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Comparative analysis of Airway Invasive Aspergillosis and Endobronchial spread of Tuberculosis on High Resolution Computed Tomography

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ABSTRACT

Background: Distinction between airway-invasive aspergillosis (AIA) and endobronchial tuberculosis (EBTB) by high-resolution computed tomography (HRCT) continues to be a diagnostic challenge, especially in TB-endemic areas with high immunosuppression rates.

Objective: To compare the high-resolution computed tomography (HRCT) imaging features, lesion distribution, and morphologic characteristics of airway-invasive aspergillosis (AIA) and endobronchial tuberculosis (EBTB) to improve diagnostic accuracy.

Methodology: Retrospective comparative study was conducted form January 2022 to February 2023 among 63 patients (30 with AIA and 33 with EBTB) on the basis of clinical, microbiological, and radiological evidence. HRCT results were evaluated by senior radiologists for definite patterns such as centrilobular nodules, tree-in-bud appearance, ground-glass opacities, halo sign, cavitation, and lymphadenopathy.

Results: Although both diseases exhibited tree-in-bud and centrilobular nodules, EBTB was typified by dense, clustered nodules with upper lobe predominance and extensive cavitation. AIA exhibited ground-glass nodules with fuzzy borders, lower lobe prevalence, and common halo sign. Morphologic distinctions among nodules and lesion distribution were statistically significant.

Conclusion: HRCT is useful to differentiate AIA from EBTB in the clinical context. Identification of these characteristic patterns may direct proper therapy, enhance outcomes for patients, and decrease diagnostic delay in situations when these infections are present.

Keywords: HRCT; Endobronchial Tuberculosis; Airway-Invasive Aspergillosis

Introduction

Respiratory infectious diseases are still a major source of morbidity and mortality globally. The diagnostic and therapeutic problems presented by Tuberculosis and invasive fungal infections such as airway-invasive aspergillosis (AIA), continues to be very challenging.[1] High-resolution computed tomography (HRCT) has revolutionized the imaging of fine airways and parenchymal changes, enabling clinicians and radiologists to identify, characterize, and follow up on these diseases with increased specificity. Of the range of pulmonary infections, endobronchial spread of tuberculosis (EBTB) and airway-invasive aspergillosis show typical but occasionally similar features on HRCT, so it is essential to understand and compare their imaging patterns clearly.[2]

Endobronchial dissemination of tuberculosis means that the TB bacteria spread through the airways.[3] It usually affects parts of the lungs in patches, especially the upper lobes of the lungs. However, it can also spread to other parts of the body. This type of TB may present as a primary infection or, sometimes as reactivation disease. The radiographic hallmark of EBTB is centrilobular nodules, tree-in-bud opacities, bronchial wall thickening, and segmental or lobar consolidation.[4] These are manifestations of active infection and caseating necrosis in the airways and adjacent parenchyma, usually with associated lymphadenopathy or cavitary lesions.

Conversely, airway-invasive aspergillosis is a type of pulmonary aspergillosis occurring most frequently in immunocompromised patients, e.g., patients with hematologic malignancies, chronic neutropenia, or post-transplantation.[5] AIA is an intermediate state between colonization and angioinvasion in which the fungal components invade the airway epithelium and the tissues around it. HRCT findings usually consist of segmental thickening of bronchial walls, peri-bronchial consolidations, centrilobular nodules, and sometimes ground-glass halos if the infection spares into the nearby parenchyma. The "halo sign" and "air crescent sign" can occur with disease progression or recovery, although they are more common in angio-invasive types of aspergillosis.[6]

Although both conditions can have some similar imaging characteristics e.g., centrilobular nodules and tree-in-bud appearance, HRCT can assist in separating the two entities. There are a number of differences in distribution, pattern, and specific features that will help in the separation. For example, EBTB more often involves the upper lobes and exhibits contiguous bronchogenic spread, AIA can present with diffuse extent with increased predominance of segmental or lobar bronchial walls mostly affecting immunocompromised individuals.[7]

Accurate and timely differentiation between AIA and EBTB on HRCT is critical because both conditions have varied therapeutic strategies, different risks for infection spreading, implications for infection control, and prognostic outcome. TB requires prolonged antibiotic treatment and public health reporting, whereas AIA needs early antifungal therapy and it often signals significant immunosuppression. Thus, radiologists need to be proficient in identifying fine differences in imaging features and combining clinical context for maximizing patient management.

