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Risk factors and Complications associated with Tuberculosis: Case series

Dr. Preeti Chhabria[1], Dr. Ketan Kargirwar[2], Dr. Rahul Kamath[3], Dr. Krunal Patel[*4]

[1]Director, Internal Medicine Department: Internal Medicine, Sir Hurkisondas Nurrotumdas Reliance Foundation Hospital and ResearchCentre

[2]Senior Consultant, Critical Care Medicine EDIC Department: Intensive Care Medicine, Sir Hurkisondas Nurrotumdas Reliance Foundation Hospital and Research Centre

[3]Clinical Associate Department: Internal Medicine, Sir Hurkisondas Nurrotumdas Reliance Foundation Hospital and ResearchCentre

[4]DNB resident - PGY2 Department: Internal Medicine, Sir Hurkisondas Nurrotumdas Reliance Foundation Hospital and Research Centre

ABSTRACT

Background: Tuberculosis (TB) remains a significant public health concern globally, with a disproportionate burden on females, particularly in India. This case series analysis explores the challenges and complications faced by 3 deceased females with TB, underscoring the need for tailored interventions.

Methods: We present three cases of Indian females diagnosed with TB at an advanced stage. All patients shared common attributes, including low body mass index (BMI), advanced disease, immunocompromised status, and delayed diagnosis. Clinical data, laboratory findings, and treatment outcomes were analyzed.

Results: Patients were diagnosed with *Mycobacterium tuberculosis*, but they exhibited poor prognostic factors such as hypoalbuminemia and anemia. Delayed diagnosis and initiation of appropriate treatment, coupled with the presence of comorbidities, and paucity of finances contributed to the disease severity and complications leading to death.

Conclusion: Indian females with TB encounter multifaceted challenges, delayed diagnosis and treatment initiation, coupled with the presence of comorbidities complicates the clinical course and severity. Early case detection, prompt initiation of appropriate treatment and managing health by targeting interventions that tackle socioeconomic determinants and gender-specific barriers, and prioritization of personal health over family needs will lead to improved treatment outcomes and a reduced overall disease burden.

KEYWORDS: Mortality, *Tuberculous meningitis*, hypoalbuminemia, anemia, *Mycobacterium tuberculosis.*

ARTICLE DETAILS

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INTRODUCTION

Tuberculosis (TB) is one of the top ten causes of death globally even in the era of effective anti-TB medication and advanced mycobacterial laboratories.[1] In 2022, an estimated 10.6 million people fell ill with TB worldwide, including 5.8 million men, 3.5 million women and 1.3 million children. Gender differentials in TB have been reported worldwide. Men are more likely to be diagnosed with TB than women, with a male-to-female ratio of 1.6:1, globally. [3,4,5] Different factors have been proposed to explain this gender gap however women have a greater likelihood of severe forms of TB and TB-HIV confection as compared to men. [5,6,7]

In this study, we report severe drug-sensitive TB infection in three female patients who succumbed to the disease despite optimal treatment.

CASE 1

A 72-year-old female with BMI of 17.2 kg/m2 was admitted with a dry cough, fever, weakness, and weight loss. She was found to be tachycardic, tachypneic, and maintaining a saturation level of 90% on room air. Her blood sugar levels

were 400 mg/dL with blood ketones at 4.9mmol/l, and she was started on a human actrapid insulin infusion. Her blood chemistry revealed anemia, hypoalbuminemia, hyponatremia, elevated CRP, and negative viral makers for HIV, Hepatitis B, and C.

