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MODESTUM

Case Report **OPEN ACCESS**

Pulmonary tuberculosis with cardiac dysfunction: An ignored combination!

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ABSTRACT

Cardiovascular involvement is rare in tuberculosis & high index of suspicion is must in diagnosing these cases in high burden setting to have successful treatment outcome. In this case report, 26-year male, presented with constitutional symptoms for three months duration with acute deterioration with tachycardia and tachypnea with hypoxia. Radiological investigations documented conglomerated miliary tuberculosis and confirmed by sputum smear microscopy. Cardiac investigations revealed sinus tachycardia in ECG, raised cardiac enzymes, and echocardiography as 'global left ventricular hypokinesia' with reduced ejection fraction. Treatment initiated with steroids with anti-tuberculosis and recorded near complete radiological resolution, bacteriological cure and restored cardiac function after six months with good compliance. We recommend cardiac workup in all pulmonary tuberculosis cases with disproportionate tachycardia.

Keywords: pulmonary tuberculosis, cardiac dysfunction, sinus tachycardia, gene Xpert MTB/Rif, global hypokinesia

INTRODUCTION

Tuberculosis primarily affects lung, and more than 80% of tuberculosis cases are pulmonary tuberculosis cases [1]. Extrapulmonary tuberculosis predominantly affects lymph nodes and pleura, while other organ systems as central nervous system, Gastrointestinal, cardiovascular system, genitourinary, and osteoarticular in descending order. Cardiovascular tuberculosis accounts for 1% to 2% of all tuberculosis cases in immunocompetent cases [2]. Cardiovascular involvement due to tuberculosis is marker of poor outcome, and tuberculous pericarditis is associated with mortality up to 40% [3]. The NET-heart project by American Society of Cardiology called "Neglected tropical diseases and other infectious diseases involving the heart" with aims to expand knowledge about the cardiovascular complications due to tuberculosis, diagnostic modalities for better management and rationale treatment to decrease mortality and morbidity [4, 5].

CASE SUMMARY

26-year-old male, petrol pump worker by occupation, no addiction history, normotensive, non-diabetic, referred to our center by family physician for acute febrile respiratory illness.

Further clinical details are, as follows:

1. Fever-for three months, intermittent, low to moderate grade without chills, and rigors associated with minimal body ache and headache. He was treated as case of enteric fever for two months by family physician and later one month as jaundice without laboratory workup documentation.
2. Cough-for three months dry and intermittent with minimal white sputum production.
3. Loss of appetite and weight loss over period of three months.
4. Weakness and myalgia with fatigability for two months.
5. Shortness of breath on exertion in the last two months.

His symptoms worsened over three months period and presented with acute febrile respiratory illness with difficulty in breathing and minimal haemoptysis for eight days. His shortness of breath worsened, and family physician referred to our center for further workup and expert management.

Clinical examination documented, as follows:

1. Restless, dry oral mucosa, cyanosis, pallor, and febrile.
2. Heart rate–156/min, respiratory rate: 46/bpm, BP–80/60 mmhg.
3. PsO_2: 82% @ room air resting & 70% @ room air on exertion.
4. Respiratory system examination revealed–bilateral breath sounds normal, bilateral crepitation's heard on both lung fields.
5. Nervous system examination–higher functions normal, no neurological abnormality, cranial nerves normal, and recent and past memory normal recall.

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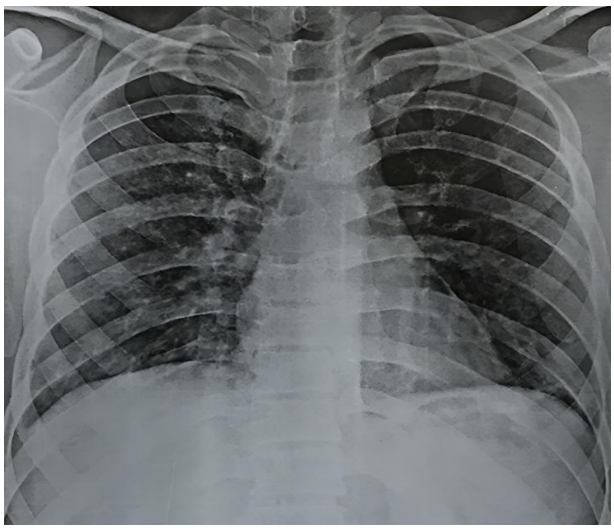

