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Case Series

Lung Cavities: Looking Beyond Tuberculosis

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I N F O

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A B S T R A C T

The spectrum of infectious and non-infectious processes associated with pulmonary cavities is vast. In a high-prevalence country like ours, it is natural albeit presumptive, to jump to the diagnosis of Tuberculosis especially when the clinical case definitions of a 'suspect' attribute 2 weeks of fever and cough with suggestive radiology to it. We have described three cases that came to us with the clinical picture of sputum-negative tuberculosis and with a lung cavity on chest X-ray. None of the primary pathogens isolated in them was *Mycobacterium*. Through this short case series, we emphasise the larger point, the need to reach a microbiological confirmation and the realization that not all that cavitates is TB.

Keywords: Lung Cavities, Prevalence, Tuberculosis, BAL

Introduction

As per the Global Tuberculosis Report of 2018, there are about 10 million incident cases of tuberculosis, which are equivalent to 133 cases per 100,000 population.[1]

In TB, the prevalence of cavities on plain chest radiographs is widely variable, but most case series report 30 to 50% of patients having cavitation. Multiple cavities are often present and frequently occur in areas of consolidation.[2,4] However, a lung cavity can be caused by protean pathological processes covering both infectious and non-infectious aetiologies. The aetiology in most hospitalised patients is diagnosed on sputum smear and culture examination. Out of them, the majority respond to the standard treatment. However, a proportion of patients fail to respond to initial therapy and require additional investigations like bronchoscopy, broncho-alveolar lavage, protected brush specimen, and/or trans-bronchial lung biopsy, and FNAC for diagnosis. We are discussing 3 cases where the etiological diagnosis was obtained after a detailed investigation where the presumptive clinical picture was pointing towards sputum-negative tuberculosis, while the CECT chest findings were suggestive of cavities and necrotizing pneumonia.

There is a need to further report such cases as our clinical judgments often get clouded by what is most commonly seen, even to the point of avoiding further evaluation. Such case reports and case series serve to prove that many times empirical therapy has to stand aside for evidence-based medicine.

Case Reports

Case 1

A 52-year-old gentleman presented with a fever for 15 days, cough for 15 days and breathlessness for 5 days. His fever was low grade with no associated chills rigours, evening rise, or night sweats. The cough was productive with around 50-60 mL of yellowish purulent expectorant which occasionally was also black in colour. There was no haemoptysis. Breathlessness had progressed over the past 5 days to make him uncomfortable even at rest. In the past, the patient had lost 12 kilograms of weight in just one month and had recently been diagnosed as a diabetic,

in the OPD evaluation, 4 days before his admission to our hospital. He was a reformed smoker and worked in manufacturing on a lathe machine.

On general examination, he had a pulse rate-110/min, Blood Pressure (BP) of 110/70 mmHg, Respiratory Rate (RR) of 25/min, SpO_2-88% on room air, and 98% with oxygen. There was no lymphadenopathy. On respiratory system examination, there was a dull percussion note and bronchial breath sounds were heard in the right infrascapular and left inframaxillary areas. The rest of the systems were normal on examination.

Investigations showed a raised WBC count of 20700/mm^3 with 90% polymorphs and 10% lymphocytes, ABG analysis showed a type 1 respiratory failure with pO_2 = 54.7mmHg. Other blood investigations such as the KFT and LFT were normal. The patient had deranged blood sugars and an HbA1c of 11.2. Chest X-Ray showed a cavitary lesion in the right middle zone (Figure 1). Following this, CECT Chest showed multiple cavitary lesions of intermediate wall thickness containing fluid with adjacent areas of ground glassing, consolidation, and nodules (Figure 2).

