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HRCT Spectrum of Pulmonary Multidrug-Resistant Tuberculosis in HIV Negative Patients: A Study in Indian Population

Dr. Anagha Rajeev Joshi[1], Dr. Saumya Mishra[2], Dr. Ashwini P Sankhe[3], Dr. Ankit Radhakrishna Bajpai[4], Dr. Vikrant Firke [5]

[1]Professor, Department of Radiology, Lokmanya Tilak Municipal Medical College and General Hospital, Sion, Mumbai-400022

[2]Fellow, Department of Radiology, Lokmanya Tilak Municipal Medical College and General Hospital, Sion, Mumbai-400022

[3]Assistant Prof, Department of Radiology, Lokmanya Tilak Municipal Medical College and General Hospital, Sion, Mumbai-400022

[4] Consultant Radiologist, Fortis hospital, Goregaon Mulund link Road, Mulund West, Mumbai - 400078

[5]Assistant Prof, Department of Radiology, Lokmanya Tilak Municipal Medical College and General Hospital, Sion, Mumbai-400022

Abstract: ***Aims: Multidrug resistant tuberculosis (MDR-TB) is a major contagious health problem in India. There is no significant difference between Multidrug resistant and drug-sensitive tuberculosis on the basis of clinical findings, therefore determination of characteristic radiological findings pointing towards multidrug resistant tuberculosis might be of help in its appropriate management. Methods: We retrospectively evaluated the spectrum of HRCT chest findings in 50 patients with clinically and microbiologically proven MDR-TB admitted to our hospital namely, consolidation, cavity (presence and number), centrilobular nodules (including a tree-in-bud pattern), fibrosis, bronchiectasis, collapse, lymphadenopathy, pleural effusion and pleural thickening. Results: Almost all i.e. 49 patients (98%) had lung involvement and amongst them majority 46 patients (92%) had bilateral lung involvement. Out of 50 patients, nodules were present in 41 patients , cavities in 26 patients, consolidation in 25 patients, fibrosis in 25 patients, 22 patients had tree in bud / V-Y pattern of nodules, 21 patients had collapse and 20 patients had bronchiectasis. Of the 26 patients who had cavities, 23 patients (88%) had multiple (>1) cavities and 3 patients (12%) had single cavity. Pleural involvement was seen in 25 patients, 14 patients had pleural effusion, 11 patients had pleural thickening. Lymphadenopathy was present in 33 patients. Conclusion: Knowledge of the typical HRCT findings of MDR-TB allows a diagnosis of suspicion, which may be useful in selecting appropriate anti-TB treatment in infected patients.***

Keywords: Multi-drug resistant tuberculosis, cavity, nodules

1. Introduction

Tuberculosis is currently the second among all infectious diseases that contribute to mortality of adults. India has the highest TB burden of any country in the world, accounting for an estimated one-fifth of global TB cases worldwide. It has an estimated prevalence of 3 million TB cases, with 2 million new cases occurring each year. About 280,000 people die from TB in India annually.

India has the second highest burden of Multidrug-resistant Tuberculosis (MDR-TB) in the world after China, with an estimated 99,000 new cases per year. [1]. MDR-TB is a problem of confirmed importance to public health worldwide. MDR-TB is defined as a strain resistant to isoniazid and rifampicin. [2]

The fundamental cause in the genesis of resistance to anti-tuberculosis drugs is the misuse of antibiotics to treat patients suffering from drug-susceptible tuberculosis, causing the mutation that occurs in the genome of Mycobacterium. Such misuse is the result of a series of actions, especially the administration of inadequate therapeutic regimens by health workers and the fact that they do not ensure that the patient follows the treatment until the end. Drug resistance arises mainly in areas where anti-tuberculosis programs are deficient. Moreover, immunodeficient patients of any background (both solid organ and bone marrow transplant, such as leukaemia or lymphoma patients and those treated with corticosteroids) are more susceptible to infection with Mycobacterium tuberculosis. [3]

2. Materials and Methods

From Aug 2016 to July 2017, we retrospectively evaluated the HRCT chest scans of 50 patients with clinically- and microbiologically-proven MDR-TB admitted to Lokmanya Tilak Municipal medical College and General Hospital, Sion, Mumbai, India. MDR-TB was defined as TB resistant to at least isoniazid and rifampin. The mode of acquisition of drug resistance was defined as ‘primary’, when it was identified in an individual who had never received any antituberculous therapy or who had had such therapy for less than 1 month. Acquired drug resistance referred to resistance that developed in a patient who had received antituberculous therapy for more than 1 month in the past. [4]

Fifty patients (15 males and 35 females; mean age, 43 years; age range, 20-82 years) were finally enrolled in this study. All 50 of these patients were HIV-seronegative as documented by negative results of a Western blot or an enzyme-linked immunosorbent assay test.