This study compares the features of HRCT of airway-invasive aspergillosis and endobronchial tuberculosis, offering a systematic approach for better diagnosis in clinical practice. Through an examination of the imaging characteristics, pathophysiologic correlations, and clinical relevance of both conditions, this research adds to the existing literature on infectious airway illnesses in the age of advanced imaging.

Objective

To compare the high-resolution computed tomography (HRCT) imaging features, lesion distribution, and morphologic characteristics of airway-invasive aspergillosis (AIA) and endobronchial tuberculosis (EBTB) to improve diagnostic accuracy.

Methodology

This retrospective, comparative observational study was performed at Nishtar Medical University, Multan between January 2022 and February 2023. There were 63 patients included in this study, divided into two groups: 30 patients diagnosed with airway-invasive aspergillosis (AIA) and 33 patients with endobronchial tuberculosis (EBTB). Patients were enrolled based on clinical suspicion, microbiological confirmation, and availability of high-resolution computed tomography (HRCT) chest imaging. Diagnosis of AIA was established on the basis of clinical presentation, risk factors like immunosuppression, and laboratory diagnosis by positive Aspergillus cultures, galactomannan antigen test, or histopathological findings of fungal invasion. Diagnosis of EBTB was established by sputum acid-fast bacilli testing, bronchoscopy findings, and histopathology or GeneXpert MTB/RIF assay.

HRCT chest images of all patients were obtained from the radiology archive of the hospital and independently read by two experienced thoracic radiologists blinded to the ultimate diagnosis. Imaging parameters examined included the presence, pattern, and distribution of centrilobular nodules, tree-in-bud opacities, bronchial wall thickening, ground-glass opacities, segmental or lobar consolidation, cavitary lesions, halo sign, air crescent sign, and lymphadenopathy. All radiological findings were noted and statistically analyzed across the two groups.

Demographic data, including age, sex, and clinical background (such as immunosuppression or comorbid-

ities), were also gathered. Statistical analysis was performed using SPSS software version 27. Categorical variables were analyzed by using the chi-square or Fisher's exact test, while continuous variables were compared by using the independent t-test. The p-value was taken to be <0.05 for statistical significance.

Results

The age of AIA patients was considerably higher (45.3 ± 6.8 years) than that of EBTB patients (36.5± 8.1 years), with a p-value of 0.01, which suggests a statistically significant difference. The gender distribution in both the groups was almost the same, with 63.3% of AIA and 66.6% of EBTB cases being male (p = 0.95), with no significant gender-related variation. There was a significantly distinct variation in immunocompromised status: 93.3% of the AIA patients were immunocompromised, whereas a mere 15.2% of the EBTB patients were immunocompromised, and this variation was extremely significant (p < 0.001). Dyspnea was present in 36.6% of AIA and 24.2% of EBTB, while fever was present in 43.3% and 48.5% respectively (Table 1).

Table 1. Demographic and Clinical Characteristics

Characteristic	AIA (n=30)	EBTB (n=33)	p-value
Mean Age (years)	45.3 ± 6.8	36.5 ± 8.1	0.01
Male Gender	19 (63.3%)	22 (66.6%)	0.95
Immunocompromised status	28 (93.3%)	5 (15.2%)	<0.001
Dyspnea	11 (36.6%)	8 (24.2%)	0.28
Fever	13 (43.3%)	16 (48.5%)	0.88

There were significant differences between the imaging findings in the two groups. Centrilobular nodules were seen in both AIA (83.3%) and EBTB (84.8%), but tree-in-bud opacities occurred much more often in EBTB (93.9%) than in AIA (70%) (p = 0.02). Ground-glass opacities (p = 0.001), halo sign (p = 0.01) and peribronchial consolidation (p = 0.007) were much more frequent in AIA. Cavitary lesions and lymphadenopathy were more characteristic of EBTB (Table 2).