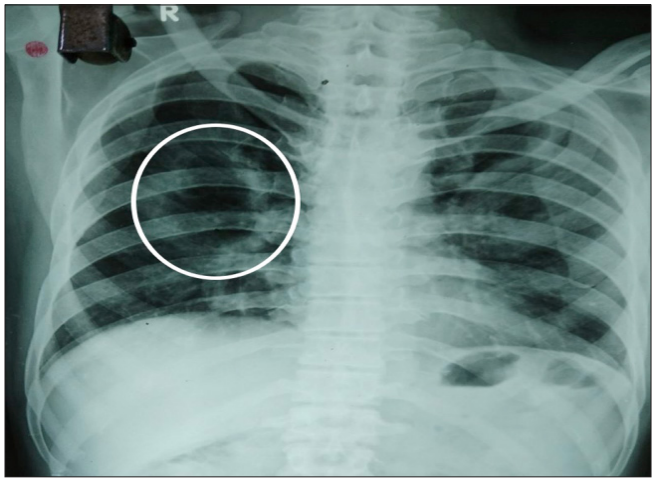

Figure 1.Cavity in the Right Middle Zone

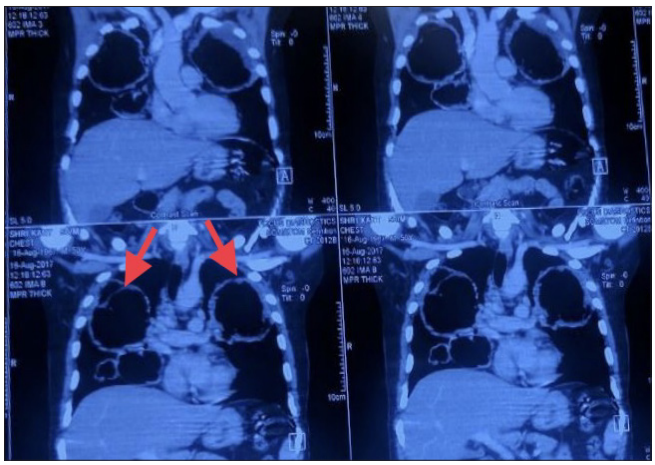

Figure 2.Bilateral Cavities

In further evaluation, his sputum studies were negative for AFB on ZN stain and for bacteria on Gram stain. Fungal culture and modified ZN stain were also negative. cANCA, HIV, HBsAg, and Aanti-HCV were all negative. Serum galactomannan was 0.3.

Video Fibre Optic Bronchoscopy (VFOB) and Broncho Alveolar Lavage (BAL) were done. The Right bronchial tree was inflamed and there were purulent secretions from the middle lobe. The Left bronchial tree was also inflamed with purulent secretions from the left upper lobe. BAL fluid galactomannan was 0.7. BAL fluid on Gram stain and culture showed *Burkholderia cepacia*.

This patient at admission had empirically been started on ceftriaxone and clindamycin covering most pneumonia-causing organisms and Insulin to control blood sugars. After the BAL fluid culture and sensitivity report, he was put on Septran and cefoperazone/ sulbactam for 2 weeks. He improved symptomatically, TLC dropped to 11400/mm^3 and type 1 respiratory failure had improved on discharge.

Case 2

A 50-year-old gentleman presented with complaints of cough for 15 days and fever for 10 days. The cough was productive with scanty, yellow, mucoid sputum and there was a history of one episode of hemoptysis a few days back. The fever was high grade, continuous but not associated with chills or rigours or any evening rise of temperature. There was no history of weight loss. He was a known diabetic, with hyperthyroidism and hypertension, on regular medications. On general examination, the patient was pale and vitals were normal. There was no lymphadenopathy. On respiratory system examination, there was a dull percussion note and bronchial breath sounds in the left infrascapular, mid-axillary, and infra-axillary areas.

The investigations showed that the haemoglobin was 8.4 g/dL, TLC 16000/mm^3, DLC 85% polymorphs, 13% lymphocytes, and 2% eosinophils. ESR was 14mm/hr and RBS was 236 mg/dL. His HbA1C was 10.7. Sputum studies were negative for gram stain and culture, AFB, and fungal culture. Serum galactomannan was 0.2. Chest X-ray (Figure 3) was suggestive of consolidation with a cavity in the left middle zone and lower zone. CECT chest (Figure 4) showed subcentimetric and borderline enlarged mediastinal lymph nodes with a large thick-walled peripherally enhancing cavitary lesion with surrounding patchy consolidation likely abscess in the left lower lobe.

We went ahead with FOB and BAL fluid analysis was done. This was negative for AFB, fungal culture, and modified ZN stain. BAL fluid galactomannan was 0.9. But here again, gram stain and culture showed *Pseudomonas aerogenosa*. Post-BAL sputum studies were again sent and this time, they were positive for AFB.

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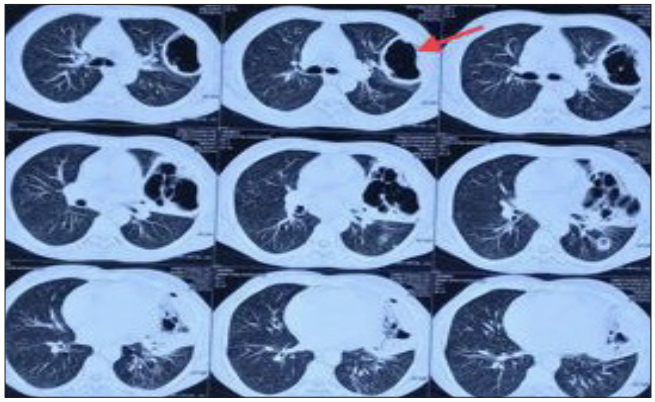

