ISSN 2664-3987 (Print) & ISSN 2664-6722 (Online)
South Asian Research Journal of Medical Sciences
Abbreviated Key Title: South Asian Res J Med Sci

| Volume-5 | Issue-2 | Mar-Apr -2023 | **DOI: 10.36346/sarjms.2023.v05i02.006**

Review Article

Cavitating Consolidation with Acute Febrile Respiratory Illness & 'Sister Cavities' Without Typical Constitutional Symptoms in Pulmonary Tuberculosis: A Rare But Possible!

Shital Patil[1*], Shubham Choudhari[2], Jayashree Dahiphale[2], Jayashree Dahiphale[2], Sanika Narkar[2], Vipul Raka[2], Gajanan Gondhali[3]

[1]Associate Professor, Pulmonary Medicine, MIMSR Medical College, Venkatesh Hospital, Latur, India
[2]Junior Resident, Internal Medicine, MIMSR Medical College, Latur, India
[3]Professor, Internal Medicine, MIMSR Medical College, Latur India

***Corresponding Author:** Shital Patil
Associate Professor, Pulmonary Medicine, MIMSR Medical College, Venkatesh Hospital, Latur, India

Article History
Received: 13.03.2023
Accepted: 25.04.2023
Published: 29.04.2023

Abstract: Community acquired pneumonia is the most common cause for lung parenchymal infiltrates in chest radiograph in scenarios with acute febrile respiratory illness. Tuberculosis in India accounts for the highest number of cases and deaths in the world. In spite of an efficient National tuberculosis control program for five decades, Tuberculosis is still the number one cause of death due to infectious agents in India and one third of total global deaths occurs in India due to this disease. Tuberculosis may present with consolidation, cavitation, coin lesion, parenchymal infiltrates and hilar mass like lesions. Acute febrile respiratory illness without typical constitutional symptoms is not frequently described in pulmonary tuberculosis. In this case report, a 69-year male, presented with acute febrile respiratory illness of short duration. He was having high grade fever, cough, shortness of breath & haemoptysis of less than two weeks duration. His symptoms were progressive and empirically treated as lower respiratory tract infection or community acquired pneumonia with oral and intravenous antibiotics by general physicians and family physicians. Family physician referred to our center for worsened general health with increased shortness of breath with episodes of minimal haemoptysis. Chest x-ray documented right lower lobe consolidation which has progressed to central cavitations and thick pericavitary rim of consolidation mimicking lung abscess. Clinically he was having crepitations in the right inframammary and infrascapular area with egophony heard. HRCT thorax showed consolidation with cavitation in the superior segment of the right lower lobe and adjacent small cavity in the posterior segment presenting as a 'Sister cavity' accompanying a large parent cavity. He was unable to produce sputum and we have processed induced sputum examination which has documented acid-fast bacilli in smear and MTB genome with rifampicin sensitivity in cartridge based nucleic acid amplification test. Initially, microbiologists refused for smear preparation due to salivary nature and poor-quality sputum. We have insisted for microbiology workup due to high chances of yield due to cavitary lung disease and noted positive yield. Treatment initiated with anti-tuberculosis (ATT). We have recorded near complete radiological resolution, bacteriological cure after eight months of ATT with good compliance. Acute febrile respiratory illness and absence of typical constitutional symptoms is not uncommon. Although cavitating consolidation is commonly described in community acquired pneumonia, presence of 'sister cavity' is a radiological clue to think and proceed to workup towards active pulmonary tuberculosis. Induced sputum has a very significant impact on diagnostic yield. Pulmonary tuberculosis should be suspected early in cases with cavitating consolidations to have a successful treatment outcome.

Keywords: Pulmonary Tuberculosis, Induced sputum, Sister cavity, Pulmonary Cavity, acute febrile respiratory illness, AFB, Gene Xpert MTB/Rif.

INTRODUCTION

Tuberculosis (TB) continues to be a major threat to global health. Cavitation is a dangerous consequence of pulmonary TB associated with poor outcomes, treatment relapse, higher transmission rates, and development of drug resistance. However, in the antibiotic era, cavities are often identified as the extreme outcome of treatment failure and are

one of the least-studied aspects of TB [1]. Pulmonary tuberculosis can have diverse presentations ranging from cavitation, consolidation, tumorous lesions, coin lesions, lower lung filed tuberculosis and endobronchial and miliary nodules [2-12]. Similarly, non-tuberculous pathologies can present with abnormalities such as consolidations, nodules, cavitations mimicking tuberculosis [2-14]. Bronchoscopy is a very crucial interventional pulmonology technique in evaluating these cases [2-14]. High risk factors for tuberculosis would be advanced age, malnutrition, pregnancy, steroids exposure, diabetes mellitus and immunosuppression [9-14]. Tuberculosis in advanced stage may cause cardiac dysfunction and systemic effects which will have poor outcome if timely treatment not received [15-17]. Final outcome in delayed treatment initiation may lead to destroyed lung as post tuberculosis sequel and proportionate number of cases may have lung function abnormalities irrespective of radiological outcome [18-20]. Tuberculosis may be misdiagnosed due to confusing or overlapping clinical and radiological features in high burden setting like India [21-25]. In present case report we have reported advanced pulmonary tuberculosis with delayed diagnosis due to lack of awareness in patient, accompanying relatives and care takers and family physicians to symptoms, available diagnostic modalities and universally acceptable and freely available treatment options for tuberculosis as per NTEP program in India.

CASE SUMMARY:

69-year-old male, farmer by occupation, tobacco addict, normotensive and non-diabetic with history of acute febrile respiratory illness of two weeks duration referred by family physician for further treatment.

Further clinical details-

1. Fever for two weeks high grade with chills and rigors associated with headache and bodyache, continuous, responding to antipyretics
2. Cough for one week, dry, intermittent, no diurnal or postural variation, with minimal hemoptysis.
3. Shortness of breath for five days before hospitalization.
4. Hemoptysis intermittent with minimal chocolate brown sputum for 3 days before hospitalization

No history of any chronic constitutional symptoms and no history of weight loss or anorexia in recent past. He was treated with oral antibiotics for 10 days by family physician and day care admission with intravenous antibiotics for 3 days before referral to our center. He has taken chest x-ray on day seven and day fourteen of symptoms. First chest x-ray taken after oral medicines and symptoms of one week. He was offered oral antibiotics and cough suppressant for a tend days. His symptoms were partially responding to oral antibiotics with persistent fever. Then treating physician decided to start intravenous antibiotics consisting beta-lactum and macrolides for three days. His symptoms worsened over three days and developed new symptoms as hemoptysis. We have reassessed his chest x-ray and documented progressive lung parenchymal abnormality with clinical worsening.

Chest x-ray documented- (Image 1 & 2)

1. Right lung parenchymal homogenous opacity in middle and lower zone with normal left lung parenchyma and hilum both sides (Image 1).
2. Radiological worsening documented as central lucency resulting into cavitation in consolidation of right middle and lower zone (Image 2).
3. Consolidation with cavitation also called cavitating consolidation in right middle and lower zone with normal lung parenchyma in right upper lobe and left lung (Image 2).
4. Hilar opacity in right side of thorax (Image 1 & 2).
5. Normal cardiac silhouette and central mediastinum (Image 1 & 2).

