients with stage II sarcoidosis offer frequently a high level of resistance upon needle advancement during EBUS and/or EUS aspiration attempts.[2] Very recently, preliminary studies of EBUS strain elastography have strengthened the hypothesis that fibrotic lymph nodes in sarcoidosis are common and may be associated with an increased inadequacy rate of EBUS samples.[10,11]

However, a "rigid" indication to the use of combined EBUS / EUS in stage II sarcoidosis has drawbacks. First, studies of strain elastography suggest that fibrotic lymph nodes can be found also in stage I sarcoidosis.[11] Second, in the study by Filarecka et al,[7] the use of combined EBUS / EUS provided added value both in stage I and in stage II; the sensitivity of the combined approach, in fact, helped the authors achieve a 100% and 82% sensitivity in stage I and II sarcoidosis, respectively.

Given these data, it would be probably interesting to investigate the role of combined EBUS / EUS in sarcoidosis using a more flexible approach which incorporates information from other useful methods such as rapid on site cytological evaluation (ROSE) and / or elastography.[12] One interesting option would be to study the added value of EUS-B-FNA, used as a rescue procedure, in patients undergoing EBUS-TBNA and showing either inadequate or inconclusive ROSE results, regardless of the disease stage. The integration of EBUS strain elastography into clinical reasoning could also be of value, especially in institutions in which ROSE is not available. It could be important, in particular, to verify whether adding EUS-B-FBNA would increase the diagnostic success of endosonography in patients whose lymph nodes exhibit low values of strain elastography mean, which suggest lymph node stiffness and may be a surrogate of lymph node fibrosis, during EBUS-TBNA.

In summary, Filarecka et al[7] should be commended as they may have opened with their study a new line of clinical research in the diagnosis of sarcoidosis using endosonography. Future studies should be aimed to establish when combined EBUS / EUS is more likely to provide added diagnostic value so that we can fine-tune the use of this approach in patients with suspected sarcoidosis.

ARTICLE INFORMATION

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