3. Image Acquisition and Analysis

All CT was performed using a multidetector row spiral CT scanner (64 slice Philips Brilliance CT). Scanning was performed at 120 kV with a 512 x 512 matrix. Scanning and image reconstruction was performed with a beam width of 0.625-10 mm and a beam pitch of 0.875-1.675 and scan data were reconstructed with a 2.5-mm section thickness for transverse images. Lung window and Mediastinal window views were acquired using contrast where necessary. Chest CT scans were reviewed by two radiologists who had no knowledge of the patients' clinical information, and conclusions were reached by consensus. The assessed patterns of parenchymal abnormalities included consolidation, cavity (presence and number), centrilobular nodules (including a tree-in-bud pattern), fibrosis, bronchiectasis, collapse, lymphadenopathy, pleural abnormalities including pleural effusion and pleural thickening. (Figure 1-8)

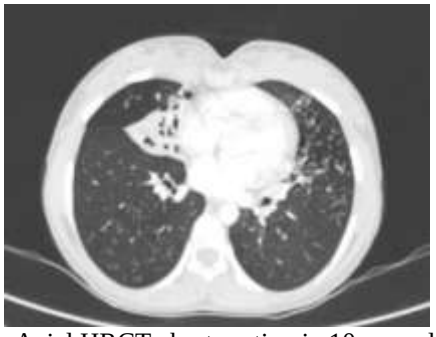
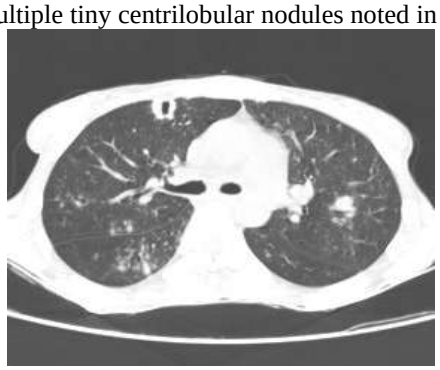
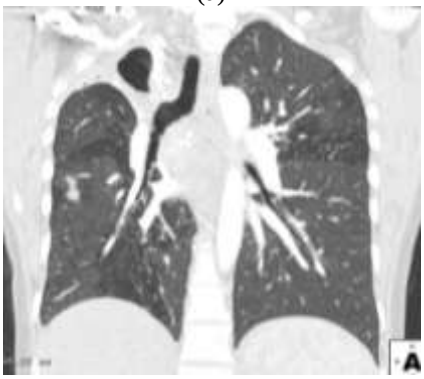


Figure 1: Axial HRCT chest section in 10 year old female patient with MDR- TB showing collapse of right middle lobe. Multiple tiny centrilobular nodules noted in lingula.

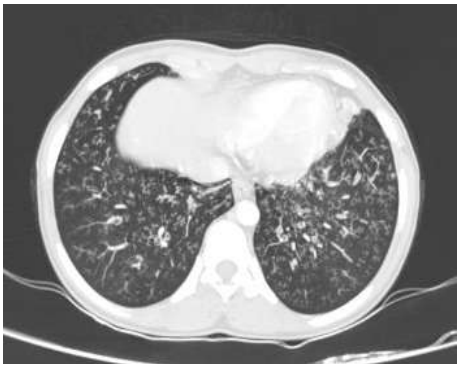


(a)

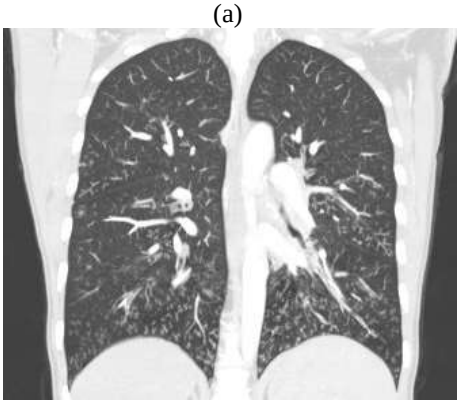


(b)

Figure 2: (a,b)–Axial and coronal HRCT chest (lung window) sections showing thick irregular walled cavities in right upper lobe associated with centrilobular nodules.



