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Editorial

Addressing the Challenges of Imaging in Tuberculosis: Need of the Hour

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Tuberculosis (TB) continues to be a raging public health concern in endemic nations across the world, including India. According to the World Health Organization TB report 2023, in the year 2022, TB was second only to coronavirus disease 2019 as cause of mortality related to infection from a single agent.[1] While lung is the initial site of involvement by the *Mycobacterium* bacillus, and pulmonary TB (PTB) is the most frequent form; subsequent hematogenous dissemination leading to extrapulmonary site infection is also common with diverse manifestations.. Extrapulmonary TB (EPTB) spares almost no organ, and the sites of involvement are both intrathoracic and extrathoracic. Lymph nodes are the most common affected site not only in the thorax, but also in the neck and abdomen. Though lung is the entry point of the organism into the body, at the time of clinical manifestation of EPTB involvement, PTB manifestation is often rather infrequently seen.

Imaging needs in patients of suspected or known TB can be diverse and varied, dependent not only on the site of involvement but also on the age of the patient, as well as available resources. Optimization of imaging hence requires cost considerations, both in terms of economic costs and radiation doses. The imaging research and resultant recommendations in this disease also need to bear in mind the diversity in practices and alignment with national programs while constantly attempting to integrate new technology. The *Indian Journal of Radiology and Imaging* featured an article on optimizing use of imaging modalities in thoracic TB in 2015.[2] The basic recommendations for deploying and interpreting modalities, including and beyond chest radiograph remain similar till date.

In case of PTB, the initial diagnosis rests on chest radiograph and microbiology, as sputum is an easily available respiratory specimen. The challenge comes in sputum negative cases, and when patients present with only systemic symptoms such fever or weight loss without respiratory localization. Herein, comes the role of computed tomography (CT) chest in diagnosis. Further, the diagnosis in cases of EPTB is more challenging than PTB. The difficulty in obtaining confirmation of diagnosis is due to two reasons, the first being that most forms of EPTB are paucibacillary, and second, several sites are relatively inaccessible to sampling. Hence, for initial diagnosis, imaging plays an even bigger role than it does for PTB. The choice of primary imaging between ultrasonography (US), CT, and magnetic resonance imaging (MRI) varies depending on the site. While CT and MRI have been extensively used and researched, US is still underutilized outside of the abdomen.

Adding to the diagnostic conundrum is the need to differentiate TB from other inflammatory disorders which closely mimic TB on imaging, but require immune-suppression therapy. The foremost among these are sarcoidosis in the chest and Crohn's disease in the abdomen. A misdiagnosis can result in inappropriate use of immunosuppressants and a resultant worsening of TB. On the other hand, several patients of sarcoidosis erroneously receive antitubercular therapy (ATT), often multiple times over years, with significant costly delay in diagnosis. Hence, the differentiation of these entities from TB has been a research interest area with several publications elaborating on the same.[3,4] Not just inflammatory disorders, but even differentiation of malignancies such as carcinoma lung from PTB, lymphoma in cases with nodal and solid organ involvement, and peritoneal carcinomatosis from TB peritonitis is often not possible without sampling.[5]

The Western world reported an increase in the incidence of TB due to rising human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) cases in the 1980s and 1990s. With the advent of effective antiretroviral therapies, this number fortunately did not show the exponential rise that was expected. On the other hand, the number of immunosuppressed individuals has been

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increasing worldwide, including India, with a rise in the number of organ transplant procedures performed, steroid use, and also the increasing number of diabetes patients.[6] Varying degrees and types of immune suppression present challenges in diagnosis and treatment of TB, requiring radiologists to be aware of atypical patterns and responses. Another factor which can confuse the interpretation of chest CT images in suspected TB is underlying exposure-related disorders. Some exposure-related disorders such as pneumoconiosis (silicosis, coal worker's pneumoconiosis) and biomass fuel exposure with resultant anthracosis/anthracofibrosis predispose the patient to TB.[7,8] Further, these patients also have a high risk of developing lung cancer. Hence, differentiation between the three possible situations, that is, exposure-related lung disease alone, or its combination with TB or lung cancer on CT, remains a pressing question.[9] In this situation, 18F-fluorodeoxyglucose positron emission tomography/CT (18F-FDG PET/CT) can prove a valuable aid.

The role of artificial intelligence (AI) in TB diagnosis has also been a focus area of research and development in recent times. Several AI models have already been developed based on different techniques, using both machine learning or deep learning.[10,11] Computer-aided detection has been used not only for detection of TB, but also for its differentiation from silicosis or delineating superadded silicosis, with a reasonable accuracy (area under the curve > 0.85, specificity $> 70\%$).[12] AI has the potential to be immensely useful as a support tool for interpretation of radiographs, allowing large-scale population-based screening/surveillance to be implemented.