The patient's radiological investigation was done represented in Figure 1(a). Sputum samples for the GeneXpert TB test came back positive with no resistance to rifampicin. The standard first-line Anti-Tubercular Treatment (ATT) was initiated, including Tab. Isoniazid, Tab. Rifampicin, Tab. Ethambutol, and Tab. Pyrazinamide. On the 5th day of admission, the patient experienced a massive haemoptysis episode (fig. 1c) and went into cardiac arrest. She was successfully resuscitated, and hemodynamic support was provided with vasopressors. Bronchial artery embolization and renal replacement therapy were offered for oliguria and severe refractory acidosis, but due to low socioeconomic status and financial constraints, the family opted for supportive care treatment. Unfortunately, on the 6th day of hospitalisation, the patient had another cardiac arrest and could not be revived, resulting in her death**.**

CASE 2

A 31-year-old female with BMI of 12.99 kg/m2 presented with fever, chills, dry cough, loss of appetite, weight loss, weakness, and fatigue. She had recently experienced a miscarriage and has been depressed since then. On admission, she was found to be poorly built and malnourished, with afebrile, tachycardic, tachypneic, and hypotensive. Blood chemistry (Table 1) revealed severe anemia and iron deficiency. She was started on IV antibiotics, fluids, and vasopressors to maintain hemodynamics. IV albumin was administered due to low serum albumin levels. Sputum culture showed acid-fast bacilli (AFB) 3+ and GeneXpert was positive for *Mycobacterium tuberculosis*. The patient was started on ATT adjusted to weight, but Pyrazinamide was withheld due to a deranged liver profile. Patient experienced hypoxia, requiring oxygen support and High-flow nasal cannula (HFNC). She developed bradycardia and asystole due to progressive hypoxia. CPR was performed, and she was revived. Financial constraints and family wishes led to supportive treatment, but she succumbed after five days of hospitalisation.

CASE 3

A 55-year-old female with BMI of 29.03kg/m^2 who has a known case of rheumatoid arthritis, hypertension, and chronic liver disease with portal hypertension presented with drowsiness and limited movement on the right side for 1 day prior to admission. She had no significant past history except a fracture in her L4 vertebra and spinal canal stenosis, which left her bedridden since August 2023. Upon admission, she had a poor Glasgow Coma Scale (GCS) score of E2M1V5, and was intubated to protect her airway. She was started on intravenous empirical antibiotics and supportive care.

Blood chemistry revealed anemia and hyponatremia, which were corrected gradually. A Computed tomography (CT) scan of her brain showed no fresh intracranial haemorrhage, but a Magnetic resonance imaging (MRI) of her brain using a stroke protocol was done (Fig. 3a). An electroencephalogram (EEG) showed bilateral intermittent slow waves, and a lumbar puncture was done. A cerebrospinal fluid analysis showed a white cell count of 35 cells/µL, with 20 cells/µL being lymphocytes and the rest being neutrophils. The protein level was measured at 77 mg/dL, and the glucose level was measured at 25 mg/dL (blood glucose was found to be 103 mg/dL). The Gram stain revealed scanty acid-fast bacilli, and the GeneXpert test was positive for acid-fast bacilli (AFB). Pyrosequencing for multi-drug resistant/extensively drug-resistant tuberculosis (M/XDR-TB) showed a positive result for tuberculosis with no evidence of resistance.

A transesophageal echocardiography showed a normal ejection fraction (EF) and no evidence of a patent foramen ovale. IV Dexamethasone was started at a dose of 0.4mg/kg/day, and she was started on weight adjusted modified anti-tubercular treatment (ATT) in view of transaminitis

During her stay in the ward, there was no improvement in her neurological condition. She was started on injections of Romiplastin and Erythropoietin once a week for anemia and thrombocytopenia. At one point, the patient had an episode of desaturation and tachypnea, with an increased need for oxygen. A chest X-ray was performed. After a detailed discussion with her relatives, a supportive care plan was made. The patient's condition gradually deteriorated on day 27 of admission, the patient succumbed after a prolonged illness.