(a)



(b)

Figure 3: (a,b)– Axial and coronal HRCT chest sections (MIP images) showing multiple discrete and confluent centrilobular nodules exhibiting the characteristic "Tree-in-bud" or V-Y pattern seen in both lungs suggesting endobronchial spread of infection.

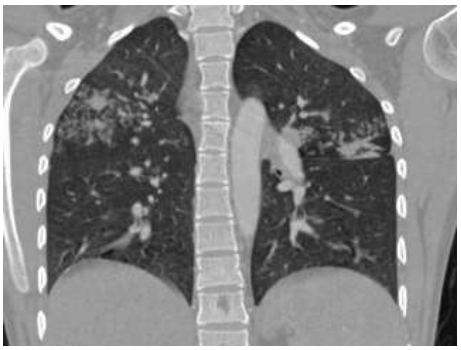
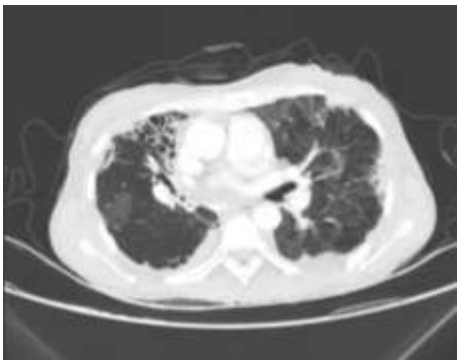
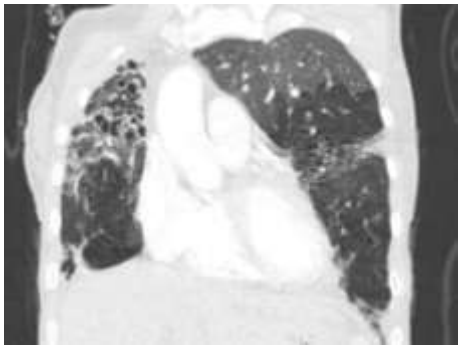


Figure 4: Coronal HRCT chest (lung window) sections showing multiple discrete and few confluent centrilobular nodules with few of them showing V-Y pattern seen in both lungs predominantly in upper lobes.



(a)



(b)

Figure 5: (a,b)–Axial and coronal HRCT chest (lung window) sections showing fibrobronchiectatic changes predominantly in the right lung. There is collapse of right middle lobe and mosaic attenuation bilateral lung

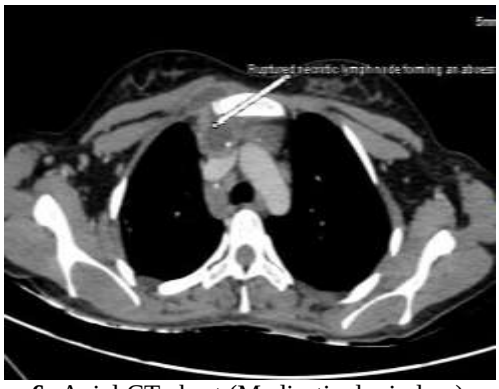


Figure 6: Axial CT chest (Mediastinal window) section showing prevascular necrotic lymphadenopathy in a 8 year old male child associated with abscess formation

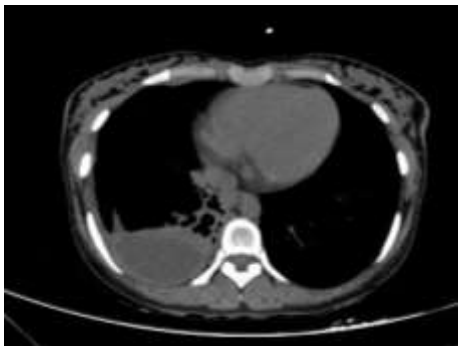


Figure 7: Axial CT chest (Mediastinal window) section showing right sided loculated pleural collection.