Figure 3.Consolidation and Cavity in Patchy Left Middle Zone and Lower Zone

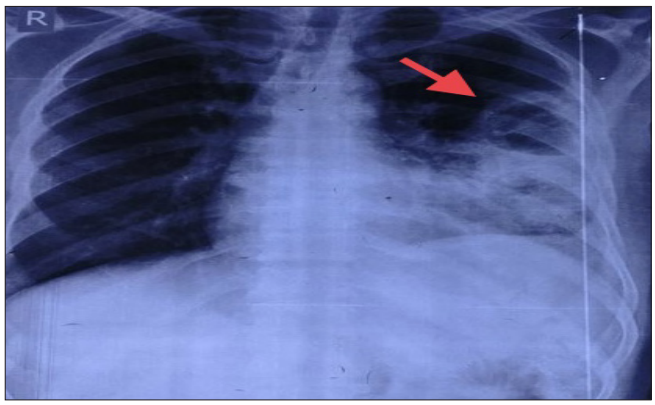

Figure 4.Cavitary Lesion with Surrounding Consolidation Likely Abscess in the Left Lower Lobe

The patient had been initially started on piperacillin/tazobactam with levofloxacin and insulin. This was changed to meropenem according to the BAL fluid sensitivity report for *Pseudomonas*. Patient symptoms improved and TLC normalised. He was started on ATT after detecting AFB in post-BAL sputum and discharged.

Case 3

A 47-year-old gentleman presented with a cough for 1 month and a fever for 20 days. The cough was productive with copious and black-coloured sputum. There was no haemoptysis. Fever was high grade, associated with chills and rigours, and with an evening rise of temperature. There was a significant weight loss of 15 kgs in the last 2 months. There was also a history of contact with a case of sputum-positive pulmonary Koch's, the patient's father, who was still on ATT. There were no previously known co-morbidities in the patient.

On examination, the patients had a pulse rate of 110/min, BP of 128/74 mmHg, RR 24/min, SpO_2 86% on Room air, and 96% with Oxygen supplementation. On respiratory system examination, there were reduced breath sounds in the left infrascapular and inframaxillary areas. Other systems were within normal limits.

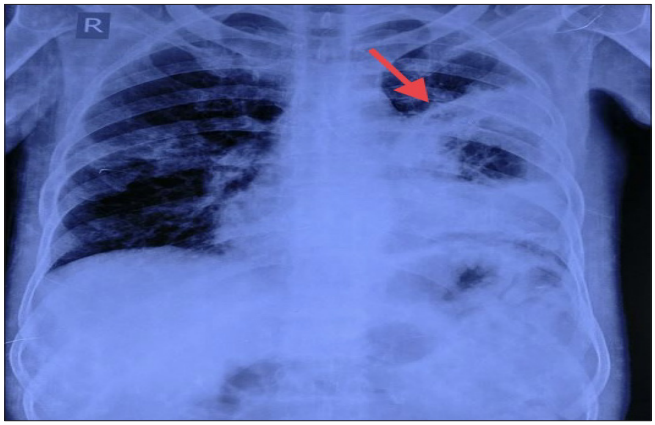

Figure 5.A Cavitary Lesion in Left Middle Zone with Surrounding Homogenous Opacity

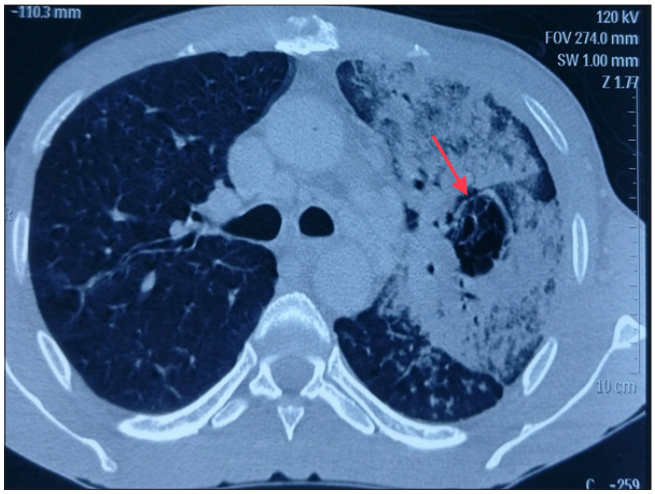

Figure 6.A Thick-walled Cavity with Thick Fluid Collection Surrounded by Areas of Consolidation