DISCUSSION

TB remains to be a global threat despite treatment modalities being available even for Extensively Drug-Resistant Tuberculosis (XDR TB). TB can affect the female reproductive system, can cause infertility, menstrual irregularities, pregnancy loss and sometimes also present as a silent Infection. [8] The mortality rate from TB is higher for women than men in India. Reasons are multifaceted such as social ones like delays in seeking care due to stigma, prioritizing family needs over their own health, and lack of economic independence. Nutritional deficiencies are more common among Indian women which further dampens immunity. Conditions like hypoproteinemia and anemia worsen TB prognosis. Co-infection with HIV are more susceptible to TB. [9]

All isolated *Mycobacterium tuberculosis* which were identified to be pansensitive to first-line ATT drugs. In addition, other confounding/poor prognostic factors like hypoalbuminemia, anemia were present in our patients. Hypoalbuminemia in TB patients can be caused by various factors, including malnutrition, chronic inflammation, and liver dysfunction. TB itself can also contribute to

hypoalbuminemia by increasing catabolism and decreasing albumin synthesis. For example, a meta-analysis found that TB patients with hypoalbuminemia had a 2.4-fold increased risk of death compared to those with normal albumin levels. [10]

One of three cases had *Tuberculous meningitis* (TBM) which is considered the most severe form of extrapulmonary tuberculosis, and it carries a higher risk of complications and mortality compared to pulmonary tuberculosis. According to a study published in the Indian Journal of Medical Research, the incidence of TBM in India is estimated to be around 22 per 100,000 population, with a higher incidence in females (24 per 100,000) compared to males (19 per 100,000). [11,12] It's important to note that the overall burden of TBM in India is influenced by several factors, including socioeconomic conditions, access to healthcare, and the prevalence of tuberculosis in general. [13] Low socioeconomic status and poor living conditions are recognized as significant risk factors for latent tuberculosis infection, along with malnutrition. [14] In India, key obstacles to controlling tuberculosis include inadequate primary healthcare infrastructure in rural regions of many states, unregulated private healthcare systems, insufficient political commitment, and administrative corruption. [15] The WHO, through its "STOP TB" strategy, has set forth a vision to eradicate tuberculosis as a public health issue worldwide by 2050.

CONCLUSION

This case series highlights the importance of considering female gender, anemia and hypoalbuminemia as important risk factors for potential pulmonary and extrapulmonary TB complications.

