Imaging in diagnosis and treatment of pulmonary tuberculosis

Sir,

I read with interest the article by Bhalla et al. and would like to humbly make the following observations:

1. The conventional classification of pulmonary tuberculosis into primary and post-primary based on radiological parameters, which the authors have elucidated, has been questioned by recent genotypic studies. Molecular methods of analysis of Mycobacterium tuberculosis isolates have revealed that radiological features are often inefficient in differentiating recent from past infection. Thus, the "classical" features of primary and post-primary tuberculosis as indicated by the imaging "pattern" often overlap and cannot indicate the remoteness of infection.

2. In the algorithm for smear-negative pulmonary tuberculosis, as described by the authors, emphasis has been laid on the combination of clinical features and chest radiographs. A systematic review of the combination of clinical parameters and chest x-rays has shown a high sensitivity (median 96%), but low specificity (median 46%) for the diagnosis of pulmonary tuberculosis. On the other hand, CT thorax has demonstrated superior specificity (more than 80% even in smear-negative patients with AIDS who have higher incidence of atypical features). In the light of the above finding, would it not be prudent to opt for a CT thorax in almost all cases (especially in a secondary/tertiary care setting) in order to rule in or rule out pulmonary tuberculosis? Whether the cost and radiation hazard of CT in these patients can be justified as against the risk of subjecting them to potentially toxic drugs over 6 months or more needs to validated in future studies.

3. In the diagnostic algorithm for pulmonary tuberculosis, besides chest x-ray and a sputum microscopy, a sputum culture and/or Xpert MTB/RIF is indicated as per the international standards for diagnosis and treatment of tuberculosis. These serve to reasonably confirm a diagnosis of tuberculosis and also may prove indispensable in guiding chemotherapeutic regimens in case of drug-resistant tuberculosis. As much as 20% and 12% cases of pulmonary tuberculosis (as diagnosed by sputum culture) may be missed by sputum microscopy and chest x-ray, respectively. Also, 37% of patients diagnosed to have tuberculosis on the basis of chest x-ray findings may not have the same confirmed by culture. So, sputum culture/Xpert MTB/RIF would serve to increase both the sensitivity and specificity diagnostics for tuberculosis.

4. In case of radiological worsening for pulmonary/nodal/pleural disease and no definite clinical improvement, the authors have suggested a prolongation of intensive phase which appears to be arbitrary. The cause of such worsening without clinical improvement can be due to a number of factors including drug resistance, paradoxical reaction, secondary infections, alternative diagnosis, etc. Hence, ruling out of the above causes seems more appropriate as also re-confirmation of the diagnosis of tuberculosis. Sputum culture (if sent at the outset) can be of paramount importance in such cases.

5. Finally tuberculosis is a great masquerader. Rare imaging findings like cannon ball shadows, cystic lesions, etc., have been reported in tuberculosis. Therefore, no radiological features should be deemed to rule out tuberculosis. Patients having suggestive clinical features should undergo microbiological tests to rule out tuberculosis irrespective of the "atypical" features offered by radiological studies.

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Conflicts of interest
There are no conflicts of interest.

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References
Author reply to comments

Sir,

We appreciate the comments of Animesh Ray. However, majority of the points raised by him have already been alluded to in the review. Following is our reply to their remarks.

1. The conventional classification of chest tuberculosis (CTB) into primary and post-primary forms helps to understand the pathogenesis of the disease and its manifestations. Though there are typical imaging features described for both, nevertheless, there is considerable overlap in the radiological patterns, as already discussed in our article. Also, since the article focuses on imaging features, molecular studies are beyond the scope of the article.

2. As authors et al. themselves state that chest radiograph (CXR) has high sensitivity, so it makes sense to employ it as an initial imaging modality, keeping in view its wide availability, low cost, and substantially less radiation. In a considerable proportion of patients, CXR along with clinical and laboratory findings would help to diagnose TB accurately and CT would be unnecessary. In the remaining patients where CXR is equivocal and/or the clinical and laboratory findings are non-contributory, CECT is justified and is the investigation of choice. Thus, CT cannot be advocated in all smear-negative patients. We agree that a section of patients (like those infected with retrovirus) usually need a CECT chest and abdomen to rule out TB (both pulmonary and extra-pulmonary) and other opportunistic infections. However, this was beyond the scope of the current article.

3. Sputum culture may be done along with smear microscopy where facilities are available and where smear examination is equivocal. We agree that Gene Xpert MTB/RIF serves as a helpful add-on test, especially in cases of smear-negative TB (because of its increased sensitivity) and to detect rifampicin resistance (in previously treated cases and contacts of drug-resistant TB patients). However, high costs and limited availability hamper the routine use. There is no definite data to justify its use in treatment-naïve, non-retroviral infected patients, and this test may have false-positive results due to detection of dead bacilli.

4. In case of radiological worsening of CTB and no definite clinical improvement, we have suggested doing a CT first to assess disease activity. This will also serve to rule out alternative diagnosis. If CT suggests residual disease activity, then intensive phase of ATT may be prolonged. At this point of time, other relevant investigations/therapies may be instituted to detect drug resistance and to treat any secondary infection. The point is well-taken that clinical/radiological worsening despite treatment should lead one to proceed with an exhaustive work-up to find the cause. We wish to highlight here that the suggested protocols may be modified depending on clinical judgment on a case-to-case basis.

5. It goes without saying that imaging findings are always interpreted in conjunction with clinical features. If there is high index of suspicion and in case of immunocompromised patients where there may be atypical radiological findings, other investigations such as bronchoalveolar lavage and tissue/fluid sampling frequently prove beneficial. Also, adequate work-up to rule out alternative diagnoses is essential in case of atypical imaging features. The purpose of the suggested recommendations is to enable judicious use of imaging in diagnosis and follow-up of CTB patients, with the caveat that they may need to be customized to the given clinical situation.

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