Clinical Diagnosis of Stage I Sarcoidosis

To the Editor:

I was perplexed to find that Tambouret and colleagues (April 2000)1 cited our article,2 referring to the pattern of asymptomatic bilateral hilar adenopathy, or bilateral hilar adenopathy accompanied by characteristic findings of sarcoidosis, ie, uveitis, arthritis, or erythema nodosum, as “clinically evocative of sarcoidosis,” and consequently advocated tissue confirmation. We conservatively estimated the positive predictive value of this pattern at 99.95% and recommended observation over biopsy confirmation. There have been no published challenges of this estimate. Our article was critically reviewed and abstracted by York University at the request of the British National Health Service as a practice guideline (http://nhscrd.york.ac.uk/). The authors of the sarcoidosis chapters in the current editions of Murray and Nadel’s textbook3 of respiratory medicine4 subscribe to this policy. Since the seminal article on the clinical diagnosis of stage I sarcoidosis was published 27 years ago,5 there have been—assuming an annual incidence of 5 × 10−8, and that half present with this stage—7 × 108 patients with stage I sarcoidosis identified in Europe and the United States (combined population, 1 billion). If our estimate of the incidence of alternative diagnoses (eg, lymphoma, tuberculosis) presenting with this pattern—5 × 10−4—we correct, there would by now be 350 such cases. During this interval, not a single reported case of this pattern due to a disorder other than sarcoidosis has appeared. This suggests that our estimate is too low. Since the authors refer to a 99.95% positive predictive value as “evocative,” one is rather curious to learn what increment in pretest probability they might require to justify a designation of “possible” or “presumptive” sarcoidosis.

When we submitted our article,2 we hoped that the long-standing issue of biopsy vs observation would finally be resolved by the overwhelming safety and economic advantages of the latter. Histologic verification of noncaseating granuloma, as the authors1 affirm, does not provide definitive evidence of sarcoidosis. This diagnosis—short of autopsy or protracted observation—is always presumptive; certainly is the limit of an asymptomatic curve of evidence. I can do no better than reiterate Dr. Kassirer’s observation: “Absolute certainty in diagnosis is unattainable, no matter how much information we gather, how many observations we make, or how many tests we perform. Our task is not to attain certainty, but rather to reduce the level of diagnostic uncertainty enough to make optimal therapeutic decisions.”6

Several shortcomings of this article1 bear mention. Sensitivity and specificity data are required for any new test. The authors reported true-positive data only for the 16 or 17 (both numbers are given) of 28 patients who underwent biopsy. Neither the false-negative rate nor specificity data were provided. Figure 2 was, for me, unsatisfying. The meaning of the last sentence—“... [fine-needle aspiration biopsy] is a cost-effective diagnostic procedure, especially for the maintenance of patients with an established diagnosis”—eluded me.

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REFERENCES


To the Editor:

We are pleased that the publication of our study (April 2000)1 afforded Dr. Reich the opportunity to elaborate his opinion concerning the futility of tissue diagnosis in stage I sarcoidosis. Unfortunately, Dr. Reich missed the point of our study. We had no intention of weighing on the best approach to the workup of stage I sarcoidosis, which is a clinical decision. We simply wanted to demonstrate that, when indicated, tissue sampling by means of fine-needle aspiration biopsy (FNAB) is as informative as open surgical biopsy but much less invasive and more cost-effective.

Sensitivity/specificity statistics would lend weight to our argument. However, we did not have sufficient data to calculate the figures. Sixteen patients had follow-up biopsies (17 inaccurately appears in the abstract). The remaining 12 patients had, to the best of our knowledge, clinical presentations compatible with sarcoidosis. In order to calculate the false-negative rate and specificity, we would have had to have a different, larger study population that would include patients with sarcoidosis in whom the FNAB did not reveal granulomas, and patients without sarcoidosis in whom granulomas were identified on FNAB.

FNAB is useful not only in the primary diagnosis of sarcoidosis but also in patients with established diagnosis of sarcoidosis in whom new lesions appear that raise the possibility of disease progression vs a second, different pathologic process. For example, one patient included in our study presented with a parotid mass without other typical symptoms of sarcoidosis. The clinical impression of the parotid mass was a pleomorphic adenoma. The FNAB revealed granulomatous sialadenitis that led to a diagnosis of sarcoidosis. Subsequently, the patient developed an enlarged axillary lymph node that on excision was found to contain nonnecrotizing granulomas compatible with sarcoidosis. Months later, a second palpable axillary lymph node was discovered to contain nonnecrotizing granulomas by FNAB, and a needless lymphadenectomy was avoided. Use of FNAB is a prudent yet conservative approach in the investigation of new mass lesions in patients with sarcoidosis.

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