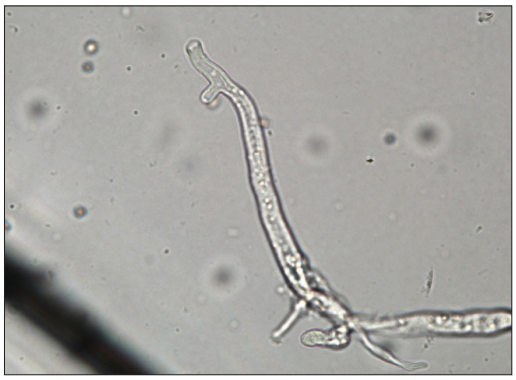

Figure 7.Aseptate Hyphae of Rhizopus Oryzae on Microscopic Examination

On investigations, his RBS was 487 mg/dL but ABG was suggestive of only type 1 respiratory failure and no acidosis. Urine for sugar was positive and negative for ketones. His Hb was 14.4g/dL, TLC 30,400/mm^3 with DLC of 85% polymorphs, 10% lymphocytes, and 5% eosinophils. KFT and LFT were normal. HIV, HBsAg, and anti-HCV were non-reactive. Serum galactomannan was 0.8. Chest X-ray (Figure 5) showed a cavitary lesion in the left middle zone

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with surrounding homogenous opacity. CECT chest (Figure 6) showed a thick-walled cavity with thick fluid collection surrounded by an area of consolidation and tree in bud appearance. Sputum studies were negative for Gram stain and culture sensitivity, AFB, and fungal stain.

On VFOB and BAL, Lt bronchial tree showed black-coloured thick secretions with areas of destroyed lung parenchyma in the left lower lobe. Blood-mixed purulent material was aspirated. Bronchial aspirate was negative for gram stain and culture, AFB, and modified ZN stain. BAL fluid galactomannan was 1.27. BAL fluid fungal stain showed a smear full of fungal hyphae and on fungal culture - *Rhizopus oryzae* was grown Figure 7.

At admission, the patient was started on piperacillin/tazobactam, clindamycin, and insulin. The patient's fever, TLC, and respiratory failure improved, but he continue to produce copious amounts of sputum. He was started on liposomal Amphotericin B following which there was a reduction in sputum production but unfortunately, on day 15 of the hospital stay, he had one episode of massive hemoptysis and succumbed to his illness. Table 1 shows the clinical profile along with the outcome of the cases.

Table 1.Clinical Profile and Outcome of the Cases

Clinical Profile	Case 1	Case 2	Case 3
Age (years)	52	50	47
Comorbidities	Diabetes	Diabetes Hypertension Hyperthyroidism	Diabetes
Chief Complaints	Fever Cough Breathlessness	Fever Cough	Fever Cough
Cavity on Chest X-ray	Single, in the Right Middle Zone	Single, in the left lower zone	Single, in the Left Middle Zone
CECT Chest	Multiple Cavities Containing Fluid with Adjacent Areas Consolidation	Borderline Enlarged Mediastinal Lymph Nodes, A Large Thick-Walled Peripherally Enhancing Cavity with Surrounding Patchy Consolidation Likely Abscess in the Left Lower Lobe	Thick-Walled Cavity with Thick Fluid Collection Surrounded by Areas of Consolidation and Tree in Bud Appearance
Organism Isolated	*Burkholderia cepacia*	*Pseudomonas aeruginosa* and AFB	*Rhizopus oryzae*
Specific Treatment	Septran and Cefoperazone/ Sulbactam	Meropenem and ATT	Amphotericin B
Outcome	Recovery	Recovery	Death

Discussion

A lung cavity can be caused by protean pathological processes including suppurative necrosis (e.g., pyogenic lung abscess), caseous necrosis (e.g., tuberculosis), cystic dilatation of lung structures (e.g., ball valve obstruction and *Pneumocystis* pneumonia), ischemic necrosis (e.g., pulmonary infarction), or displacement of lung tissue by cystic structures (e.g., *Echinococcus*).[5] Additionally, malignancies may also cavitate.[6,7]

According to the Global Tuberculosis Report 2018, there are an estimated 10 million incident cases of tuberculosis, equivalent to 133 cases per 100,000 population.[1] There are a significant number of national and international programs targeting its elimination. India particularly is home to 27% of the global burden. The estimated incidence of tuberculosis in India is 204 per 100,000 population in 2017.[1] With this background, a lung cavity with a history of fever, cough lasting more than 2 weeks, and weight loss become subjected to inadvertent bias towards Tuberculosis, particularly in primary healthcare, OPD, and resource-poor setting.