Distribution of lesions differed considerably across groups. EBTB mainly involved the upper lobes (75.7%), while AIA had a predilection for basal segments of the lower lobes (86.6%). Diffuse pulmonary involvement was more frequently observed in patients with AIA (66.7%), while EBTB had more focal and bronchogenic extension (Table 3).

There were marked variations in TIB nodule morphology. Sharply defined, dense nodules predominated in EBTB,

Table 2. HRCT Imaging Features Comparison

Imaging Feature	**AIA (n=30)**	**EBTB (n=33)**	**p-value**
Centrilobular Nodules	25 (83.3%)	28 (84.8%)	0.63
Tree-in-Bud Appearance	21 (70%)	31 (93.9%)	0.02
Bronchial Wall Thickening	26 (86.7%)	21 (63.6%)	0.01
Ground-Glass Opacities	19 (63.3%)	5 (15.1%)	0.001
Halo Sign	8 (26.6%)	1 (3%)	0.01
Cavitation	6 (20%)	13 (39.3%)	0.17
Lymphadenopathy	4 (13.3%)	10 (30.3%)	0.04
Peribronchial Consolidation	14 (46.7%)	4 (12.1%)	0.007

Table 3. Distribution of Lesions on HRCT

Distribution	AIA (n=30)	EBTB (n=33)	p-value
Upper Lobe Involvement	7 (23.3%)	25 (75.7%)	0.001
Lower Lobe Predominance	26 (86.6%)	4 (12.1%)	<0.0001
Diffuse Pattern	20 (66.7%)	5 (15.2%)	0.0005
Segmental Involvement	23 (76.6%)	9 (27.2%)	0.002

whereas AIA had ground-glass nodules and fuzzy, ill-defined borders. Clusters of nodules were detected in 48.4% of the cases with EBTB but not in AIA (Table 4).

Discussion

This current study offers a detailed comparison of the high-resolution computed tomography (HRCT) findings of airway-invasive aspergillosis (AIA) and endobronchial tuberculosis (EBTB). HRCT offers high spatial resolution, enabling accurate assessment of lung structures, making it essential in diagnosing and monitoring these pulmonary conditions.[8,9] Both these conditions are radiologically overlapping but clinically different pulmonary infections. From a retrospective review of 63 patients, 30 with AIA and 33 with EBTB, we noted multiple statistically significant differences in imaging patterns, lesion morphology, and lesion distribution that contribute to the radiologic distinction between these diseases. These findings are very important for treatment and patient outcomes, especially in areas where both tuberculosis and fungal infections are common.

One of the most important findings from our research was the significant contrast in the demographic and clinical history between the two patient groups. AIA patients were significantly older on average and much more likely to be immunocompromised (93.3% vs 15.2%), as would be expected for airway-invasive aspergillosis pathogenesis. The existence of immunocompromised conditions like hematologic malignancies, solid organ transplant, or prolonged neutropenia provides a susceptible host status to Aspergillus spp. to evolve from colonization to airway mucosa invasion. According to Jenks et al. (2021), Invasive aspergillosis (IA) is becoming increasingly recognized as an important infection among critically ill ICU patients.[10] Kim et al. (2015) documented that Tree-in-bud opacities on HRCT, although frequently associated with TB, can also be found in airway-invasive aspergillosis (IA), particularly among immunocompromised patients. TB is characterized by dense, defined nodules, cavitation, and upper or diffuse lung involvement. In IA, ground-glass, blurry nodules with a basal predominance and more peri-bronchial consolidation are found in his study.[11] On the other hand, other studies documented that clusters of centrilobular nodules, peribronchial consolidations, and bronchial wall thickening, were more common in patients with AIA.[12,13]

