Tissue Sampling in Suspected Sarcoidosis: Can We Avoid Mediastinal Procedures?

To the Editor:

We read with interest the recent American Thoracic Society clinical practice guidelines (1) for the diagnosis and detection of sarcoidosis. We are grateful to the guideline group for producing an important evidence-based document to guide clinicians across the world.

We would like to comment on the recommendation about tissue sampling for patients with suspected sarcoidosis on the basis of mediastinal and/or hilar lymphadenopathy, which forms Question 2 of the document: Should Patients with Suspected Sarcoidosis and Mediastinal and/or Hilar Lymphadenopathy, for Whom It Has Been Determined That Tissue Sampling Is Necessary, Undergo EBUS-guided Lymph Node Sampling or Mediastinoscopy as the Initial Mediastinal and/or Hilar Lymph Node Sampling Procedure?

The committee has recommended endobronchial ultrasound (EBUS)-guided lymph node sampling—rather than mediastinoscopy—as the initial procedure of choice to use the relatively less invasive of the two procedures. However, we believe that there is scope for an even lesser invasive approach in the scenario addressed in Question 2, applicable to a significant fraction of patients.

We have recently evaluated our experience (2) of performing ultrasound-guided core-needle biopsy of cervical lymph nodes in 25 patients suspected of sarcoidosis who had mediastinal and/or hilar lymphadenopathy on thoracic computed tomographic scans. It is important to note that the lymph nodes sampled following ultrasound were not generally enlarged, many with a short axis dimension <10 mm, and that in many cases, the lymph nodes were sonographically normal. Where a neck node could be biopsied, granulomatous inflammation was nearly always confirmed.

This technique is considerably cheaper than either EBUS–transbronchial needle aspiration or mediastinoscopy and less invasive than either. We therefore would strongly recommend that neck ultrasound be considered a first-line tool when pulmonologists are confronted with a patient with lymphadenopathy and tissue sampling is considered necessary to confirm granulomatous inflammation.

Moreover, the approach may have value (on a case-by-case basis) in the scenario posed in Question 1: Should Lymph Node Sampling Be Performed in a Patient Presenting with Asymptomatic Bilateral Hilar Lymphadenopathy? As these patients may be reluctant to undergo mediastinal procedures because of invasiveness and risk of complications, ultrasound assessment with a view to cervical lymph node sampling would be more acceptable.

We would recommend that pulmonologists and radiologists be more widely aware of the advantages of this approach and feel that dissemination of this option as an initial diagnostic modality could benefit a large number of patients and offer cost savings.

Finally, and importantly, it provides an attractive option during the current coronavirus disease (COVID-19) pandemic as a diagnostic modality with a lower crossinfection risk.

Author disclosures are available with the text of this letter at www.atsjournals.org.

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References

1. Crouser ED, Maier LA, Wilson KC, Bonham CA, Morgenthau AS, Patterson KC, et al. Diagnosis and detection of sarcoidosis: an official American Thoracic Society clinical practice guideline. Am J Respir Crit Care Med 2020;201:e26–e51.

2. Fahim A, Qasim MM, Rosewarne D. Neck as mediastinal extension: diagnosis of sarcoidosis by core biopsy of cervical lymph nodes. Clin Respir J 2020;14:16–20.

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Confirmatory Tissue Sampling in Clinical Stage I Sarcoicosis

To the Editor:

A policy of tissue verification of stage I sarcoidosis (SIS) in subjects presenting with asymptomatic bilateral hilar lymphadenopathy (ABHL) to identify an alternative diagnosis (AD) simulating SIS that might be materially benefited by earlier diagnosis (lymphoma or tuberculosis [TB]) appears to be a self-evident, categorical good. This view was challenged by Winterbauer and colleagues on grounds that ABHL is such a stereotypical feature of sarcoidosis that one can
make a confident provisional clinical diagnosis (1) (with confirmation by mandated follow-up), thus sparing individuals with ABHL, who comprise the vast majority of subjects presenting with ABHL, from an invasive procedure. In the 50+ years since its publication, to my knowledge, not a single verified exception has been published. The decision to proceed thus rests on a quantitative assessment: What proportion of ABHL is caused by AD? What is the benefit of their earlier ascertainment? How many persons with ABHL must undergo an invasive procedure to confirm an AD? What are the harms and costs of a confirmatory invasive procedure?

I reviewed the abstract or text of the case series cited by the authors of the guideline policy (2) and found that most confounded their analysis by conflating BHL with cases demonstrating radiographically evident mediastinal lymphadenopathy, a feature characteristic of lymphoma. Collectively, they reported 1.96% with an AD, more than 100-fold a prior estimate in which ADs presented as ABHL (3). None furnished a documented instance. Some guideline authors commented on rare reports of metastatic hypernephroma presenting in this fashion. Because earlier diagnosis confers no material benefit, we did not consider it an AD. Based on the product of the incidence and radiographic presentation of AD, we estimated that they comprise ≤0.05% of persons presenting with ABHL (3). We reported that a delay in diagnosis of lymphoma would have, at most, a trivial effect on its course, that primary TB was typically unilateral and self-limited in 95% of cases, and that both lymphoma and progressive primary TB would become evident during mandated follow-up.

Major complications of transbronchial needle aspiration (TBNA) appear to be infrequent, but, absent a reporting requirement or incentive, they cannot be quantified.

Under the assumption that our estimate of the positive predictive value of a clinical diagnosis of S1S based on ABHL underestimated AD by a twofold order of magnitude (i.e., ≤0.05% vs. 1.96%), that TBNA is 100% sensitive for AD and sarcoidosis, that it is complication free, and that the procedural (99–232) charge is $5,000, if 102 persons with ABHL were submitted to TBNA, the net charge would be a half-million dollars, 100 would receive no offsetting, tangible benefit, and 2 would be found to have a lymphoma or TB. Under our estimate of ≤0.05% AD, under the same assumptions, if 10,005 persons with ABHL underwent TBNA, the net charge would be 50 million dollars, 10,000 would receive no tangible benefit, and, at most, 5 persons with an AD might be marginally benefited by an earlier diagnosis (vs. mandated clinical follow-up).

Tissue confirmation of S1S is indicated in the occasional patient with high-risk history (e.g., lymphoma, renal cell carcinoma, or TB exposure), but, because of the extreme rarity with which an AD (whose earlier diagnosis would be materially beneficial) presents in this fashion, tissue confirmation is not required; it imposes numerous individuals destined to spontaneous resolution to an invasive and costly procedure not offset by commensurate benefit. In the exquisitely rare individual (none have been reported!) with an AD simulating S1S, the diagnosis will become evident with routine, mandated follow-up with trivial to no harm imposed by the diagnostic delay.

The disproportion between potential benefits versus collective harms (including the procedure as a harm) and costs strongly favor a provisional clinical diagnosis of S1S over tissue confirmation.