Figure 1. Chest X-ray PA-1 showing bilateral upper and middle zone inhomogeneous opacities

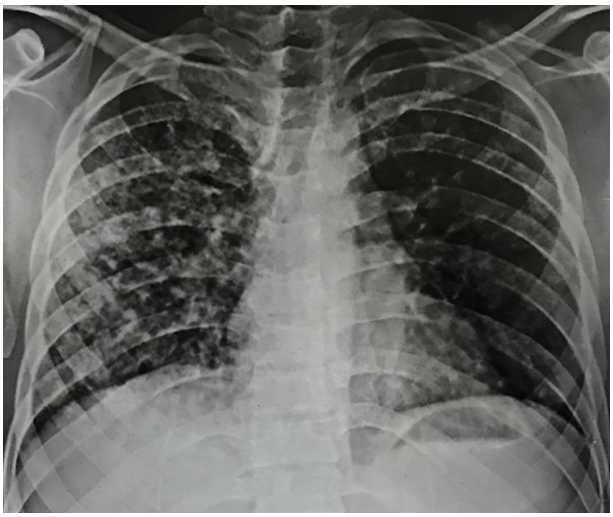

Figure 2. Chest X-ray PA-2 new nodular opacities and increased inhomogeneous opacities as in upper, middle, and lower zones

6. Cardiovascular and gastrointestinal systems were normal.

We have assessed past records of hospitalization as chest X-ray showing bilateral upper and middle zone inhomogeneous opacities (**Figure 1**) and chest X-ray done at our center during hospitalization documented new nodular opacities and increased inhomogeneous opacities as in upper, middle, and lower zones as compared to previous (**Figure 2**). Duration between two X-rays were two months and received antibiotic treatment targeting enteric fever and jaundice.

Laboratory examination during hospitalization documented, as follows:

1. Hemoglobin–10.5 gm% total white blood cells–16,000/mm3 polymorphs–70%, platelet count–70,000/uL.
2. CRP–245 mg/L (0-6 mg/L), random blood sugar level–134 mg%, and HbA1C–5.60%.
3. LDH–1,290 IU/L (70-470 IU/L) and uric acid–3.4 mg (3.5-7.5 mg/dL).

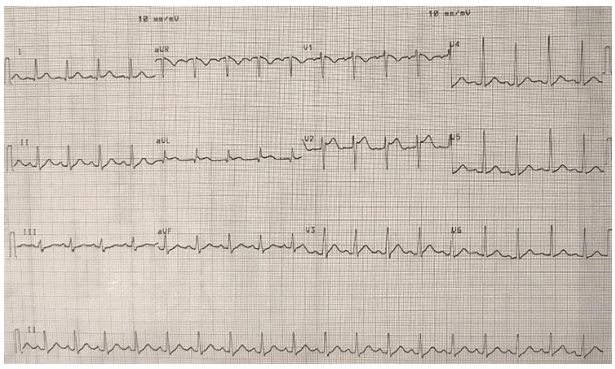

Figure 3. ECG showing sinus tachycardia

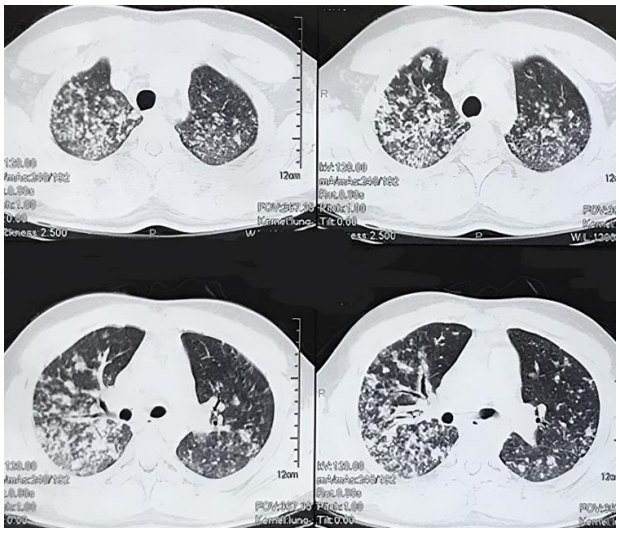

Figure 4. HRCT thorax-1 suggestive of bilateral, peripheral multifocal nodular opacities in upper middle and lower lobes