Cavitating consolidation is defined as are of central lucency in consolidated lung parenchyma with or without fluid level i.e., cavitation surrounded by homogenous opacification with or without air bronchogram.

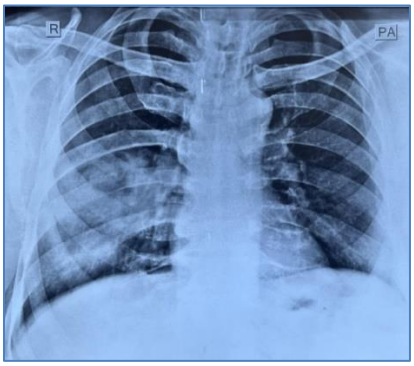

Image 1: Chest x-ray PA showing consolidation in right middle and lower zone

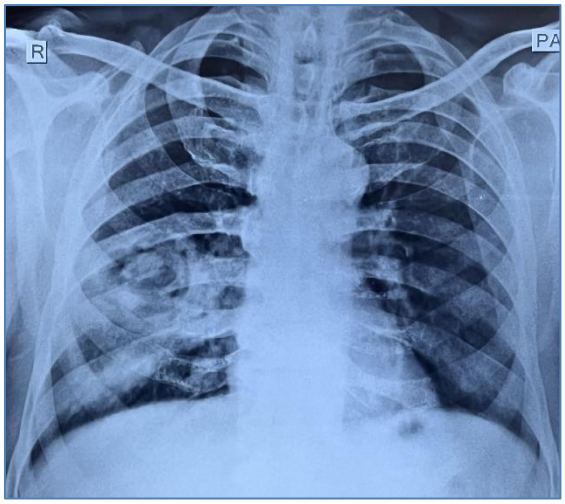

Image 2: Chest x-ray PA showing cavitating consolidation in right middle and lower zone

Clinical examination documented as-

Thin built, febrile, no pallor or cyanosis or clubbing.
Heart rate-118/min Respiratory rate: 24/bpm, BP-90/60 mmhg
PsO2: 90% resting & 88% on routine walk @ room air
Respiratory system examination revealed- coarse crepitation with decreased breath sounds in right intrascapular and lower axillar & inframammary area. Decreased vocal resonance on auscultation in right inframammary, intrascapular and lower axillary area.
Cardiovascular, gastrointestinal & nervous system examination were normal.

Laboratory Examination during hospitalization documented as-

Hemoglobin-11.0 gm% total white blood cells- 19000/mm3 Polymorphs-90%, Platelet count-270000/uL
CRP- 145 mg/L (0-6 mg/L), random blood sugar level-134 mg% HbA1C-5.60 %
LDH-790 IU/L (70-470 IU/L)
Serum electrolytes: Sodium-131 meq/L (135-145 meq/L) Potassium-3.7 meq/L (3.5-5.5 meq/L) Ionic calcium-1.39 meq/L (1.09-1.36 meq/L)
D-dimer-780 ng/ml (<500 ng/ml)
IL-6-26.98 pg/ml (0.00-7.00 pg/ml)
Serum creatinine-1.1 mg/dL (0.7-1.4 mg/dL)
Liver function tests- normal
Thyroid functions-normal
ECG was showing sinus tachycardia.
Pro-BNP- 96 pg/ml (<125 pg/ml)
CPK-MB- 10.33 IU/L (0-25 IU/L)
Trop-I- (cardiac troponin)-.12 ng/L (0-19 ng/L)
COVID-19 RT PCR test and results documented Negative for SARS-CoV-2
Viral markers such as HIV-II and HIV-II antibody negative and Australia antigen negative
We have done HRCT thorax with contrast for cavitating consolidation in right lower lobe.

HRCT Thorax documented as- (Image 3 & 4)

1. Thick-walled cavity of size 3cmx4cm in superior segment of right lower lobe. Wall is thick, margins are smooth, contains minimal air fluid level. Pericavitary consolidation and satellite nodules are also seen randomly distributed in right lower lobe basal segment (Image 2).
2. 'Sister cavity' is also seen in posterior segment of right upper lobe. Sister cavity is defined as small sized lung cavity developed on same side of thoracic cavity containing large pulmonary cavity with radiological signs of active pulmonary tuberculosis. Sister cavities are very frequently observed in pulmonary tuberculosis which is marker of advanced pulmonary tuberculosis (Image 3 & 4).
3. Thick pleural based cavity in right lower lobe. Left lung parenchyma, mediastinal structures such as pulmonary vessels and lymph nodes are normal (Image 4).

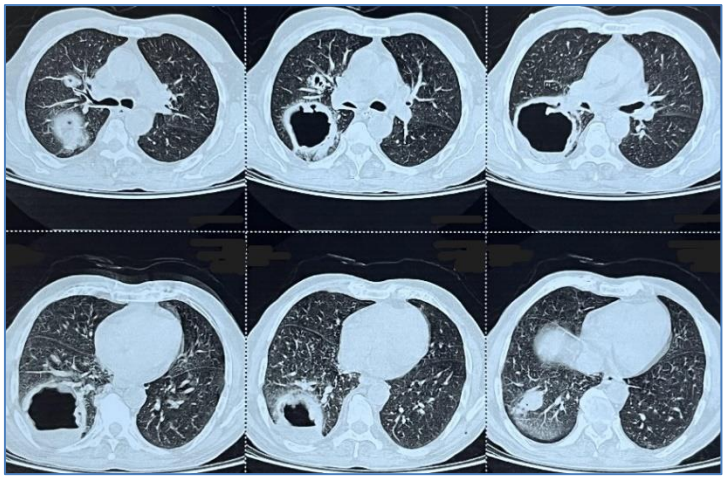

Image 3: HRCT thorax showing large thick-walled cavity in superior segment of lower lobe with accompanying 'sister cavity' in posterior segment of upper lobe

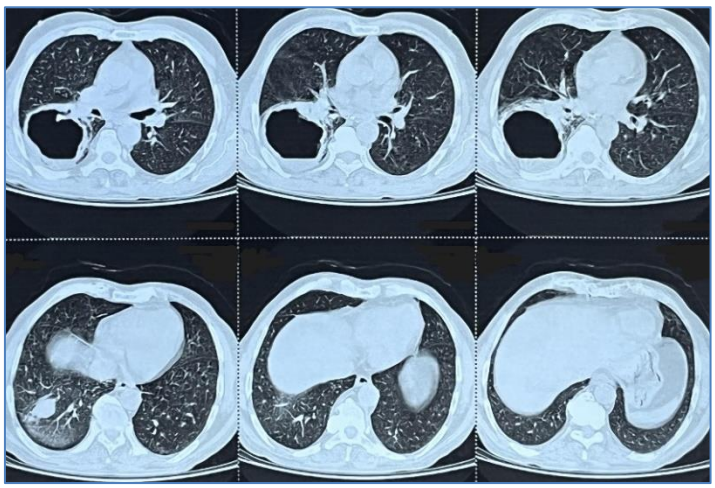

Image 4: HRCT thorax showing thick-walled cavity with air fluid level in superior segment of right lower lobe

Sputum examination after induction documented acid fast bacilli and TB Gene Xpert MTB/RIF were documented MTB genome and rpo-b mutation negative.

