Thoracic sarcoidosis versus tuberculosis: Need for a multi-disciplinary approach

Sir,

We read with great interest the article titled "Dilemma of diagnosing thoracic sarcoidosis in tuberculosis endemic regions: An imaging based approach" by Bhalla *et al*.[1] in the October-December 2017 issue of the *Indian Journal of Radiology and Imaging* (Volume 27, Issue 4). The article focused and succeeded in projecting in great detail the nuances of differentiating between sarcoidosis and its close mimic tuberculosis (TB). The algorithm, proposed by the authors, unifies clinical, radiological, laboratory, and pathological evidence to serve as an effective diagnostic tool. We would like to make a few pertinent points in this regard.

The authors in their review have rightly regarded thoracic imaging by contrast-enhanced computed tomography (CECT) as central to the evaluation of sarcoidosis in a high TB burden population, which when highly suggestive can be sufficient ground for starting appropriate therapy. However, in a significant proportion of these cases wherein non-specific (NS) findings are obtained, pathological confirmation of granulomatous inflammation is relied upon to clinch the diagnosis. This, however, has various pitfalls. First, although granulomatous inflammation with caseous necrosis has been classically described for TB, non-caseating granulomas can also occur in cases of TB. In this regard, cytopathological grading of tubercular lymphadenitis has been published previously (grade I: epitheloid granulomatous reaction with caseation, grade II: epitheloid granulomatous reaction without caseation, grade III: non-granulomatous reaction with necrosis), emphasizing that non-caseating granulomas can be commonly seen in TB.[2,3] Furthermore, granulomatous inflammation with caseous necrosis has been reported in sarcoidosis as well. This uncommon entity, called necrotizing sarcoid granuloma (NSG), represents 1.6%-4% of pulmonary sarcoidosis, where extra-pulmonary involvement is deemed extremely rare.[4] Histology is characterized by granulomatous angitis with necrosis, most often misdiagnosed and treated as TB.[5] In a recent study evaluating the role of endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) in mediastinal lymphadenopathy, 206 cases of granulomatous inflammation were obtained and the presence of caseation and/or acid-fast bacilli was considered confirmatory for TB. While TB was diagnosed in 76 cases (36%), the etiology could not be ascertained conclusively in 123 cases (59.7%) with non-caseating granulomas.[6] Although theoretically few small loose lymphocyte "depleted" granulomas are obtained in sarcoidosis and numerous compact lymphocyte "rich" granulomas are likely to be tubercular, these subtle differences are insufficient to guide treatment decisions.

For the physician, this implies that in cases with NS findings, other characteristics are to be relied upon to zone in to the diagnosis, namely, history of confirmed TB in the past, contact or family history of confirmed TB, result of tuberculin skin testing, and response to empirical anti-TB therapy.

We believe that the addition of microbiological tests for TB to routine cyto/histopathology evaluation could prove beneficial in this regard. Apart from ZN staining for acid-fast organisms, pathology samples should be processed for mycobacterial culture and Xpert MTB/RIF (cartridge-based nucleic acid amplification test/nested polymerase chain reaction (PCR)). In an Indian study involving 63 patients of granulomatous lymphadenitis diagnosed by endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA), 35 were diagnosed as TB. Of these, three patients (9%) had microbiological positivity as the sole diagnostic feature.[7] This was re-iterated in another Korean study on EBUS-TBNA in granulomatous lymphadenitis, wherein of the seven patients with NS cytology and negative smear results, Xpert MTB/RIF gave the diagnosis in four cases (57%).[8] Among the microbiological tests performed on TBNA samples, Xpert MTB/RIF appears to provide the highest yield. The percentage positivity for AFB in smears of TB with non-caseating granulomas is low, varying from 1.9% to 20%.[3,9] While a sensitivity close to 60% has been reported for Xpert MTB/RIF in material obtained by TBNA and EUS-FNA, it remains to be specifically seen whether this rate would be maintained in specimens with non-caseating granulomas.

Finally, differentiation of thoracic sarcoidosis and TB in a TB endemic setting can be extremely difficult, often requiring a multidisciplinary approach involving pulmonologists, radiologists, pathologists, and microbiologists. Even after this, a therapeutic trial of anti-TB therapy may be required in difficult-to-diagnose cases, as atypical manifestations of TB are more common than typical presentation of sarcoidosis in our setting. Microbiological testing of the pathology specimen should be appended to the algorithm to increase the diagnostic yield.

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Conflicts of interest

There are no conflicts of interest.

Agrima Mian, Animesh Ray

Department of Medicine, AIIMS, New Delhi, India
E-mail: doctoranimeshray@gmail.com

References

1. Bhalla AS, Das A, Naranje P, Goyal A, Guleria R, Khilnani GC. Dilemma of diagnosing thoracic sarcoidosis in tuberculosis-endemic regions: An imaging-based approach. Part 2. Indian J Radiol Imaging 2017;27:380-8.
2. Navani N, Molyneaux PL, Breen RA, Connell DW, Jepson A, Nankivell M, *et al*. Utility of endobronchial ultrasound-guided transbronchial needle aspiration in patients with tuberculous intrathoracic lymphadenopathy: A multicentre study. Thorax 2011;66:889-93.
3. Bezabih M, Mariam DW, Selassie SG. Fine needle aspiration cytology of suspected tuberculous lymphadenitis. Cytopathol 2002;13:284-90.
4. Binesh F, Halvani H, Navabii H. Systemic sarcoidosis with caseating granuloma. BMJ Case Rep 2012;2012:bcr0520114278.
5. Chong Y, Lee EJ, Kang CS, Kim TJ, Song JS, Shim H. Necrotizing sarcoid granulomatosis: Possibly veiled disease in endemic area of mycobacterial infection. J Pathol Transl Med 2015;49:346-50.
6. Manucha V, Kaur G, Verma K. Endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) of mediastinal lymph nodes: Experience from region with high prevalence of tuberculosis. Diagn Cytopathol 2013;41:1019-22.
7. Thangakunam B, Isaac BTJ, Christopher DJ. Endobronchial ultrasound experience in a high tuberculosis prevalence setting. Indian J Tuberc 2017;64:196-200.
8. Eom JS, Mok JH, Lee MK, Lee K, Kim MJ, Jang SM, *et al*. Efficacy of TB-PCR using EBUS-TBNA samples in patients with intrathoracic granulomatous lymphadenopathy. BMC Pulm Med 2015;15:166.
9. Prasoon D. Acid-fast bacilli in fine needle aspiration smears from tuberculous lymph nodes. Where to look for them. Acta Cytol 2000;44:297-300.

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