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Commentary

Exudative pleural effusion in chronic kidney disease: An aetiological dilemma

The aetiological diagnosis in patients with exudative pleural effusion has always been a diagnostic dilemma. This predicament becomes all the more obvious in patients having exudative effusion with co-morbid illnesses like chronic kidney disease (CKD). In tuberculosis (TB)-endemic countries, patients with exudative pleural effusion and prolonged low grade fever in the absence of any other localization are "presumed" to be of tubercular origin in "clinical perception" and empirically administered antituberculosis therapy.

In this issue, Kumar *et al*[1] have addressed this clinical dilemma in patients with CKD and exudative pleural effusion. It is imperative to note that perhaps this is the first study to evaluate medical thoracoscopy in exudative pleural effusion in CKD patients in India. In a prospective observational study done in a tertiary care hospital of north India, the authors have performed nucleic acid amplification tests (NAAT) and adenosine deaminase (ADA) assay and compared these with medical thoracoscopy. Conventional investigations in pleural fluid like smear for acid-fast bacilli (AFB) and Lowenstein-Jensen (LJ) medium culture were also done. They observed that in patients with CKD, uraemia was the most common cause of exudative pleural effusion even in a TB-endemic country like India[1]. Further, this study reveals that ADA has a low sensitivity (67%) in patients with exudative effusion with a cut-off value of 40 IU/l. In patients with CKD, haemodialysis is a confounding factor as it reduces the levels of ADA. However, the limitation of ADA in the diagnosis of tubercular pleural effusion is increasingly being appreciated even in patients without co-morbid disease like CKD. In a study from Japan, it was observed that tubercular pleural involvement was significantly common in patients with less than 50 IU/l ADA levels in pleural effusion[2]. Over the years, it has been also proposed that determination of ADA isoenzymes may help in differentiating the aetiology of pleural effusion. ADA has two isoenzymes- ADA1 and ADA2. Increased ADA 2 activity is more indicative of tubercular pleural effusion as compared to ADA 1 activity[3,4]. Recently, *Mycobacterium tuberculosis* antigen-specific gamma interferon enzyme-linked immunospot performed on pleural fluid mononuclear cells has been shown to provide an accurate and rapid diagnosis of tubercular pleural effusion as compared to ADA[5,6].

The limitation of pleural fluid smear for AFB and L-J medium culture in diagnosis of tubercular pleural effusion has further been confirmed in this study[1]. All patients with TB had negative pleural fluid smear AFB and sterile culture with L-J medium. In one study from Taiwan, it has been observed that BACTEC liquid culture medium may have an advantage over solid L-J medium in patients with tubercular pleural effusion in high TB-endemic regions[7].

Another important observation of this study[1] was that amongst the NAAT multiplex polymerase chain reaction (PCR) employing IS6110, protein antigen b, and MPB 64 had higher diagnostic accuracy for tubercular pleural effusion as compared to 65kDa *M. tuberculosis* gene PCR. Both the sensitivity and specificity of multiplex PCR were 100 per cent as compared with 65kDa PCR where sensitivity was 100 per cent and specificity was 50 per cent only. In a study from Taiwan, amplified *Mycobacterium tuberculosis* direct test (AMTD), a commercial test of NAAT approved by the US Food and Drug Administration was used for diagnosing tubercular pleural effusion[8]. It was observed that pleural effusion AMTD sensitivity and specificity were 36.4 and 84.5 per cent, respectively[8].

Medical thoracoscopy is evolving as an important diagnostic tool in the management of respiratory

diseases especially involving the pleura in India. The study done by Kumar *et al*[1] has highlighted the role of medical thoracoscopy as a safe and effective technique in evaluation of patients with exudative pleural effusion in CKD. They have rightly proposed that this single centre trial is hypothesis-generating and needs to be validated with multicentric trials. The only caveat to these findings in a resource-limited country like India is the lack of availability of trained health care personnel to perform medical thoracoscopy and/or NAAT.

The authors have observed that in their centre, closed pleural biopsy is not routinely performed and all patients of undiagnosed pleural effusions are subjected to medical thoracoscopy. A randomized controlled trial from Turkey has compared the role of Abrams needle pleural biopsy under CT scan guidance (CT-ANPB) with that of medical thoracoscopy in 124 patients with undiagnosed exudative pleural effusion. This study recommends the use of CT-ANPB as the primary method of diagnosis in patients with pleural thickening or lesions observed on CT scan. However, in absence of these CT findings, the patients should be subjected to medical thoracoscopy[9].

Medical thoracoscopy also has the benefit of visual diagnosis in patients with tubercular pleural effusion. The direct visualization of pleural nodules had a sensitivity of 83 per cent and specificity of 100 per cent[1]. Recently, a study from China has also suggested that experienced healthcare personnel performing medical thoracoscopy can visually diagnose tubercular pleural effusion[10]. The visual findings on medical thoracoscopy indicative of TB included necrosis, diffuse miliary nodules, hyperemic edematous thickened pleura, single/multiple pleural nodules and pleural adhesions/ fibrotic septa.

The study by Kumar *et al*[1] is a major step forward in appraisal of different modalities of investigation in CKD patients with exudative pleural effusion. It has put in perspective the fact that even in TB-endemic countries like India, other diagnoses need to be considered before presuming that most exudative effusions are tubercular in aetiology. It has also highlighted the role of newer modalities like medical thoracoscopy and NAAT in the management of these patients. Of course, these results need to be validated in a multicentric trial before these can be generalized for a vast resource-limited country like India. Operational research particularly multicentric trials are the need of the hour in India to generate indigenous evidence-based medicine for appropriate diagnosis and management of both communicable as well as non-communicable diseases.

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