4. Serum electrolytes: sodium–130 meq/L (135-145 meq/L), potassium–3.7 meq/L (3.5-5.5 meq/L), and ionic calcium–1.39 meq/L (1.09-1.36 meq/L).
5. D-dimer–780 ng/ml (<500 ng/ml).
6. IL-6–1.75 pg/ml (0.00-7.00 pg/ml).
7. Serum creatinine–2.7 mg/dL (0.7-1.4 mg/dL).
8. Liver function tests–normal.
9. Thyroid functions–normal.
10. Sputum examination documented acid fast bacilli and TB gene Xpert MTB/RIF were documented MTB genome and rpo-b mutation negative.
11. ECG was showing sinus tachycardia (**Figure 3**).
12. Pro-BNP–96 pg/ml (<125 pg/ml).
13. CPK-MB–38.33 IU/L (0-25 IU/L).
14. Trop-I-(cardiac troponin)–324.3 ng/L (0-19 ng/L)
15. COVID-19 RT PCR test and results documented negative for SARS-CoV-2.

Echocardiography done to rule out myocarditis and structural heart disease in presence of sinus tachycardia and raised cardiac enzymes. Echocardiography examination shown dilated left ventricle, global left ventricular dysfunction with reduced ejection fraction, and without structural pericardial or myocardial abnormality. HRCT thorax suggestive of bilateral, peripheral multifocal nodular opacities in upper middle and lower lobes (**Figure 4**).

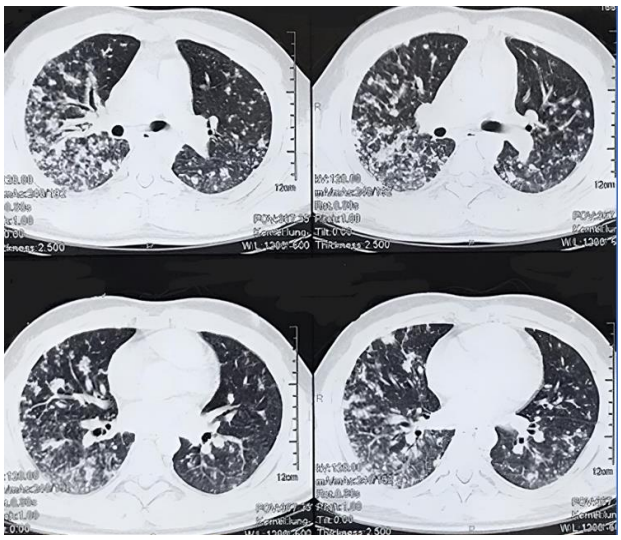

Figure 5. HRCT thorax-2 showing Nodular opacities were isolated, randomly placed at some point and in groups forming conglomerated appearance to consolidations involving upper and middle lobes

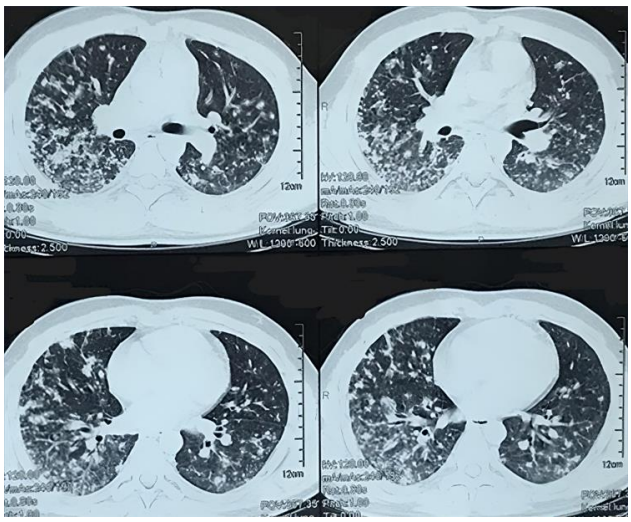

Figure 6. HRCT thorax-3 showing Nodular opacities with decreasing frequency to lower lobes as comparison to upper and middle lobes

Nodular opacities were isolated, randomly placed at some point and in groups forming conglomerated appearance to consolidations involving upper and middle lobes predominantly with decreasing frequency to lower lobes (**Figure 5** and **Figure 6**).