Conversely, EBTB, caused by the bronchogenic spread of Mycobacterium tuberculosis, was found to be more common in comparably younger, immunocompetent persons in our study. This is how tuberculosis typically arises in nations such as ours, with widespread prevalence of the disease. In these environments, individuals tend to get reinfected or experience reactivation of latent TB, particularly within the airways, as a result of poor living conditions and environment. The imaging characteristics in our EBTB group, including upper lobe predominance, dense and clustered centrilobular nodules, and cavitation are the radiologic signs of active endobronchial tuberculosis. Wetscherek et al. (2022) emphasized newer imaging characteristics in TB patients and describes signs such as the reversed

Table 4. Morphologic Characteristics of TIB Opacities

TIB Morphology	AIA (n=30)	EBTB (n=33)	p-value
Dense Nodules	0 (0%)	30 (90.9%)	<0.0001
Ground-Glass Nodules	24 (80%)	0 (0%)	<0.0001
Fuzzy Margins	26 (86.7%)	2 (6.06%)	<0.0001
Clustered Nodules	0 (0%)	16 (48.4%)	0.0008

halo, galaxy, and cluster signs.[14]

One significant and new finding of our study is the comparative analysis of tree-in-bud (TIB) morphology in the two groups in detail. Although TIB pattern is more or less seen in both AIA and EBTB, our analysis revealed a difference in the quality of these nodules. TIB nodules in AIB were mainly ground-glass density with fuzzy, ill-defined edges, indicating partial bronchiolar lumen filling with secondary peribronchiolar inflammation. In contrast, in EBTB, the TIB nodules were closely packed, well-demarcated, and often found in clusters, in keeping with caseating granulomatous inflammation characteristic of tuberculous infection. A study by Franquet et al. (2001) has shown that Aspergilloma is seen as a soft-tissue mass in a cavity with an "air crescent" sign. Nodules and a "halo sign" are seen in angioinvasive aspergillosis.[15]

Another significant finding of our study was the lobar distribution and the pattern of involvement variability. While 75.7% of the cases of EBTB had upper lobe predominance. AIA had a strong affinity for the lower lobes, with diffuse parenchymal dissemination. This diffuse pattern of lower lobe involvement in AIA presumably suggests both gravity-dependent deposition and hematogenous dissemination of the spores in immunocompromised lungs. Garg et al. (2015) showed that middle lobe syndrome (MLS) is one of the mildest presentations of endobronchial tuberculosis (EBTB).[16] Meanwhile, a study conducted by Agarwal et al. (2012) reported that Allergic bronchopulmonary aspergillosis (ABPA) can present with normal imaging, and central bronchiectasis is not a consistent or defining feature.[17]

The halo sign, noted in 26.6% of AIA compared with merely 3% in EBTB, represents the angio-invasive tendency of Aspergillus and is not typical in tuberculosis, pointing to an important pathophysiological distinction. Cavitation and lymphadenopathy, by contrast, were more frequent in EBTB, cavitation resulting from caseating necrosis and nodal hypertrophy consistent with active TB. Cavitation may indeed occur in chronic aspergillosis, but it was less often encountered in AIA. Importantly, research such as Nguyen et al. (2021) has demonstrated a significant risk of chronic pulmonary aspergillosis (CPA) in post-TB patients who have residual cavities, resulting in the distinction between TB, AIA, and CPA becoming an emerging diagnostic challenge in high-endemic settings.[18]

Aspergillus infections might be present with tuberculosis, and thus radiologists have to pay close attention to the imaging distinctions between the two. Rapid and correct diagnosis is critical since treatment protocols are extremely different; TB involves antibiotics and public health protocols, while AIA involves antifungal agents and strict observation. TB continues to need mandatory reporting and isolation, whereas AIA, particularly in compromised immune patients, tends to rapidly worsen and requires immediate attention.

Conclusion

Our study highlights the role of HRCT as an essential imaging tool in the early diagnosis and AIA-EBTB differentiation. Although both diseases can have superimposable features, such as centrilobular nodules and tree-in-bud opacities, by further studying the morphology and distribution of the lesions, associated findings (e.g., halo, consolidation, lymphadenopathy), and patient's clinical history, a more secure and earlier diagnosis can be obtained. Additional prospective multicenter trials with high subject numbers and inclusion of sophisticated imaging analysis software are needed to confirm and extend our observations.

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