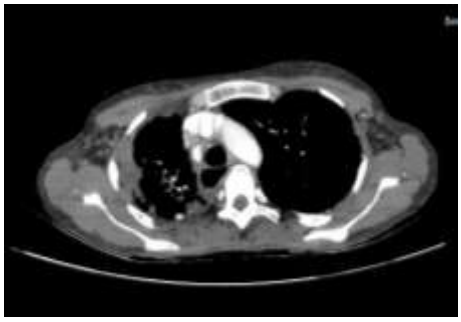


Figure 8: Axial CT chest (Mediastinal window) section showing right sided irregular pleural thickening. It suggests a chronic infective sequelae.

4. Results

Of the 50 Multidrug resistant tuberculosis patients enrolled in the study, 35 were females (70 %) and 15 were males (30 %). The mean age of the patients was 25.7 years (Min age- 4 months, Max age - 60 years)

Age Group	*No. of Patients*
0-15	08 (16%)
15-30	30 (60%)
30-45	06 (12%)
45-60	06 (12%)

44 patients had secondary MDR and 6 had primary MDR.

Spectrum of HRCT Findings

Almost all i.e. 49 patients (98%) had lung involvement and only 1 patient (2%) had no lung involvement. Out of 49 patients, 46 patients (92%) had bilateral lung involvement and 3 patients (6%) had unilateral lung involvement.

HRCT Pattern	*No. of Patients*
Nodules	41
Cavity	26
Consolidation	25
Fibrosis	25
Tree in Bud	22
Collapse	21
Bronchiectasis	20

Out of 50 patients, nodules were present in 41 patients , cavities in 26 patients, consolidation in 25 patients, fibrosis in 25 patients, 22 patients had tree in bud / V-Y pattern of nodules, 21 patients had collapse and 20 patients had bronchiectasis.

Of the 26 patients who had cavities, 23 patients (88%) had multiple (>1) cavities and 3 patients (12%) had single cavity Lymphadenopathy was present in 33 patients.

Pleural involvement was seen in 25 patients, 14 patients had pleural effusion, 11 patients had pleural thickening.

5. Discussion

Nearly one-third of the world population, i.e., two billion people, are infected with Mycobacterium tuberculosis and are at risk of developing the disease. Following HIV/AIDS, TB is the world's second commonest cause of death from infectious diseases. Annually, more than eight million people develop active TB, of whom about two million die.[5,6]. The WHO estimates that 50 million people worldwide are infected with MDR-TB, and that 273,000 (3.1%) of the 8.7 million new TB cases in the year 2000 were caused by MDR-TB.

Tubercle bacilli are continually undergoing spontaneous mutations that create resistance to individual anti-TB drugs. However, the frequency of these single mutations is sufficiently low that if the appropriate combination chemotherapy is administered and reliably ingested, no clinically significant resistance will occur.[7]

Most commonly, the development of acquired drug resistance occurs when there is a large multiplying bacillary population, such as what occurred in pulmonary cavities—when an inadequate drug regimen (inappropriate drugs, insufficient dosages, etc) is prescribed, or when there is a combined failure of both the patient and the provider to ensure that an adequate therapeutic regimen is taken. [8] Rarely, malabsorption of one or more anti- TB drugs may account for acquired resistance.[9]

Drug-resistant TB represents a threat to TB control programmers. Erratic and inappropriate use of currently available medications, HIV-TB co-infection, and concerns about transmission of drug-resistant strains in the general population, all contribute to a worrying picture. Unfortunately, the practitioner's error and poor patient adherence to the treatment may result in resistance and hence, treatment failure. [10]

Obviously a critical element for the future control of MDR-TB is prevention. For already existing strains of drug-resistant M. tuberculosis, it is vital to halt their transmission in community or hospital, in particular, in our country where an outbreak of MDR-TB is highly probable . Health workers are in contact with a large number of patients with MDR-TB in referral hospitals. Early identification of cases with MDR-TB plays a crucial role in its prevention. Therefore, we must be watchful of any signs that could help us to predict and prevent another catastrophic event. One of those signs would be obtained from imaging modalities.

