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A Case Series of Reactivation of Fungal Ball in the Patients with Covid-19 Pneumonia: Awakening of A Titan

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Abstract

Background: Due to the use of immunosuppressants and immune modulator property of the corona virus, co-infections are proportionately increased in the second wave of Covid-19 infection. Aspergillosis is an air-borne opportunistic fungal pathogen that primarily affects immunocompromised hosts.

Method and results: We studied ten patients who had severe Covid-19 infection with superimposed pulmonary Aspergillosis. All these patients had an old history of tuberculosis. All of these patients were managed as per standard Covid-19 protocol and were on immunosuppressants. Sugar level was found to be deranged during the course of management. Fungal culture and galactomannan test from the respiratory specimen was done to help diagnosed these cases early. Computed Tomography (CT) scan was highly sensitive and demonstrated large thick-walled cavitary lesions with internal soft tissue density and several other supportive findings such as air crescent, reverse halo sign and ground-glass densities to ascertain the early diagnosis.

Conclusion: Myriads of Co-infections are associated with Covid-19 infection leading to significant morbidity. Early diagnoses of co-infections are thus essential to modulate the management. CT scan proved to be an essential tool not only to measure the severity of Covid-19 infection, but also in diagnosing associated co-infections. It is also advised to keep an eye for the possibility of the reactivation of the pulmonary Aspergillosis in a Covid-19 patient who presents with severe breathlessness.

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Introduction

Aspergillosis is a mycotic disease led by Aspergillus species, usually A. fumigatus. Aspergillus is an air-borne opportunistic fungal pathogen that predominantly acts on immunocompromised hosts. The Aspergillus species are omnipresent in the environment and typically do not cause any human pathology, providing that the lungs are structurally healthy and the host immunity is unharmed. If either of these is impaired, then there is a probability that this otherwise benign fungus may become pathological. The clinical, histological, and radiological demonstration of pulmonary Aspergillosis is intended by the number of organisms, organisms' virulence and the patient's immune response.

Pulmonary Aspergillosis can be segregated into five categories: (a) aspergilloma (saprophytic Aspergillosis), (b) allergic bronchopulmonary Aspergillosis, which is a type of hypersensitivity reaction, (c) semi-invasive (chronic necrotizing) Aspergillosis, (d) air-way-invasive Aspergillosis (acute tracheobronchitis, bronchiolitis, bronchopneumonia, obstructing bronchopulmonary Aspergillosis), and (e) angioinvasive Aspergillosis.

Saprophytic Aspergillosis (aspergilloma) is illustrated by Aspergillus infection without tissue encroachment. It usually gives rise to the accumulation of inter-twined fungal hyphae mixed with mucus and cellular fragments within an earlier pulmonary cavity or ecstatic bronchus. Tuberculosis and sarcoidosis are the most common underlying causes. At radiography, mycetomas are characterized by a solid, round or oval mass with soft-tissue opacity within a lung cavity. Commonly, the mass is segregated from the cavity wall by air space of variable size and shape, resulting in the "air crescent" sign.

Airway-invasive Aspergillosis is characterized at histologics interpretation by the presence of Aspergillus organisms deep to the airway basement membrane. It occurs most typically in immunocompromised neutropenic patients and patients with AIDS. Clinical presentation includes acute tracheobronchitis, bronchiolitis, and bronchopneumonia.

In recent times, Covid-19 has escalated the threat for invasive fungal Aspergillosis, and we establish that Aspergillus species can cause co-infection in a patient with Covid -19, especially in severe/critical illness.

The radiologist plays a considerable part in the opinion of pulmonary Aspergillus infection.

Case presentation and imaging findings

This descriptive observational study includes ten cases with severe Covid-19 infection. All ten cases were between 30-40 years of age and were RT-PCR positive with an old history of tuberculosis, presented with severe respiratory distress. The patients were supervised as per standard Covid-19 guidelines and were on immunosuppressants. Their diabetic status was not known; however, sugar level was found deranged during the course in the ward. Non-contrast Computed Tomography (CT) thorax was done in all ten patients.

CT scan showed Covid-19 findings as ground-glass densities in peripheral and basal distribution, being the most usual finding, a ground-glass pattern in amalgam with thickened interlobular and intralobular lines (crazy paving). Vascular dilatation, and traction bronchiectases and in some cases architectural abnormality with the formation of subpleural bands were also noted (Figure 1).