During hospitalization emergency care management done with oxygen supplementation by nasal canula with target oxygen saturation 91%, Injection methylprednisolone 40 mg three times and antibiotics as meropenem and linezolid. We have stopped antibiotics after sputum examination documented as tuberculosis and started anti-tuberculosis treatment (ATT) as per weight band with isoniazid, rifampicin, pyrazinamide, and ethambutol. Cardiac enzymes were raised, and ECG was showing sinus tachycardia, cardiologist consultation suggested to add metoprolol 25 mg OD to control the heart rate. Nephrologist consultation taken for renal involvement and decided for wait and watch for renal functions and concluded myocardial dysfunction as cause for renal dysfunction. Renal functions were completely recovered after one week after stabilization of heart rate.

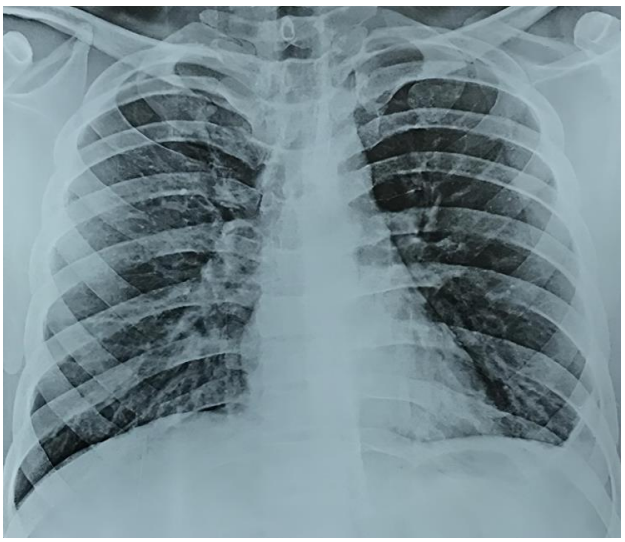

Figure 7. Chest X-ray PA at two months showing Radiological response with significant decrease in nodular opacities in bilateral lung fields

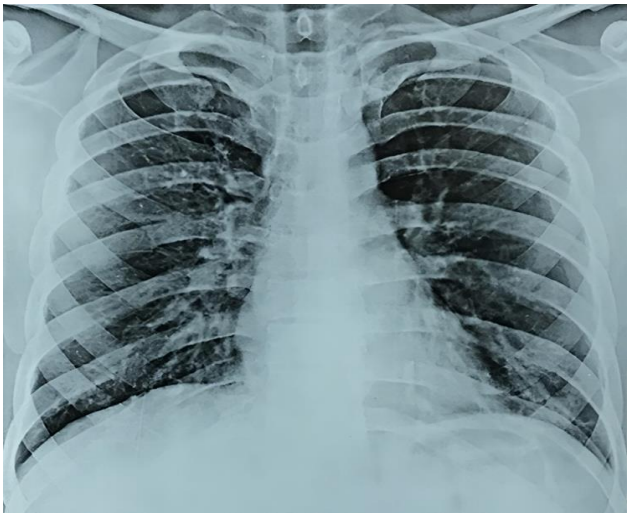

Figure 8. Chest X-ray PA at four months showing near complete resolution of opacities in upper, middle, and lower lung fields

He was tolerating antituberculosis treatment without any liver or renal dysfunctions, dose of methylprednisolone decreased from 40 mg three times to one time daily after one week after stabilization of heart rate and decrease in oxygen requirement. His improvement in oxygen saturation, no oxygen requirement and normal heart rate (60-90 beats/minute) took 10 days in intensive care unit. He was discharged to home after two weeks of treatment, with four drug ATT and oral methylprednisolone 40 mg tapered over to eight weeks to four mg daily. After two months of treatment, radiological response documented with clearance of radiological abnormalities. Radiological response documented as significant decrease in nodular opacities in bilateral lung fields (**Figure 7**).