FIGURES

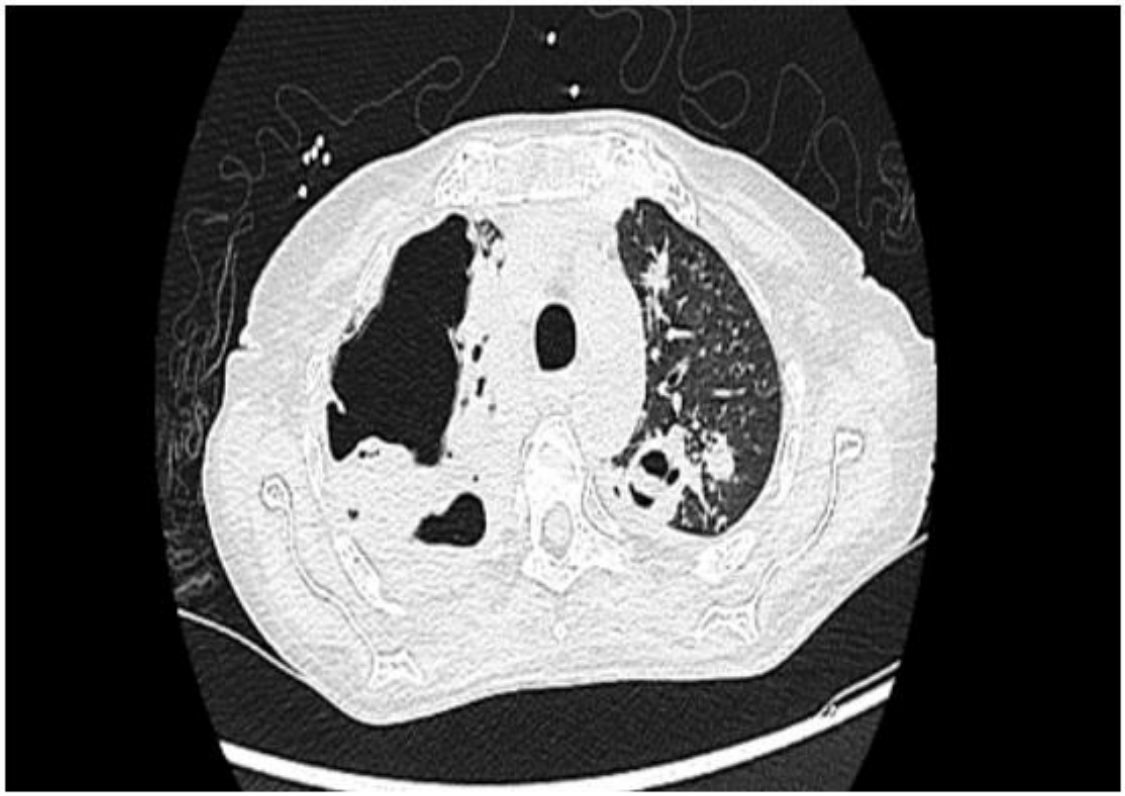


Fig. 1(a) - HRCT Chest- Extensive clusters of centrilobular subsolid to solid non-calcified nodules showing 'tree-in-bud' branching pattern likely due to Disseminated Active Pulmonary tuberculosis

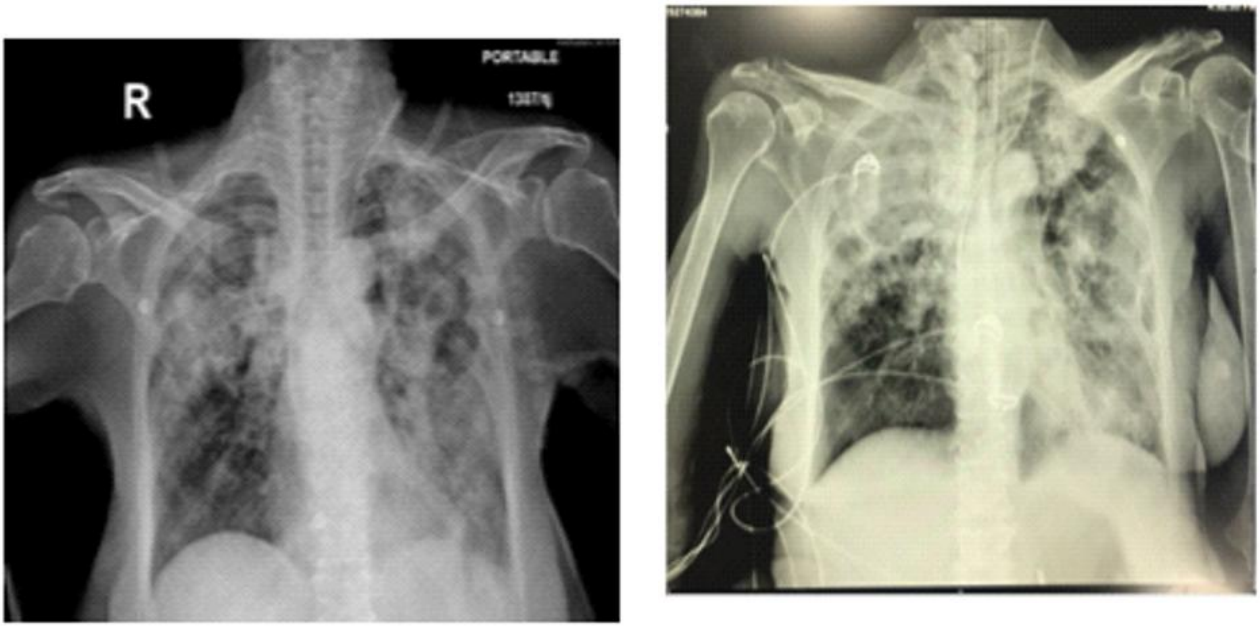


Fig. 1(b) – Chest X-ray- Dense consolidations seen bilaterally upper and mid zone right side and left lung field .Fig1.(c) Chest X-ray Post-Haemoptysis(Day 5) Bilateral consolidations seen suggestive of extensive Pulmonary tuberculosis