Microbiologist initially told that sputum sample quality is inadequate due to salivary nature of induced sputum. Usually induced sputum contains more frothy and watery contents as compared to classically described mucoid or mucopurulent sputum. We have informed microbiologist regarding induced sputum and possibility of good diagnostic yield due to cavitary lung disease which contains high bacterial load. Induced sputum although looks salivary contains enough bacterial load to document AFB in smear and MTB genome in Gene Xpert MTB/RIF analysis.

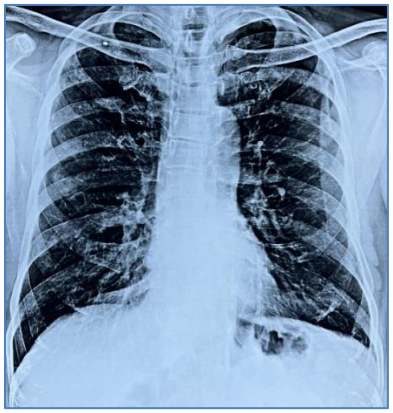

Image 5: Chest x-ray PA showing near complete resolution with parenchymal infiltrates

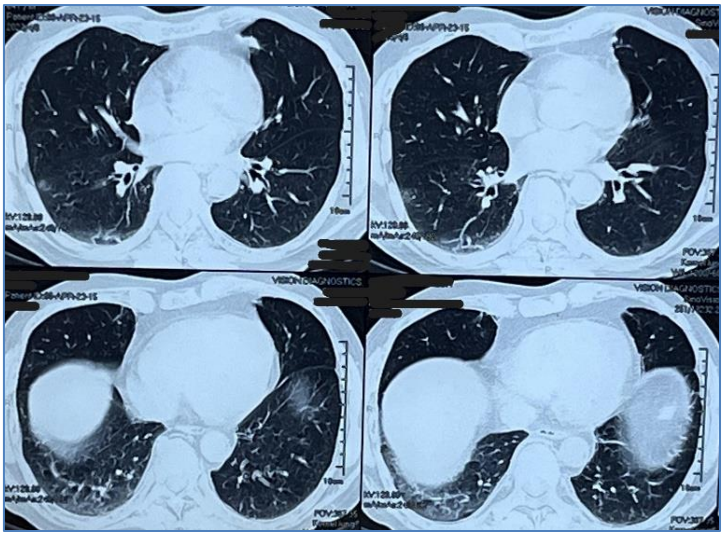

Image 6: HRCT Thorax showing minimal right lower lobe infiltrates without any lung parenchymal abnormality

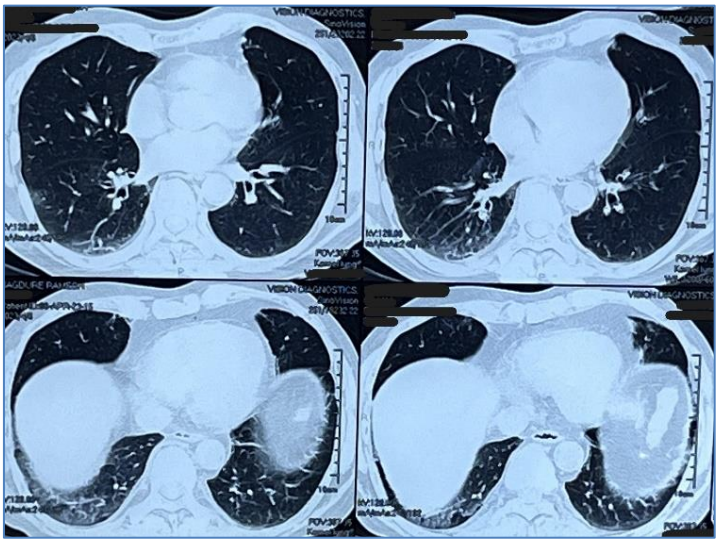

Image 7: HRCT Thorax showing minimal right lower lobe infiltrates and parenchymal bands without any lung parenchymal abnormality

We have started anti-tuberculosis treatment (ATT) as per the NTEP (National tuberculosis elimination program) protocol according to weight band containing four drugs isoniazid (H), rifampicin (R), ethambutol (E), and pyrazinamide (Z). She was discharged to home with advice for strict anti-TB treatment as four drugs in the first 2 months (HRZE) and three drugs in the next 6 months (HRE) as per the NTEP national guidelines for TB treatment. Microbiological examination documented negative MTB genome in sputum at 2 months of treatment. Radiological resolution of lung cavity has documented after five months of ATT treatment. We have documented weight gain and general health improvement with best compliance to anti-TB treatment and observed the importance of counselling. He was regularly monthly followed for 8 months; clinical and radiological assessment was done in every visit. We have documented clinical, microbiological and radiological 'cure' after eight months of treatment (Image 5-7).

DISCUSSION

Cavitation is a seminal event and a key pathological feature of human TB. It has negative implications not only for the patient - associated with poor treatment outcomes, including delayed sputum culture conversion, relapse after treatment, and development of drug resistance, but is also a public health threat, since cavitation greatly increases the risk of person-to-person transmission [1]. In humans, cavitary lesions show a strong preference for the apices of the lung. Based on this distribution, it has long been presumed that cavities form preferentially at sites of high ventilation: perfusion ratios, which favor bacterial growth. However, in addition to receiving the highest relative ventilation, the apices of the human lung are also the site of highest mechanical stress. Transpulmonary pressure (TPP), the tension force applied to the lung by negative pressure within the pleural space, follows a vertical gradient owing to the interactions of

gravity and thoracic wall shape. In humans, the area of greatest TPP therefore corresponds to the apices of the lung [26, 27].

Proposed mechanism of cavity genesis and progression [28]

In the context of tuberculosis, these smooth-type cavities suggest a novel mechanism for cavity formation. The necrotic granuloma is fundamentally a sphere with a rigid fibrotic exterior and a soft caseous interior. Inspiration produces a rapid decrease in pleural pressure, translating to the application of external tension and development of negative pressure within the sphere. Fibrous tissue is inelastic, and therefore prone to failure under repetitive mechanical stress. A tear occurring in the fibrotic wall that extended to the necrotic center would allow air to be sucked into the soft interior on inspiration, with rapid subsequent enlargement of the lesion. Upon expiration, the tension force would be released, resulting in positive pressure within the lesion and temporary closure of the tear. This is similar to the one-way valve theory postulated by Coryllos and Ornstein, [29] Coryllos, [30] and Eloesser, [31] and explains the finding that cavities frequently contain pressurized interiors. Cavities with smooth morphology are younger on average, confirming that this most likely represents an early stage of cavitation. An extreme example of air-trapping also may explain the presence of similarly young fibrous-type cavities, with their large central space and thin walls reminiscent of balloons. Experiments by Coryllos [29] in 1938 corroborate this mechanism by the introduction of a small-diameter thoracoscope into human cavities and injection of small amounts of dye or saline. When suction was applied to the cavity interior, Coryllos observed a "bubbling of air" [29] inward through the bronchial outlet, with simultaneous drainage of the instilled fluid. However, when positive pressure was applied, no movement of air or saline occurred, indicating that the outlet had been obstructed temporarily [29].