Pulmonary MDR-TB exhibits a wide range of radiological signs most of them having severe patterns.

An essential question regarding the role of radiological findings is about their effectiveness on determining the morbidity and mortality of patients suffering from MDR-TB. We know MDR-TB is associated with higher rates of failure and death than is drug susceptible TB. However, the association between the extension of lesions on radiography and the mortality rate among patients with MDR-TB is still unclear. [11]

To the best of our knowledge, only few studies have evaluated imaging findings in MDR-TB.

In one of the studies, they compared chest X-rays of patients with MDR-TB and drug-susceptible TB and speculated that the overall radiographic findings and patterns among the two groups are similar.[12] They found that once a patient developed MDR-TB during an outbreak, the predominant radiographic pattern was similar to that of a primary TB. In those patients who acquired MDRTB due to low adherence to treatment protocol, most findings were consistent with that of secondary TB. In the latter condition, they found cavitatory lesions in 50% of patients. However, about one-third of the patients did not show the expected radiographic pattern.

Kritski et al, in 1997 performed a study among patients requiring re-treatment and found that the presence of cavitatory lesions was significantly associated with an unfavourable outcome. However, this finding was not associated with MDR-TB. In that study, presence of cavitatory lesions had a positive predictive value of 54% for an unfavourable outcome.[13]

Those findings were reproduced by Yew et al, in China. They performed a study to evaluate the outcome in patients with MDR-TB. Cavitatory lesions were found in 50.8% of patients and significantly correlated with a poor outcome.[14]

Two other studies, previously showed the relation between cavitatory disease and MDR-TB.[15,16] In one study performed in Argentina, the authors reported radiological findings as minimal, moderate and advanced and noted significant differences between the primary and acquired MDR-TB: The patients with acquired MDRTB presented with a higher prevalence of advanced lung lesions (as high as 75% of subjects).[17]

Based on these data, Long in 2000 suggested that one of the criteria for presuming MDR-TB was the presence of cavitatory disease. He concluded that these lesions harbour greater numbers of bacilli so that the likelihood of MDR-TB rise in the presence of them.[18]

In comparison with the above studies, a recently published article which was on community-based therapy in MDR-TB done in Peru, found that 66.6% of patients have bilateral pulmonary disease and cavitatory lesions, and that only 6% of patients have neither bilateral disease nor cavitatory lesions. Cavitatory lesions were absent in residual subjects. Surprisingly, the presence of cavitatory lesions was not associated with adverse disease outcome.[19]

Multiple cavities are more frequently observed in MDR-TB patients than those with DS TB infections.[20,21]. In our study, cavitatory lesions were present in 52% patients and majority (88%) of patients with MDR-TB had multiple cavities. Our results are similar to previous results.[2,10,22]

Finally, in management of pulmonary MDR-TB, imaging modalities could be as a guiding tool whenever surgical resection of involved lung area is the treatment option.[23]

6. Conclusion

As compared with patients with drug-sensitive (DS) pulmonary TB, non-AIDS patients with MDR TB are younger and the patients have a more frequent history of previous TB treatment and show multiple cavitatory lung lesions as seen on CT.

Our study shows that the HRCT chest imaging findings of pulmonary MDR-TB reflects more frequently the extensive and destructive pattern. Physicians always ask themselves whether their patients are at risk for MDR-TB or not. Some authors suggest certain criteria for this concern.[24]
We consider that radiological features in certain patients could raise suspicion of MDR-TB.

Our study revealed some radiological findings that could be used as markers of MDR-TB; when a patient presents with multiple cavitatory lesions associated with the sign of “tree

in bud", centrilobular nodules, consolidations and bronchiectasis, of bilateral distribution, the possibility that it is a case of MDR-TB should be considered.

Radiologists should be familiar with different patterns in pulmonary MDR-TB and related complications in each finding so that they can inform clinicians so as to suspect MDR TB. Knowledge of the typical CT findings of MDR-TB allows a diagnosis of suspicion, which is useful for selecting proper anti-TB treatment in infected patients before reaching a definitive diagnosis based on bacteriology. This, together with good therapeutic compliance, is the best strategy for controlling this important public health problem that is MDR-TB.

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