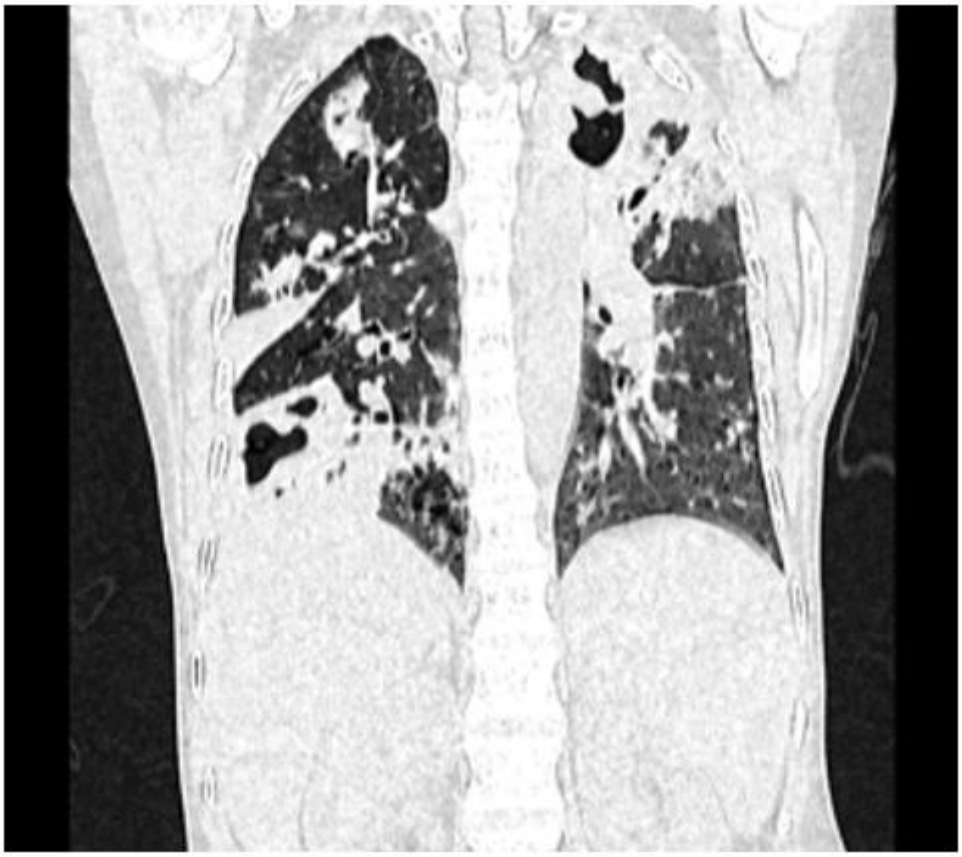
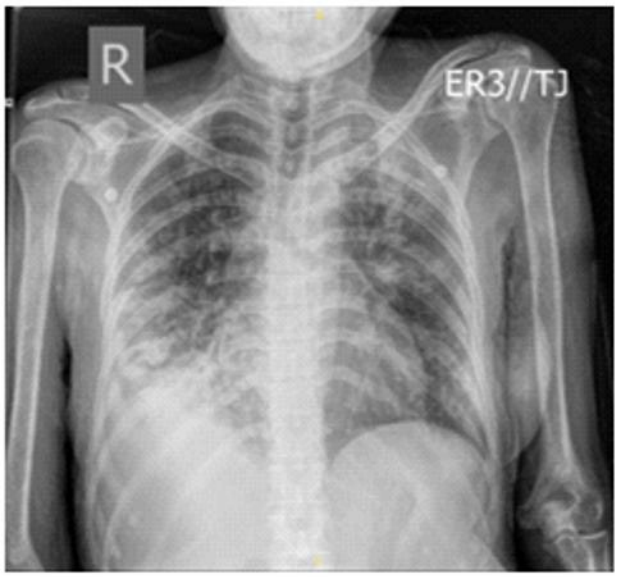