Follow-up of patients with TB requires even more judicious use of imaging, bearing in mind the need for repeated imaging in some. In children and young adults particularly, radiation-free modalities should be chosen whenever feasible. Hence, the need for enhancing the role of US and MRI in this setting, particularly US, due to its added cost and logistical advantages. Another advanced modality which has been researched in TB is 18F-FDG PET/CT. It has some niche indications, however, cost, radiation dose, and availability preclude its routine use in this setting. This is especially so when used for response assessment, as this requires repeated imaging. As in the case of several other infections, drug resistance has emerged as a major challenge in effectively controlling TB. This resistance may be primary, or acquired during treatment. Drug resistance poses unique imaging challenges, particularly during follow-up. When a worsening picture is seen on follow-up, it could reflect drug-resistant (DR) organisms, immune reconstitution inflammatory syndrome (IRIS), or even an alternate etiology. Hence, meticulous analysis of findings and familiarity with differentiating features are required to guide further management decisions including the need for and site of additional tissue sampling. For instance, IRIS was initially reported in HIV/AIDS patients, but is now recognized even in immunocompetent individuals. Since the treatment regimens for DR TB are longer, the number of imaging studies required are more. In fact, decisions regarding complete clearance of infection or residual activity have become rather challenging.

In the management of TB, it is not just active disease, but also its sequelae resulting from fibrosis or cicatrization that present myriad challenges. Consequences of healed TB are most frequently encountered following pulmonary disease and are now referred to as post-tubercular lung disease (PTLD) or post-tubercular lung abnormality. These include dyspnea, recurrent infections, hemoptysis, chronic obstructive pulmonary disease, and can even result in pulmonary arterial hypertension. In endemic regions, the number of people affected by PTLD are staggering, several of them being young adults.[13] Interpretation of imaging in these symptomatic patients with symptoms mirroring active TB, is challenging. Similar clinical presentation can be a consequence of reactivation of TB or secondary bacterial infection in the bronchiectasis and cavities. Another possibility is colonization by *Aspergillus* species, causing chronic pulmonary aspergillosis (CPA). Aspergillomas are the key imaging finding to be recognized.[14] CPA not only causes hemoptysis but also systemic symptoms. These patients, with radiographs resembling active TB, often end up receiving ATT inappropriately, due to missed diagnosis. Hence, radiologists play a key role in making the diagnosis and also recognizing the subtype of CPA.

Interventional radiology (IR) plays an important role at several stages of the disease. Image-guided biopsy/cytology is used most often for initial diagnosis in lymph nodes, and less frequently for focal lesions in solid organs. Pleural and pericardial fluid aspiration, as well aspiration from other sites such as psoas abscess is best done under US guidance. While the role of aspiration for diagnostic purposes is clear, role and timing of catheter drainage in effusions and collections is less standardized, and often varies across institutions. Further, vascular interventions in the active phase are primarily required for pseudoaneurysms resulting from necrotizing inflammation. Coil embolization is most frequently required for pulmonary or gastroduodenal arteries, these being the most frequently involved. Aortic pseudoaneurysms have also been reported as a consequence of spinal TB.[15] The most common performed vascular procedure in patients with PTLD is bronchial artery embolization (BAE), performed in patients presenting with hemoptysis due to hypertrophied arteries.[16] In TB endemic regions, PTLD with or without CPA is the dominant indication of BAE, unlike the nonendemic regions where it is bronchiectasis. Hence, TB continues to remain an important factor governing variations in IR practices not only among endemic and nonendemic regions, but also within endemic regions depending on the socioeconomic strata of the patients that an institution caters to. In fact, CPA also contributes to high recurrence rates of hemoptysis in PTLD patients due to progressive infection, and resultant recanalization of previously embolized arteries.

The current special issue of *Indographics* focused on imaging in TB goes beyond PTB, and aims to address

extrathoracic (EPTB) sites also. This special issue is planned keeping several objectives in mind. Since TB is a multisystem disorder with myriad presentations, it is often overcalled in TB endemic regions. On the other hand, when the presentation is atypical, there can be an inadvertent delay in diagnosis. As a radiology community practicing in a high endemicity area, we not only need to remain updated about the advances in TB imaging and management, we also need to find solutions that can work at a community level to enhance early diagnosis, screening, and surveillance. Authors in this issue come from numerous institutions across the country and have been selected based on their subspecialty expertise. We hope that the collated articles are found to be a useful resource by radiologists across the country.

Conflict of Interest
None declared.

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