A cavity begins when mechanical action disrupts the necrotic granuloma by causing a tear in the fibrotic wall. With inspiration, external tension in the surrounding lung tissue pulls air into the necrotic center, causing a smooth cavity. If at any point the outlet is severely obstructed creating a ball-valve effect, extreme air trapping occurs and causes the cavity to assume a thin-walled fibrous balloon-like morphology. If the outlet is open or only partially obstructed, air accumulates less rapidly, resulting in smaller cavities that may progress or wax and wane. The mechanical actions of respiration continue to act on these lesions, causing eventual disruption and loosening of the retained caseum. This newly freed material is coughed up in the sputum to continue the transmission cycle, leaving behind a mixed or rough cavity with a wall of progressively crumbling caseum. Finally, any of these lesions may spontaneously close and resolve, leaving a residual scar.

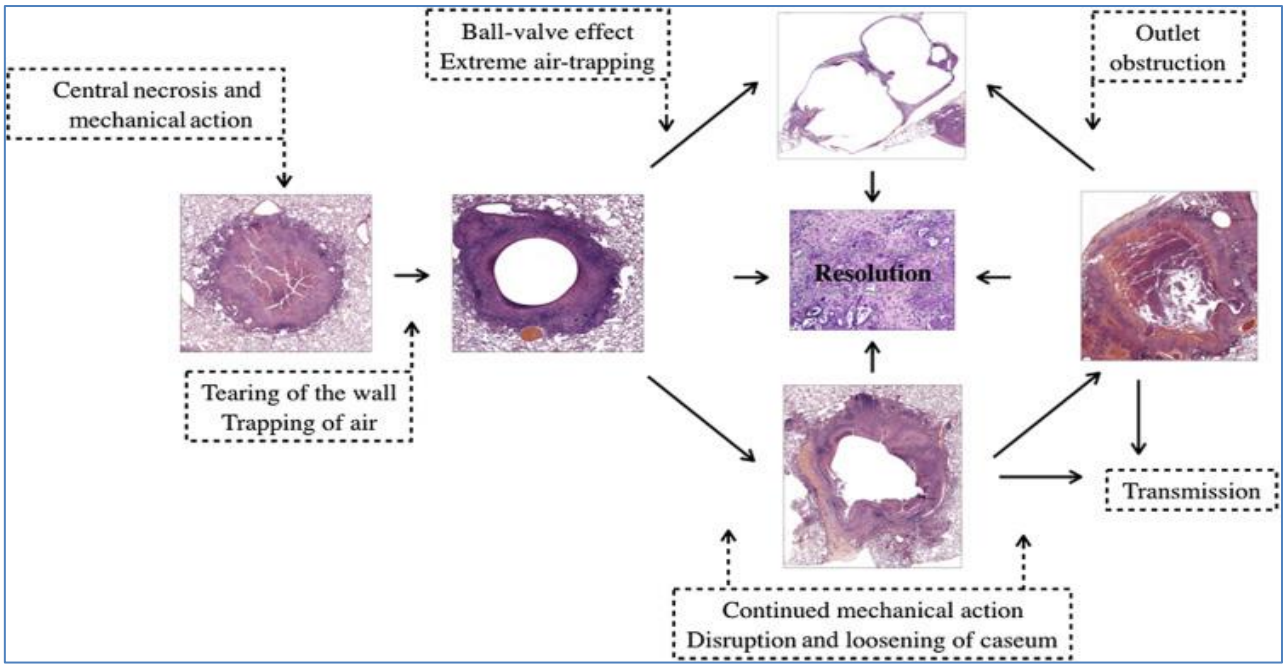

Figure 1: Showing proposed mechanism for cavity formation [28]

Cavity formation is the conversion of immune accessible lung tissue to immune sheltered surfaces continuous with the external environment. We consider TB cavitation as a complex phenotype driven by biochemical, biophysical, immunological, and microbiological processes, which have important roles during the different stages of cavitation and therefore could be targeted for prevention of extensive lung destruction, disease transmission, and the emergence of drug-resistance [1].

Overview of the drivers of pulmonary cavitation in TB [1]

1. **Biochemical drivers:** Proteolytic depletion of the ECM in the lung is necessary for TB cavitation. More recently, host-expressed extracellular collagenases, such as matrix metalloproteinases (MMPs) and cysteine cathepsins, have been described as key mediators of the ECM degradation that precedes cavitation in TB. Higher expression of the MMP-1, 3, 7, 8, 9, 12, 13, and the cysteine cathepsin K have been described at the wall of TB cavities and granulomas. Hypoxia augments monocyte and neutrophil MMP secretion acting through the hypoxia inducible factor (HIF)-1α transcription factor, an important regulator of the host response to oxygen deprivation. Elevated concentrations of MMP-1, 2, 3, 8, and 9 have also been reported in respiratory fluids from pulmonary TB patients and correlate with severity of disease and number of cavities. MMPs likely play complex roles in immune signaling and vascular permeability within TB lesions [31-32].
2. **Biophysical drivers:** A possible physical determinant of cavitation is proximity to an airway. Not every necrotic lesion cavitates, and this could be due to the lack of access to an airway leading to an inability to evacuate its caseous contents into the bronchial tree and form a cavity. Nagasawa et al. investigated the relationship between cavity size and bronchial drainage and found that larger cavities were drained by larger bronchi, suggesting that the size of the pre-cavity focus must match an appropriately sized airway for cavitation to occur [33].
   Similarly, increased air pressure inside the cavity from a caseous one-way-valve between the cavity and the draining bronchus may lead to the initial cavity formation [34].