Fig. 2(a) - HRCT chest - Multifocal large cavitating consolidations with air bronchograms and surrounding ground glass haziness as well as multiple clusters of branching centrilobular nodules with a tree in bud appearance in bilateral lung parenchyma suggestive of Pulmonary tuberculosis



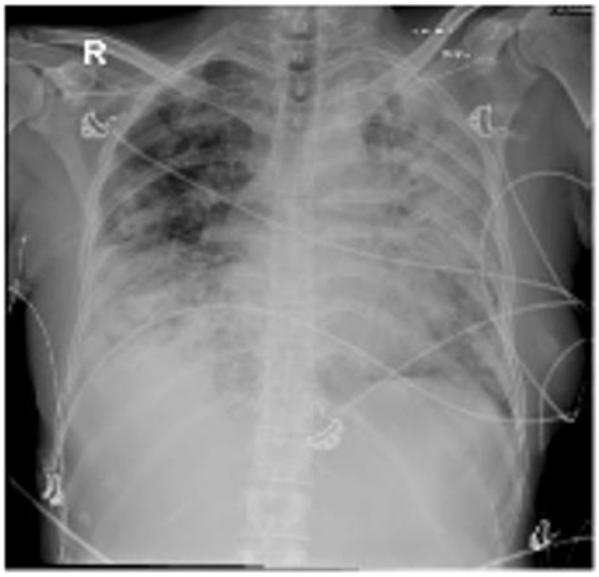
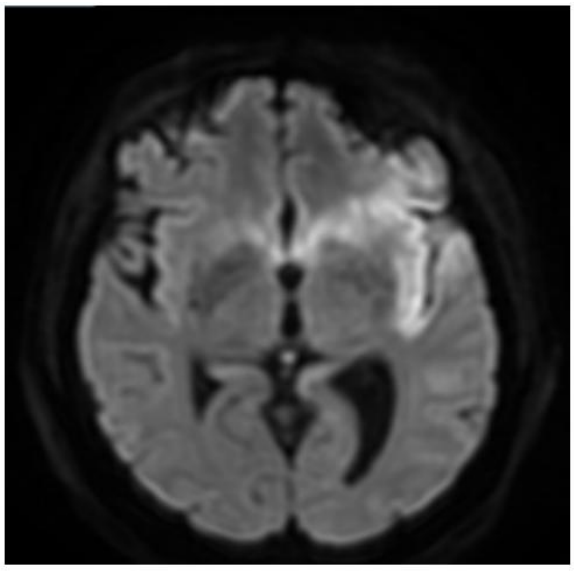


Fig. 2(b) - Chest X-Ray - Patchy opacities in the right mid -lower zones and upper zone and small right pleural effusion suggestive of Pulmonary Tuberculosis Fig. 2(c) - Chest X-Ray -diffuse patchy cavitary consolidation of both lungs due to acute Pulmonary tuberculosis