In TB the prevalence of cavities on plain chest radiographs is widely variable, but most case series report cavitation in 30 to 50% of patients. Multiple cavities are often present and frequently occur in areas of consolidation.[2,4] Cavities can be variable in size and can have both thick and thin walls.[2,8,9]

However, TB is not the only infection that cavitates. As a general rule, organisms that cause subacute or chronic pulmonary infections (e.g., mycobacteria and fungi) are more frequently associated with cavities than organisms that cause acute pulmonary infections (e.g., viruses and *S. pneumoniae*). There are some exceptions to this norm such as necrotizing pneumonia associated with *Staphylococcus aureus* and *K. pneumoniae*.

Thus, it would serve us well to seek microbiological reaffirmation in every tuberculosis suspect and even in

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those diagnosed clinically with TB. As we have seen, in all three of the above cases, the responsible organisms were isolated on BAL, even though the sputum studies sent were normal.

BAL, performed during fiberoptic bronchoscopy, is a useful diagnostic adjunct to lung biopsy for non-neoplastic lung diseases. In localised disease, lavage of the involved segment is likely to yield the best results. In diffuse disease, the right middle lobe or lingula is lavaged most commonly. BAL fluid should be transported to the lab on ice but can be stored or transported at room temperature if processing occurs in less than 1 hour. The cells in BAL fluid remain viable for up to 4 hours when stored at 25°C. BAL allows sampling of innate (lung macrophage), cellular (B-and T-cells), and humoral (immunoglobulin) responses within the lung. It allows the safe sampling of the distal lung for specific pathogens in patients unable to expectorate diagnostic sputum.

There is an increased sensitivity and specificity (60% and 90% respectively) to diagnose AFB in BAL fluid when sputum is negative for AFB. BAL has been used to detect antigens causing fungal infections increasing the diagnostic yield and the inflammatory cells in BAL fluid are examined to detect ILD.

A point to emphasize is the relevance of post-bronchoscopy sputum studies. There has been a noted increase in yield as seen in the second case. This has been previously reported in a retrospective study of 236 patients who were smear-negative for AFB, post bronchoscopy 33.3% converted to sputum positive and 8.8% were exclusively positive in post-bronchoscopic sputum examination. The AFB culture yield increased by 7%. Thus, PBS analysis can provide a simple rapid way of diagnosing PTB.[10]

In our first case, *Burkholderia cepacia*, an aerobic gram-negative bacillus, was isolated. It is a frequent colonizer rather than an invader and is described usually in patients with cystic fibrosis or chronic granulomatous disease, with a fatal outcome. Outside hospital acquisition of this infection suggests environmental exposure. There are only a few cases reports on cavitary lung lesions in non-cystic fibrosis patients.[11]

The second organism isolated was *Pseudomonas* aeruginosa. It is an opportunistic pathogen. It is highly fulminant with the mortality rate with CAP reported to being around 61.1%.[12] It occasionally induces rapid and progressive tissue destruction, leading to the formation of cavitary lesions and abscesses.[13] Therefore, early diagnosis and treatment make all the difference in this disease.

The third case was of zygomycoses. Zygomycoses refers to the infection caused by saprophytic fungi of the Zygomycete family- Rhizopus, Mucor, Cunninghamella, Apophysomyces, and Absidia. Zygomycetes are also opportunistic pathogens. Patients usually present with acute onset of cough, and fever and less frequently with hemoptysis. Pulmonary disease is the most common manifestation of zygomycosis in patients with underlying malignancy, while diabetics and patients with other risk factors more frequently present with extrapulmonary disease.[14] Pulmonary infiltrates are usually found on chest radiographs, with cavitation noted in 26 to 40% of cases.[15,16]

Conclusion

In conclusion, we would like to draw attention to the fact that not all cavitates, even in the clinical setting of fever with evening rise, cough, and weight loss needs to be tuberculosis. This is of particular relevance in the setting of diabetes mellitus. Bronchoscopy and BAL fluid analysis and even a post bronchoscopy sputum analysis must be encouraged to isolate an incriminating organism in those who are sputum negative for AFB. Also one should not hesitate in going ahead with further diagnostic procedures even if you have isolated one organism because chronic cavitary lesions might harbour secondary bacterial pathogens while the primary aetiology is a tubercular or fungal infection. This needs to be emphasised in a patient with an immunocompromised state.

So, reaching a microbiological diagnosis should be aimed at all patients. Although it was a small case series it clearly brings out the importance of detailed workup and isolation of specific microorganisms. Further studies with larger sample sizes are needed to prove this with statistical significance.

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Conflict of Interest: None

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