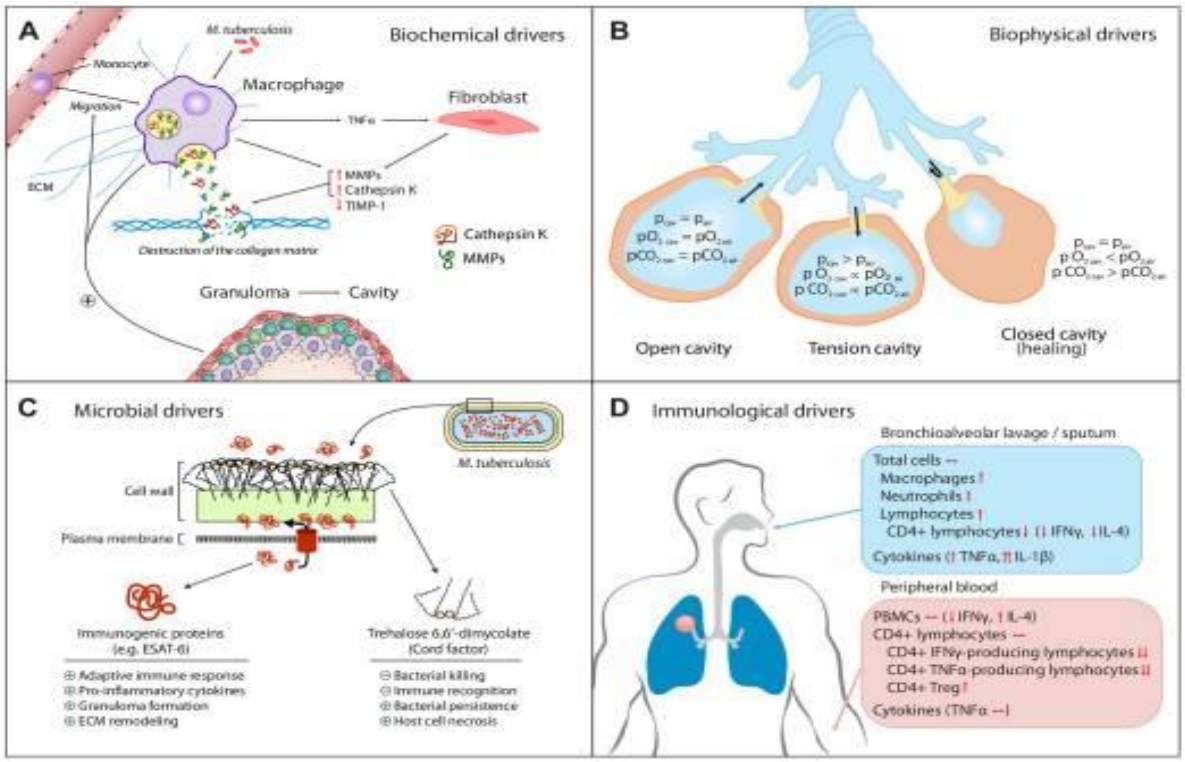

Figure 2: Showing Overview of the drivers of pulmonary cavitation in TB [1]

However, while a positive-pressure model may explain early cavitation events, many large cavities have open connections between the cavity-space and the draining bronchus. The preferred location of cavities in the lung apices could also have a role in cavity formation. In addition to receiving the highest relative ventilation, the apices of the human lung are also the site of the highest mechanical stress. Recently, Ihms *et al*., suggested that the pull of lung-tissue at the periphery of the cavity wall also aides during cavity formation and growth [35].

The biophysical mechanisms of large-cavity growth remain largely unresolved and further investigations are required to evaluate tissue-level biophysical changes that could be contributing to cavity formation and subsequent enlargement. For instance, the combined influence of vascular necrosis and increased oxygen demand from immune cell influx within large granulomas may create a hypoxic environment focused at the center of a lesion which drives central necrosis in the pre-cavity nodule [36, 37].

3. **Microbial Drivers:** While many infectious and non-infectious diseases can form lung cavities, TB causes an especially high rate of cavitation. Since M. tuberculosis is dependent on aerosolization for transmission, the

bacillus may have evolved specific virulence factors that promote cavitation. However, there is little evidence that intrinsic molecules of M. tuberculosis are capable of directly mediating tissue destruction leading to cavitation. Rather, most models propose that M. tuberculosis causes cavities indirectly by promoting an immune response that leads to cavitation. A possible exception is the recent characterization of tuberculosis necrotizing toxin which induces host-cell necrosis. There are also some suggestions of heterogeneity in the ability to cause tissue destruction among M. tuberculosis strains. Bacteria isolated from efficient TB spreaders can lead to more necrosis and lesions that resemble caseating granulomas when used to infect mice, compared to bacilli isolated from inefficient TB spreaders. The combined injection of M. tuberculosis or M. bovis cell wall protein mixed with a mycobacterial long branched-chain fatty acid glycolipid, such as trehalose 6,6′-dimycolate (TDM), was able to cause cavities in rabbits. Immunogenic proteins like ESAT-6, encoded by genes of virulent M. tuberculosis-complex, but lost from the BGC genome, are known to promote granuloma formation. Similarly, TDM stimulates macrophages to release pro-inflammatory cytokines leading to fibrosis and necrosis [38-41].

4. **Immunological Drivers:** The innate immunity plays a major role in the host's response to M. tuberculosis. Macrophages are the first line of defense and their response can either control the infection or favor its development. While there is extensive data describing the role of the innate immune response in pulmonary TB, there is still more work to be done to better understand its role leading to cavitation. Necrosis is associated with cavitation in many processes (e.g. squamous cell carcinoma, pyogenic lung abscess). Similarly, the relative tendency toward cell necrosis over apoptosis during the inflammatory response to M. tuberculosis infection is a likely factor affecting cavitation. Therefore, cell-signaling pathways that favor necrosis over apoptosis could also bias the inflammatory response toward cavity formation [42-45]. The adaptive immune response also plays a role in cavitation. Cavitary TB patients have decreased total CD4+ lymphocytes but increased proportion of Th2 lymphocytes compared to non-cavitary controls. An emerging model suggests that a Th2 cytokine, pro-fibrotic adaptive immune response predominates in cavitary TB patients. Higher levels of TNFα, IL-6, and IL-1β measured in bronchoalveolar lavage of pulmonary TB patients correlates with cavitary disease. In humans, neutrophils may also play a major role in cavity formation. An alternative hypothesis propose that severe TB is the result of a progressive immune response to mycobacterial antigens [45-47].

Mycobacterial ecology at the cavity wall [1]

One of the most intriguing perspectives on cavitation considers the internal surface of the cavity as a biofilm. A biofilm is a microbial community growing on a biotic or abiotic surface within a self-assembled polymeric matrix. For bacilli at the cavity surface, caseum of the cavity wall acts as a protective matrix for growth and dissemination. The outstanding concession in this model is that caseum is not strictly self-assembled, but rather results from pathogen-induced host-cell necrosis at the cavity surface. However, in many other ways, M. tuberculosis' niche within cavity caseum behaves as a biofilm [48-49].

The caseum is a substrate for bacilli in different states of metabolic dormancy and active replication. Although predominately studied in vitro or in non-cavitating necrotic granulomas; oxygen, and nutrient gradients throughout the NL likely control hypoxia responses, sigma factor expression, and the mycobacterial stringent response leading to a three-dimensional organization of bacteria in different metabolic and transcriptional states. While necrotic granulomas are known to be hypoxic, the increased oxygen tension within the caseum of newly formed cavities also likely activates resuscitation-promoting factors to drive bacillary replication and disease transmission. The caseous niche also provides protection to M. tuberculosis. Since caseum is devoid of vascularization, drug penetration is dependent on diffusion which can lead to subinhibitory concentrations of some anti-TB compounds. Moreover, caseum is a strong binding environment and further limits the availability of some drugs. Together with reduced access of the immune system to necrotic areas, these conditions promote genetic diversification and the acquisition of drug resistance, which are also hallmarks of biofilms [50-54].

Bacilli present in caseum are mostly extracellular and exhibit altered cell wall biochemistry. Although unproven in vivo, M. tuberculosis seems to preferentially grow in caseum as genetically regulated necrosis-associated extracellular clusters to enhance persistence, reduce antibiotic susceptibility, and promote transmission events. Therefore, the ultrastructural identity of M. tuberculosis biofilms in vivo could also be clusters and cords bacilli growing within the favorable caseous environment at the inner edge of the cavity. Many aspects of microbial ecology within the cavity remain unstudied, probably because of the difficulty in modeling TB cavities and obtaining specimens. However, with the recent advances in modeling, it is now possible to conduct detailed studies on bacterial physiology and growth-state within cavities [55-57].

Tuberculous Cavity:

Tuberculous cavity has special features which can be differentiated from other causes such as lung abscess, malignancy, infarct, sarcoidosis, bulla, and Wegner's granulomatosis.