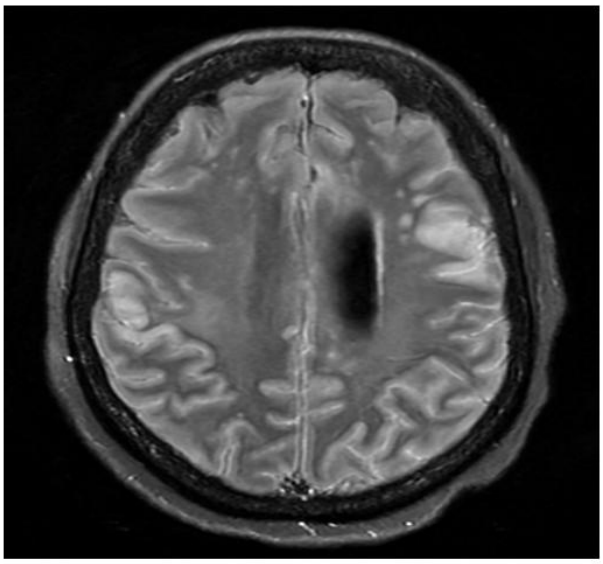


Fig. 3(a) - Completed acute non-haemorrhagic infarctions in the left middle cerebral arterty and left anterior choroidal / PCA distribution. On contrast, diffuse enhancement is identified in the sulcal spaces within both cerebellar hemispheres, and within the sylvian fissures and basal cisterns suggestive of acute basal exudative meningitis causing vasculitis

Table 1. Baseline investigations of three cases of TB

Investigations	Case 1	Case 2	Case 3
Haemoglobin (g/dl)	9.9	5.4	9.8
Total Leucocyte count (x10^9/L)	10.90	18.81	7.9
Platelet count (x10^9/L)	150	590	303
Blood Urea Nitrogen (mg/dl)	15.93	8.22	20.23
Urea (mg/dl)	34.1	17.6	43.43
Creatinine (mg/dl)	0.504	0.376	0.581
Sodium (mmol/L)	132.7	129.5	115

Potassium (mmol/L)	4.05	4.41	5.04
Total Bilirubin (mg/dl)	0.385	0.384	1
Alanine Transaminase(U/L)	12	19.8	89.5
Aspartate Transaminase (U/L)	13.3	36.4	47
Gamma Glutamyl Transferase (U/L)	55.3	178	132
Alkaline Phosphatase (U/L)	112	407	134
Total Protein (g/dl)	4.99	6.37	6.45
Albumin (g/dl)	1.82	2.29	3.3
Human Immunodeficiency Virus	Non-reactive	-	Non- reactive
Hepatitis B Virus	Non-reactive	-	Non-reactive
Hepatitis C Virus	Non-reactive	-	Non-reactive
C-Reactive Protein (mg/dl)	19.7	23.2	0.92
GeneXpert TB (Sputum)	Very low detected	High detected	-
GeneXpert TB (CSF)	-	-	Low detected
Rif resistance	Not detected	Not detected	Not detected
CSF Examination			
* Cell count (Cells/ µL)	-	-	WBC 35, RBC 1
* Protein (mg/dl)	-	-	77.4
* Sugar (mg/dl)	-	-	25
* ADA (U/L)	-	-	2.1
* AFB	-	-	Positive
* Pyogenic Culture	-	-	No growth

Table 2. Summary of patient characteristics, co-morbidities, radiological findings, treatment, complication and outcome of three cases of TB

Age/Sex	Co-Morbidities	Radiologic Features	Treatment	Complication	Outcome
72/F	Diabetes Mellitus	HRCT Chest - 'tree-in-bud' branching pattern, Multiple cavitating small to large consolidations scattered in bilateral lung parenchyma, mediastinal adenopathy	First line ATT and other supportive treatment	Haemoptysis	Deceased
31/F	None	HRCT chest – 'tree in bud' appearance, Multifocal large cavitating consolidations, multiple calcified granulomas in bilateral [R > L], multiple subcentimeter size and enlarged mediastinal nodes	First line ATT and other supportive treatment	ARDS	Deceased

55/F	Rheumatoid arthritis, Chronic liver disease, Hypertension	MRI Brain - Completed acute non-haemorrhagic infarctions in the left MCA and left anterior choroidal / PCA distribution. Post contrast - diffuse enhancement within sulcal spaces of both cerebellar hemispheres, and within the sylvian fissures and basal cisterns; suggestive of acute basal exudative meningitis causing vasculitis	IV Steroid, PO Isoniazid, PO Pyrazinamide, PO Ethambutol, IV Amikacin, IV Levofloxacin, Moxifloxacin, PO Trizidone [3]	TB meningitis	Deceased

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