After completion of intensive phase, she was shifted to continuation phase with isoniazid, rifampicin, and ethambutol without steroids. Radiological follow-up examination done at four months shown near complete resolution of opacities in upper, middle, and lower lung fields (**Figure 8**). He was having abnormal renal functions initially during hospitalization, we recommended monthly follow-up in outdoor unit with kidney functions and liver functions tests monitoring. He tolerated

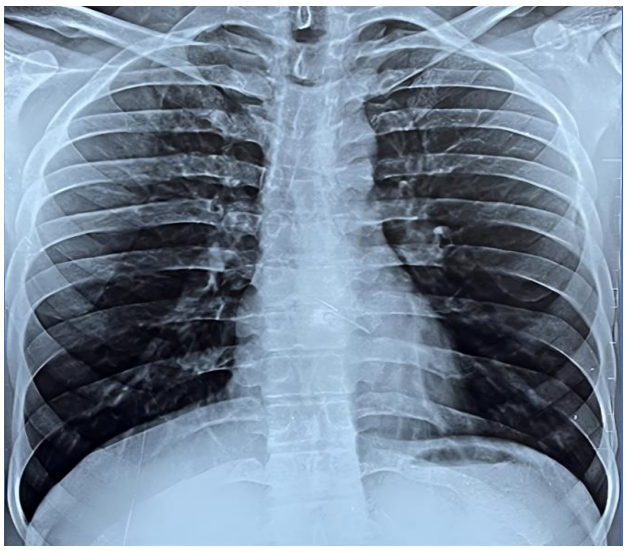

Figure 9. Chest X-ray PA at six months showing complete resolution of radiological abnormalities

complete course of ATT for six months as per national guidelines and documented 'cure' of tuberculosis. Sputum smear microscopy done at two months and six months documented absence of acid-fast bacilli, and we confirmed as cure from disease.

Clinical and radiological response documented after completion of ATT with complete resolution of radiological abnormalities in chest X-ray (**Figure 9**). Echocardiography done after completion of ATT documented normal cardiac chambers, normal systolic and diastolic left ventricular function with normal ejection fraction and without structural pericardial or myocardial abnormality.

DISCUSSION

Tuberculosis is most common communicable disease in India, caused by mycobacterium tuberculosis. Pulmonary tuberculosis is leading cause of mortality due to infectious disease and is among the top 10 causes of death globally. TB is having significant impact on mortality and morbidity in in low- and middle-income countries (LMIC), where it generates a significant burden of disease [6]. Global burden of tuberculosis is considered as public health emergency since last 25 years and irrespective of efforts form health department disease remains uncontrolled in terms of incidence, prevalence, mortality, and morbidity. China, India, Indonesia, Nigeria, and South Africa rank first to fifth, respectively, in terms of the incident TB cases [7]. India accounts for highest number of new cases, and total cases on treatment across the world. As per figures by WHO (during 1999 to 2020) one billion more peoples will be newly infected, 200 million will get sick and 70 million will die if aggressive control measures will not be taken and universal diagnosis and treatment options are not strengthened [8].

Tuberculous myocarditis is very rare disease with only few cases reported in literature. Tuberculous myocarditis usually resulted form lymphogenous or hematogenous dissemination of tubercle bacilli form lung parenchymal focus and sometimes direct spread from primary pericardial disease [9, 10]. Myocarditis usually a bi-ventricular disease with diffuse involvement of myocardium. Some times isolated left or right ventricle may be involved, and this is associated with lung involvement on respective side. Sinus tachycardia is predominant electrocardiographic abnormalities in these cases with abnormally raised cardiac enzymes such as creatin phosphokinase–MB (CPK-MB) and cardiac troponins. We have documented similar finding in our case. Although myocardial biopsy is specific for myocarditis, it is less sensitive. In one of the studies with endomyocardial biopsy, biventricular involvement was noted in approximately 70% of patients and alone RV myocarditis in 8% [11]. Echocardiography is sensitive tool to diagnose myocardial involvement and abnormalities documented as regional or global wall motion abnormality, dilated chambers and systolic or diastolic ventricular dysfunction and reduced ejection fraction [12]. Echocardiography is not specific for myocarditis unless myocardial echogenicity is present.