Location: Usually located in upper lobe but possible in any part of lung. Upper lobe, middle lobe, lingula and then lower lobes are involved in tuberculous cavitations. Right upper lobe apical or posterior segment and right lower lobe superior segment are commonest sites of lung cavities seen in tuberculosis. Central lung cavities are more common in tuberculosis than pleural based locations. Pleural based cavities are commonly described in Wegner's granulomatosis.

Number: usually single, sometimes multiple cavities are also documented. Multiple cavities, bilateral and variegated with bizarre shape is seen in Wegner's granulomatosis.

Size: medium to large sized cavities are documented in tuberculosis. Size of 2 cm or less are rarely seen, and maximum would be eight centimeters documented in tuberculosis.

Shape: round or oval is typical feature of pulmonary tuberculosis. Bizarre shape, variegated, irregular is seen in Wegner's and malignant lung process.

Wall: usually thick-walled cavities are seen in tuberculosis. Wall thickness of more than 5 mm is common. Wall thickness of more than one centimeter is commonly documented in pyogenic and malignant pathology.

Margins: Smooth margins is characteristic feature of tuberculosis. Irregular, crenated and indentations are seen in malignancy and pyogenic process.

Content: Minimal or less than one third of fluid level is described in tuberculosis. More than half fluid is indicator of pyogenic process.

Pericavitary consolidation: consolidation surrounding the air containing space or cavity is called as pericavitary consolidations. This is unique feature tuberculous cavity. Pericavitary consolidation is marker of wall thickness and indicates moderate wall thickness cavities in tuberculosis.

Satellite nodules: Nodular opacities, discretely or randomly noted around cavity in called as satellite nodules. Satellite nodules are observed in anatomically same segment or lobe. Satellite nodule is indicator of lymphatic or bronchogenic spread. Satellite nodules are unique feature of tuberculosis pathology. Satellite nodules are tiny acinar and intestinal nodules seen in pulmonary tuberculosis. Distant nodules i.e. in different lobe or other lung is not satellite nodules which is indicator or hematogenous dissemination and present as miliary nodules. Tree in bus opacities are not satellite nodules which is indicator of lymphatic dissemination or bronchogenic spread to different lobe or another lung.

Ancillary features: mediastinal adenopathy, pleural effusion and calcification in cavity wall, central versus eccentric cavitation will help in differentiating tuberculous from other causes. Other ancillary features such as acute respiratory versus chronic constitutional symptoms with special inclusion of anorexia, weight loss and low-grade fever will guide further confirmation of pathology and diagnostic approach. Acute illness is common in community acquired pneumonia but not uncommon in tuberculosis. Constitutional symptoms are common in tuberculosis but also seen in malignancy.

'Siter Cavity': "Sister cavity is first time reported in literature. Sister cavity is defined as presence of cavitary lesion on same side of lung with large cavitary lesion either in same lobe or different lobe."

Unique features of 'sister cavity' are-

1. Sister cavity is smaller size than parent lung cavity. Usually more than one in number.
2. Anatomically located in same lung, same lobe, same segment or different lobe and different segment on same side of thoracic cavity.
3. Sister cavity doesn't contain fluid level.
4. Sister cavity is considered as primitive cavity and as duration of illness increase it will increase in size.
5. Sister cavity formation is indicator of lymphatic or bronchogenic dissemination of pulmonary tuberculosis.
6. Sister cavities are usually thick-walled than parent cavities.
7. Sister cavities are usually not associated other features of tuberculous cavities such as pericavitary consolidation and satellite nodules.
8. Sister cavity is marker of active pulmonary tuberculosis. Its association with nontuberculous pathologies such as pyogenic and malignant lung process is extremely rare.
9. Cavities documented in other lung of primary lung cavity are not 'sister cavities.'

CONCLUSION

In the present case report, we have reported an acute febrile respiratory illness in geriatric patient without constitutional symptoms with cavitating consolidation presented as community acquired infections. HRCT workup

showed a typical tuberculous cavity with first time rereported in medical literature 'Sister cavity'. Induced sputum examination has shown acid fast bacilli in smear with MTB genome and rifampicin sensitivity in nucleic acid amplification test. Excellent clinical and radiological outcome observed as cure after eight months of ATT. We have confirmed Pulmonary tuberculosis as presenting feature of acute febrile respiratory illness with cavitating consolidation.

Learning points

1. Acute febrile respiratory illness without constitutional symptoms such as weight loss, anorexia and low-grade fever, cough and shortness of breath with or without hemoptysis is rarely described in active pulmonary tuberculosis and most common in community acquired pneumonia.
2. Cavitating consolidation with acute febrile respiratory illness may be seen in active pulmonary tuberculosis and comes after the community acquired pneumonia. Other ancillary radiological features will give radiological clues to suspect tuberculosis over community acquired pneumonia.
3. Conventional chest radiograph is a less sensitive technique and all cases should undergo HRCT thorax to investigate further. This will have additional advantage of documenting the extent and nature of parenchymal abnormalities with pleural, vascular and mediastinal abnormalities.
4. Tuberculous cavity has very typical characteristics and is described as a soft cavity with minimal air fluid level, usually single large and solitary to multiple in number. These cavities are classically associated with pericavitary consolidations and satellite nodules.
5. 'Sister cavity' not commonly described in medical literature. Sister cavity is the presence of a distant cavity to parent cavity which is not anatomically related such as different lobe, different lymphatic drainage. Presence of 'sister cavity' is considered as a radiological clue to suspect tuberculosis etiology and workup accordingly.
6. Sputum production and its yield in cavitary lung disease associated with pulmonary tuberculosis depends on size of cavity, anatomical location, bronchus communication of cavity and quantity of sputum production.
7. Induced sputum has a very significant impact on diagnostic yield and the most cost-effective technique in ruling out active pulmonary tuberculosis. It is a sensitive technique when smear examination is considered and its specificity increased with cartridge based nucleic acid amplification of Gene Xpert MTB/RIF test in cases with cavitary lung disease.
8. Induced sputum looks like salivary or less mucoid due to its methodology. We recommend it as routine and it will decrease the need for more invasive tests such as bronchoscopy. Bronchoscopy guided sampling such as BAL has significant yield in sputum negative cavitary lung diseases. Induced sputum is cost effective, easily performed technique and its sensitivity is comparable with bronchoscopy in cavitary lung disease. In the absence of cavitary lung disease, bronchoscopy is superior to conventional microscopy in smear after induced sputum examination.
9. Pulmonary tuberculosis should be suspected early in cases with cavitating consolidations to have a successful treatment outcome. Important quote which is a real misnomer as 'rare things rare to happen' for cases with Cavitating consolidation with acute febrile respiratory illness & 'sister cavities' without typical constitutional symptoms in Pulmonary Tuberculosis & now, 'rare things not rare to happen but possible', because acute febrile respiratory illness with cavitating consolidation tuberculosis in uncommon but TB is not uncommon.