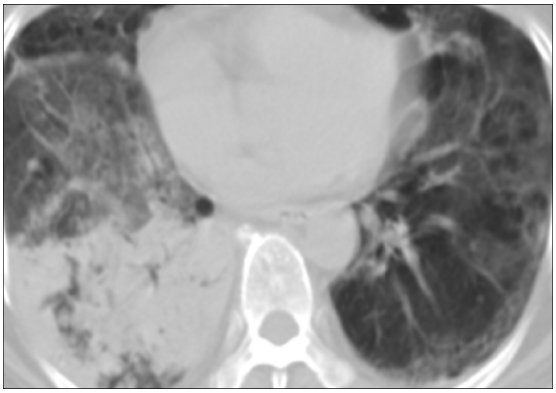

Figure 1: Axial thin-section chest CT in lung window shows right lower lobe consolidation (white arrow) with surrounding ground glass densities (black arrow). Peripheral ground glass densities are observed in left lung fields suggesting Covid-19 infection.

In seven cases, internal round shaped soft tissue density was noted in the dependent position of the cavity, forming the air crescent sign (Figure 2). CT scan demonstrated common finding as a rounded mass within a large thick-walled, cavitatory lesion with adjacent consolidation and nodular opacities seen segregated from ground glass density in Covid-19. In the prone position, this soft tissue density was received on the dependent position (Figure 3 and 4). In three cases, central ground-glass densities surrounded by denser consolidation of crescentic shape was noted, forming reverse halo sign (Figure 2).

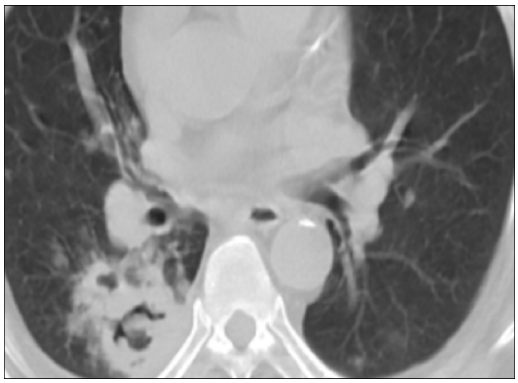

Figure 2: Axial unenhanced thin-section of chest CT images shows the classical appearance of an aspergilloma (white arrow) (well-formed cavity with a central soft tissue attenuating rounded mass surrounded by an air crescent sign).

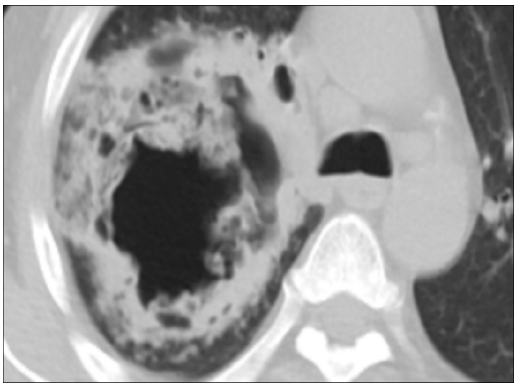

Figure 3: Axial section from high-resolution chest CT images shows thick walled cavitating lesion with surrounding consolidation (black arrow). Characteristic air- inclusions without fluid levels.

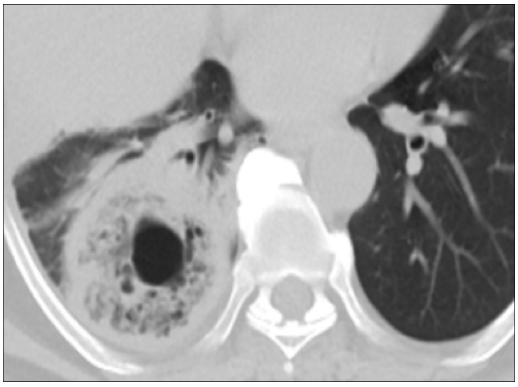

Figure 4: Axial unenhanced chest CT images shows thick walled cavity with surrounding consolidation and invasion.

Out of ten patients, three patients displayed centrilobular nodular opacities, placed in linear branching arrangement forming tree in bud appearance in distant sites such as various lobes of the ipsilateral lung and contralateral lung indicative of the air-way-invasive aspergillosis (Figure 5 and 6).

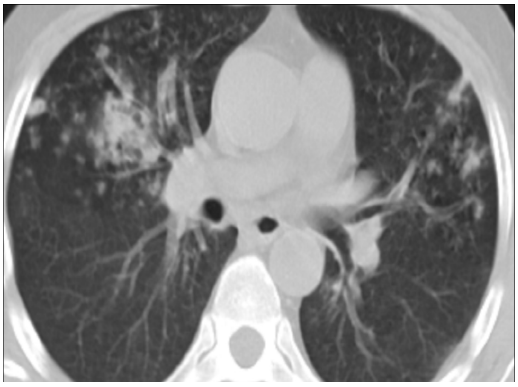

Figure 5: Axial section from chest CT images shows multiple nodular densities in bilateral para cardiac lung fields developing into consolidations.