Thus, myocarditis is a challenging diagnosis to establish, and there is no clear in vivo gold standard since a negative endomyocardial biopsy result does not exclude the diagnosis and echocardiography is not specific [13]. Although echocardiography is the preferred imaging modality for the heart, CT and MR imaging are likely underutilized due to their capacity to increase lesion visibility and characterization. In present study, cardiac MR (CMR) is not performed due to cost constraint. CMR outperforms echocardiography in detecting tuberculous myocardial involvement, analogous to what has been reported in the western European series on myopericarditis [14, 15].

Treatment of cardiovascular tuberculosis is not validated for myocardial involvement and advocation of steroids along with ATT were not widely studied due to less prevalence and reporting. Steroids with ATT are recommended in pericardial disease for 12 weeks in tapering doses with significant impact on mortality and final outcome [16]. In our case report with myocardial Tuberculosis, steroids were used for four weeks in tapering order with ATT backup.

Issues Needs Further Global Research

1. Is cardiac dysfunction possible without direct involvement of heart or structural heart disease in pulmonary tuberculosis?
2. Whether systemic inflammatory surge is leading cause for cardiac dysfunction as measured by CRP titer in pulmonary tuberculosis?
3. Whether direct and or indirect myocardial involvement due to Tuberculosis pathology leading to cardiac dysfunction?
4. Direct involvement due to TB is underestimated due to less expertise in invasive diagnostic modalities as myocardial samplings and reliability of these modalities is real concern.
5. Indirect myocardial Involvement occurs due to inflammatory surge and adrenal suppression. Adrenal suppression is common with or without adrenal involvement resulted into cardiac dysfunction.
6. Whether steroids should be added with ATT in these cases as steroids will help in two ways, first cutdown inflammatory surge and second adrenal support.
7. Global hypokinesia is hallmark of cardiac dysfunction especially in these cases with myocardial suppression and cardiac pump failure resulting into tachycardia and shock.

In present case report, we have documented cardiac dysfunction in radiologically advanced lung disease with disproportionate tachycardia and tachypnea with hypoxia. Abnormal cardiac enzymes, sinus tachycardia in ECG and abnormal echocardiography conformed myocarditis as cause for cardiac dysfunction. We have successfully treated with steroids and ATT with radiological resolution, bacteriological cure in pulmonary tuberculosis and normal cardiac function after six months.

Key Learning Points From This Case Report

1. Cardiac dysfunction in active pulmonary tuberculosis is underestimated and less evaluated routinely.
2. Disproportionate tachycardia and tachypnoea with or without shock are clinical indicators to suspect early, especially in cases with risk factors like advanced pulmonary TB on chest radiograph with abnormal cardiac enzymes.
3. Echocardiography examination shown normal cardiac chambers, global left ventricular dysfunction with reduced ejection fraction and without structural pericardial or myocardial abnormality.
4. Treatment with short course of steroids with ATT backup is showing significant improvement in clinical status and have significant impact on final cardiac outcome.
5. Cardiac dysfunction is not rare, actually it's a double trouble in sick and critical cases with pulmonary TB.
6. We recommend always look for cardiac dysfunction in pulmonary TB cases in cases with unstable cardiorespiratory parameters. Echocardiography is basic bedside non-invasive, reliable tool to diagnose cardiac dysfunction in expert hands.
7. Learning point from this case report is never hesitated to give steroids even in advanced cases with ATT backup, which will significantly impact final outcome in both, TB, and cardiac dysfunction.

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Ethical statement: Authors stated that the study is approved by the Institutional Review Board/Ethics Committee of MIMSR Medical college, Venkatesh chest Hospital and Critical Care Center, Latur, India. Authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal.

Declaration of interest: No conflict of interest is declared by authors.

Data sharing statement: Data supporting the findings and conclusions are available upon request from the corresponding author.

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