Conflicts of Interest: Nil

Research Funding: Nil

REFERENCES

1. Urbanowski, M. E., Ordonez, A. A., Ruiz-Bedoya, C. A., Jain, S. K., & Bishai, W. R. (2020). Cavitary tuberculosis: the gateway of disease transmission. *The Lancet Infectious Diseases*, *20*(6), e117-e128.
2. Patil, S., & Gajanan, H. (2014). Cavitary Lung Disease: Not Always due to Tuberculosis! Primary Lung Cancer with Smear Positive Pulmonary Tuberculosis-A Case Report. *American Journal of Medical Case Reports*, *2*(8), 164-166.
3. Shital, P., Anil, J., Sanjay, M., & Mukund, P. (2014). Tuberculosis with diabetes mellitus: clinical-radiological overlap and delayed sputum conversion needs cautious evaluation-prospective cohort study in Tertiary Care Hospital, India. *J Pulm Respir Med*, *4*(2), 1-5.
4. Shital, P., & Kasture, L. (2014). 'Tennis Racket cavity'on Chest Radiograph: Strong Predictor of Active Pulmonary Tuberculosis!–A Case Report. *American Journal of Medical Case Reports*, *2*(9), 167-169.
5. Shital, P., Choudhary, C. R., Kasture, L., & Rujuta, A. (2015). Endobronchial Tuberculosis Presenting as a Post-obstructive Pneumonia, Para-hilar Mass Lesion in Chest Radiograph and 'Tumorous' Endobronchial Lesion during Bronchoscopy: A Case Report. *American Journal of Infectious Diseases*, *3*(5), 147-151.
6. Patil, S., Dahiphale, J., Raka, V., Narkar, S., Choudhari, S., & Gondhali, G. (2023). „Coin Lesion" in Chest Radiograph Presenting as Round Pneumonia with Eccentric Cavitation in HRCT Thorax: Tuberculosis or Malignancy-A Real Puzzle. *South Asian Res J Med Sci*, *5*(2), 33-40.

7. Patil, S., Dahiphale, J., Raka, V., Narkar, S., Choudhari, S., & Gondhali, G. (2023). „Stepladder Lung Cavities" with „Starry Sky Pattern" in HRCT Thorax with Constitutional Symptoms: A Strong Predictor of Active Pulmonary Tuberculosis. *SAR J Med*, *4*(2), 32-42.
8. Patil, S., Narwade, S., & Mirza, M. (2017). Bronchial wash Gene Xpert MTB/RIF in lower lung field tuberculosis: Sensitive, superior, and rapid in comparison with conventional diagnostic techniques. *Journal of Translational Internal Medicine*, *5*(3), 174-181.
9. Patil, S., & Gondhali, G. (2017). Short course of high dose steroids used for non-pulmonary indication like anaphylaxis caused flare up of tuberculosis & presenting as acute pulmonary tuberculosis with pleural effusion: a case report. *European Journal of General Medicine*, *15*(1), 37-42.
10. Patil, S., & Mirza, M. (2018). Tuberculous Lymphadenitis of Hilar Lymph Nodes as a Cause of Right Middle Lobe Syndrome: A Case Report. *Respiratory Case Reports*, *7*(2), 90-96.
11. Patil, S., & Patil, R. (2018). Fleeting pulmonary infiltrates in allergic bronchopulmonary aspergillosis Misdiagnosed as tuberculosis. *Int. J. Mycobacteriol*, *7*, 186-190.
12. Patil, S., & Jadhav, A. (2019). Short course of high-dose steroids for anaphylaxis caused flare up of tuberculosis: a case report. *Journal of Translational Internal Medicine*, *7*(1), 39-42.
13. Patil, S., & Gondhali, G. (2021). Pulmonary Melioidosis Masquerading as Tuberculosis: A Case Report. Electron J Gen Med. 2021; 18 (5): em310.
14. Patil, S., & Gondhali, G. (2021). COVID-19 pneumonia with pulmonary tuberculosis: double trouble. *The International Journal of Mycobacteriology*, *10*(2), 206-209.
15. Shital, P., & Mirza, M. (2018). Laryngeal & Lower lung field tuberculosis in pregnancy: A case report. Electronic Journal of General Medicine, 15(2), em06
16. Patil, S. V., Toshniwal, S., & Acharya, A. (2023). GondhaliG. Cardiac dysfunction in active pulmonary tuberculosis: Mysterious facts of TB's pandora. *Electron J Gen Med*, 2023; 20(2): em452.
17. Patil, S., Gondhali, G., & Bhadake, M. (2022). Disproportionate tachycardia and tachypnea in pulmonary tuberculosis: A marker of concurrent cardiac dysfunction. *Journal of Association of Pulmonologist of Tamil Nadu*, *5*(3), 124.
18. Patil, S. V., Narwade, G., & Gondhali, G. (2020). Cardiac Dysfunction in Active Pulmonary Tuberculosis: Double Trouble!!. *European Respiratory Journal*, 56, 1604.
19. Patil, S. V., Patil, R., & Gondhali, G. (2020). Cardiac Dysfunction in Active Pulmonary Tuberculosis: Underestimated, Missed Routinely and Have Impact on Clinical Outcome!; Prospective Study of 600 Cases in Tertiary Care Setting in India. In *C53. GLOBAL EXPERIENCES IN TB AND NTM CARE* (pp. A5435-A5435). American Thoracic Society.
20. Patil, S., Narkar, S., Raka, V., Dahiphale, J., Choudhari, S., & Gondhali, G. (2023). Destroyed lung'as Post Tuberculosis Sequel: A Preventable Stigma of 'disease of concern'of Millennium. *Saudi J Med*, *8*(3), 112-119.
21. Patil, S., Patil, R., & Jadhav, A. (2018). Pulmonary functions' assessment in post-tuberculosis cases by spirometry: Obstructive pattern is predominant and needs cautious evaluation in all treated cases irrespective of symptoms. *The International Journal of Mycobacteriology*, *7*(2), 128-133.
22. Patil, S. V., Toshniwal, S., & Gondhali, G. (2023). Cavitating lung disease is not always due to tuberculosis! Wegener's granulomatosis with mycetoma with deep vein thrombosis lower limb: Case report with review of literature. *Electron J Gen Med*, 2023; 20(1), em425.
23. Patil, S., & Gondhali, G. (2022). Bronchus sign on HRCT thorax: presenting sign of Wegener granulomatosis with lung involvement—misdiagnosed as TB in presence of acino-nodular pattern on imaging. *The Journal of Association of Chest Physicians*, *10*(2), 105-111.
24. Patil, S., & Patil, D. (2022). Wegener's granulomatosis mimicking like pulmonary tuberculosis and presenting as cavitating lung disease with mycetoma: A case report with review of literature. *Med Sci Res*, *13*, 103-109.
25. Patil, S., Gondhali, G., & Patil, D. (2022). Chronic febrile respiratory illness with acino-nodular consolidations as presenting feature of granulomatosis with polyangiitis: A case report with review of literature. *Journal of Association of Pulmonologist of Tamil Nadu*, *5*(3), 116-120.
26. Cardona, P. J. (2011). A spotlight on liquefaction: evidence from clinical settings and experimental models in tuberculosis. *Clinical and Developmental Immunology*, *2011*, 868246.
27. West, J. (1971). Distribution of mechanical stress in the lung, a possible factor in localisation of pulmonary disease. *The Lancet*, *297*(7704), 839-841.
28. Coryllos, P. N., & Ornstein, G. G. (1938). Giant tuberculous cavities of the lung: pathogenesis, pathologic physiology, and surgical treatment. *Journal of Thoracic Surgery*, *8*(1), 10-54.
29. Coryllos, P. N. (1939). Physics applied to tuberculosis, *J Franklin Inst*, 227, 287-304.
30. Eloesser, L. (1937). Blocked cavities in pulmonary tuberculosis, *J Thorac Surg*, 7, pp. 1-22.
31. Elkington, P., Shiomi, T., Breen, R., Nuttall, R. K., Ugarte-Gil, C. A., Walker, N. F., ... & Friedland, J. S. (2011). MMP-1 drives immunopathology in human tuberculosis and transgenic mice. *The Journal of clinical investigation*, *121*(5), 1827-1833.