Figure 6: Axial unenhanced thin-section chest CT images show the classical appearance of a reactivated aspergilloma (white arrow). (Irregular thick-walled cavity with a central soft tissue attenuating rounded mass with internal air foci and surrounding consolidation). Ground glass densities are also depicted in bilateral visualized lungs in basal and peripheral distribution (black arrow).

Discussion

Coronavirus was first found in 1960 and is a class of enveloped RNA virus (single-stranded) [1]. Based on their genetic make-up and morphology, they are categorized into Alpha, Beta, Gamma, and Delta coronavirus [2]. The Alpha and Beta variants of this virus infect humans by affecting the respiratory and gastrointestinal systems; the rest of the two variants affect birds. Symptom includes shortness of breath, cough, fever, loss of taste, and generalized weakness.

During the second wave of Covid-19, it was stated that affected patients had superimposed fungal infections. The most usual fungal pathogen, which caused superimposed infection, was the aspergillosis species. The most typical presentation of patients affected by Aspergillus species was the formation of aspergilloma, allergic bronchopulmonary aspergillosis and invasive pulmonary aspergillosis, tracheobronchial and chronic pulmonary aspergillosis [3]. Aspergilloma is a fungal ball that derives in preformed thick-walled cavities. Initially, patients with accidental findings on chest radiography were asymptomatic, although they can progress to hemoptysis due to vascular damage caused by mechanical effects of the fungus ball and fungal toxins [3]. Allergic bronchopulmonary aspergillosis is triggered due to hypersensitive reaction to Aspergillus species antigens, usually noticed in steroid-dependent asthmatics and cystic fibrosis patients [3].

Invasive aspergillosis occurs mainly due to Aspergillosis sp invading through tissue and blood vessels into the bloodstream and infecting distant tissues, including the heart, brain, and eyes, and it is the most dangerous form of pulmonary aspergillosis. It usually occurs as a superimposed infection in severe influenza pneumonia [4]. It is a well-known complication of immunocompromised patients, especially with haematological malignancies. There are sporadic cases of invasive aspergillosis described in conjunction with Covid-19 infection [5].

Tracheobronchial aspergillosis is rare, typically and exclusively encountered in lung and heart-lung transplant patients at the bronchial anastomotic sites. Chronic pulmonary aspergillosis comprises chronic cavitation, subacute IPA, and chronic fibrosing. The chronic pulmonary aspergillosis is accompanied by new cavity formation, although without surrounding lung parenchyma invasion. Chronic cavitary pulmonary aspergillosis is lesser invasive than subacute IPA. They are typically seen in patients with immunosuppression and arise within a thin-walled cavity. In disparity to aspergilloma, subacute IPA destroys surrounding lung tissue. Extensive fibrosis around the cavity is usually seen in conjunction with chronic fibrosing type [3].

Pulmonary aspergillosis mainly affects structurally abnormal lungs with preceding thin-walled well-formed cavities [6]. They mainly involve the posterior segment of the upper lobe and the superior segment of the lower lobe. Pulmonary TB is one of the most common risk factors for pulmonary aspergillosis. Other common preexisting conditions linked with pulmonary aspergillosis are pulmonary sarcoidosis, bronchiectasis, and other pulmonary cavities (e.g., bronchogenic cysts) [7].

These cavities were noted on a prior chest radiograph or CT scan on the admission of these Covid-19 patients, suggesting the latent infection with the fungus. During the course of Covid-19 pneumonia, these cavities become thick-walled with surrounding consolidations and nodular densities. As with any other bacterial or fungal infection, superimposed infection with pulmonary aspergillosis significantly increases morbidity and mortality, primarily when associated with conditions like Covid-19.

Conclusion

During this Covid-19 pandemic, pulmonary aspergillus can cause superimposed infection in a patient with SARS-CoV-2 de-

spite not having a traditional risk factor of aspergillus infection. The outcome of Covid-19 associated pulmonary aspergillosis is poor and cautious use of an antifungal agent is recommended to avoid complications like drug-drug reaction and adding cardiovascular toxicity to the anti-SARS-CoV-2 agent. CT scan is the ideal modality for diagnosis of this superadded infection.

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