32. Ong, C. W., Elkington, P. T., & Friedland, J. S. (2014). Tuberculosis, pulmonary cavitation, and matrix metalloproteinases. *American journal of respiratory and critical care medicine*, *190*(1), 9-18.
33. Nagasawa, N., Yamashita, M., & Okamoto, H. (1953). Studies on the relationship between pulmonary tuberculous cavities and draining bronchi, by injecting acrylic resin. *Acta tuberculosea Japonica*, *3*(2), 35-47.
34. Coryllos, P. N. (1936). The mechanics and biology of tuberculous cavities. *American Review of Tuberculosis*, *33*(5), 639-660.
35. Ihms, E. A., Urbanowski, M. E., & Bishai, W. R. (2018). Diverse cavity types and evidence that mechanical action on the necrotic granuloma drives tuberculous cavitation. *The American journal of pathology*, *188*(7), 1666-1675.
36. Via, L. E., Lin, P. L., Ray, S. M., Carrillo, J., Allen, S. S., Eum, S. Y., ... & Barry III, C. E. (2008). Tuberculous granulomas are hypoxic in guinea pigs, rabbits, and nonhuman primates. *Infection and immunity*, *76*(6), 2333-2340.
37. Datta, M., Via, L. E., Chen, W., Baish, J. W., Xu, L., Barry, C. E., & Jain, R. K. (2016). Mathematical model of oxygen transport in tuberculosis granulomas. *Annals of biomedical engineering*, *44*, 863-872.
38. Gadkowski, L. B., & Stout, J. E. (2008). Cavitary pulmonary disease. *Clinical microbiology reviews*, *21*(2), 305-333.
39. Barry 3rd, C. E., Boshoff, H. I., Dartois, V., Dick, T., Ehrt, S., Flynn, J., ... & Young, D. (2009). The spectrum of latent tuberculosis: rethinking the biology and intervention strategies. *Nature Reviews Microbiology*, *7*(12), 845-855.
40. Sun, J., Siroy, A., Lokareddy, R. K., Speer, A., Doornbos, K. S., Cingolani, G., & Niederweis, M. (2015). The tuberculosis necrotizing toxin kills macrophages by hydrolyzing NAD. *Nature structural & molecular biology*, *22*(9), 672-678.
41. Verma, S., Bhatt, K., Lovey, A., Ribeiro-Rodrigues, R., Durbin, J., Jones-López, E. C., ... & Salgame, P. (2019). Transmission phenotype of Mycobacterium tuberculosis strains is mechanistically linked to induction of distinct pulmonary pathology. *PLoS pathogens*, *15*(3), e1007613.
42. De Martino, M., Lodi, L., Galli, L., & Chiappini, E. (2019). Immune response to Mycobacterium tuberculosis: a narrative review. *Frontiers in pediatrics*, *7*, 350.
43. Kumar, V., Abbas, A. K., & Aster, J. C. (2018). Lung. Robbins Basic Pathology. 10 ed. Philadelphia, Pennsylvania: Elsevier.
44. Dheda, K., Booth, H., Huggett, J. F., Johnson, M. A., Zumla, A., & Rook, G. A. (2005). Lung remodeling in pulmonary tuberculosis. *The Journal of infectious diseases*, *192*(7), 1201-1210.
45. Ravimohan, S., Kornfeld, H., Weissman, D., & Bisson, G. P. (2018). Tuberculosis and lung damage: from epidemiology to pathophysiology. *European respiratory review*, *27*(147).
46. Elkington, P. T., Green, J. A., Emerson, J. E., Lopez-Pascua, L. D., Boyle, J. J., O'Kane, C. M., & Friedland, J. S. (2007). Synergistic up-regulation of epithelial cell matrix metalloproteinase-9 secretion in tuberculosis. *American journal of respiratory cell and molecular biology*, *37*(4), 431-437.
47. Mazzarella, G., Bianco, A., Perna, F., D'AURIA, D., Grella, E., Moscariello, E., & Sanduzzi, A. (2003). T lymphocyte phenotypic profile in lung segments affected by cavitary and non-cavitary tuberculosis. *Clinical & Experimental Immunology*, *132*(2), 283-288.
48. Dutta, N. K., & Karakousis, P. C. (2014). Latent tuberculosis infection: myths, models, and molecular mechanisms. *Microbiology and Molecular Biology Reviews*, *78*(3), 343-371.
49. Basaraba, R. J., & Ojha, A. K. (2017). Mycobacterial biofilms: revisiting tuberculosis bacilli in extracellular necrotizing lesions. *Microbiology spectrum*, *5*(3), 5-13.
50. Lenaerts, A. J., Hoff, D., Aly, S., Ehlers, S., Andries, K., Cantarero, L., ... & Basaraba, R. J. (2007). Location of persisting mycobacteria in a Guinea pig model of tuberculosis revealed by r207910. *Antimicrobial agents and chemotherapy*, *51*(9), 3338-3345.
51. Rustad, T. R., Harrell, M. I., Liao, R., & Sherman, D. R. (2008). The enduring hypoxic response of Mycobacterium tuberculosis. *PloS one*, *3*(1), e1502.
52. Kaushal, D., Schroeder, B. G., Tyagi, S., Yoshimatsu, T., Scott, C., Ko, C., ... & Bishai, W. R. (2002). Reduced immunopathology and mortality despite tissue persistence in a Mycobacterium tuberculosis mutant lacking alternative σ factor, SigH. *Proceedings of the National Academy of Sciences*, *99*(12), 8330-8335.
53. Mukamolova, G. V., Turapov, O., Malkin, J., Woltmann, G., & Barer, M. R. (2010). Resuscitation-promoting factors reveal an occult population of tubercle bacilli in sputum. *American journal of respiratory and critical care medicine*, *181*(2), 174-180.
54. Vadwai, V., Daver, G., Udwadia, Z., Sadani, M., Shetty, A., & Rodrigues, C. (2011). Clonal population of Mycobacterium tuberculosis strains reside within multiple lung cavities. *PloS one*, *6*(9), e24770.
55. Ryan, G. J., Hoff, D. R., Driver, E. R., Voskuil, M. I., Gonzalez-Juarrero, M., Basaraba, R. J., ... & Lenaerts, A. J. (2010). Multiple M. tuberculosis phenotypes in mouse and guinea pig lung tissue revealed by a dual-staining approach. *PloS one*, *5*(6), e11108.
56. Orme, I. M. (2014). A new unifying theory of the pathogenesis of tuberculosis. *Tuberculosis*, *94*(1), 8-14.
57. Wong, K. W., & Jacobs Jr, W. R. (2016). Postprimary tuberculosis and macrophage necrosis: is there a big ConNECtion?. *MBio*, *7*(1), e01589-15.