

## Case Report

# Cryptic tuberculosis: a missed diagnosis and an unusual presentation

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### ABSTRACT

Cryptic tuberculosis is a rare and atypical clinical presentation of disseminated hematogenously spread tuberculosis, in which the usual diagnostic criteria for tuberculosis, especially the roentgenographic evidence, are lacking. Here we report a case of an elderly female with prolonged respiratory distress, persistent anaemia, with thrombocytopenia and hypoproteinaemia; in spite of long term treatment and normal X-ray chest. Diagnosis of cryptic tuberculosis was established only after histopathology report of a late appearing axillary lymph node during the course of treatment. The incidence of these occult forms of tuberculosis, where diagnosis is often established too late or entirely missed, is significant. This possibility must be kept in mind in severe infectious conditions and pyrexia of unknown origin without obvious aetiology.

**Keywords:** Bacterial infection, Diagnosis, Respiratory tract, Treatment, Tuberculosis

### INTRODUCTION

Cryptic disseminated tuberculosis is an insidious form of hematogenously spread tuberculosis, most commonly affecting middle aged and elderly. Cryptic form includes some cases where there is reactivation of a primary complex as well as those with a small, sometimes undetected, chronic focus.<sup>1</sup> In immune-compromised patient, cryptic tuberculosis may alter the diagnosis and is often missed or possibility of tuberculosis is not even considered. Late and unusual presentation may lead to difficulty in diagnosis and increased mortality.

### CASE REPORT

A 62 year old female patient presented to emergency department of hospital with chronic productive cough since 4 months, associated with muco-purulent, non-foul smelling, non-blood tinged expectoration. She also had shortness of breath since last one month, which was insidious in onset, gradually progressive, from MMRC

grade 2 to 4 over 20 days, associated with non-pleuritic, no radiating, dull chest pain on right side since fifteen days. There was no history of fever, loss of appetite, loss of weight.

No previous history of tuberculosis, diabetes mellitus, bronchial asthma, hypertension, coronary artery disease and cerebrovascular disease. She had undergone partial thyroidectomy ten years back due to some mass in thyroid but concerned documents were not available. Family history was not significant. At the time of presentation, patient's general condition was poor, she was dyspnoeic and irritable but conscious, oriented to time, place and person.

On examination there was tachycardia and tachypnea; oxygen saturation was 78 % on room air. Patient was pale with bilateral pitting pedal edema and no lymphadenopathy. On respiratory examination, there were decreased breath sounds on right mammary area, interscapular area, infrascapular area, infra axillary area

and on left infrascapular area and infraaxillary area. In per abdomen examination, abdomen was distended fluid thrill, shifting dullness was present, no organomegaly. Cardiovascular examination showed loud P2 and neurological examination was normal. Due to past history of thyroid mass, possibility of malignant pleural effusion was considered.

Patient was admitted to ICU started on non-invasive ventilation, arterial blood gas analysis was suggestive of hypoxia. Complete blood count revealed anaemia (Hb 7gm/dl) and thrombocytopenia (platelets 58000). ESR was 18 mm. Liver function tests were normal except for serum protein, which was persistently low. Renal functions, Thyroid function tests, ECG, 2D Echo were normal. Chest X-ray was suggestive of right massive pleural effusion and left moderate pleural effusion (Figure 1).

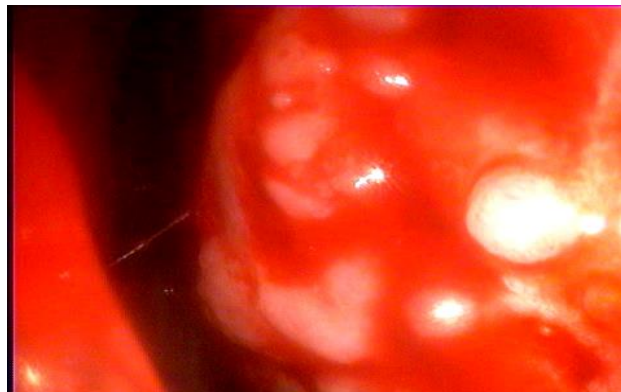


**Figure 1: CXR at the time of admission.**

USG chest revealed bilateral pleural effusion (Massive on right side and mild to moderate on left side). USG whole abdomen revealed thickened gall bladder and mild to moderate ascites. Thoracocentesis was done from right side; approximately 1200 ml haemorrhagic fluid was aspirated and sent for analysis. Pleural fluid analysis was as follows: Sugar -68, Total protein -2.39, Albumin -1.00, Cell count- 80, Neutrophils -10, Lymphocytes -75, Mesothelial- 10, RBC- 9200/cmms, and ADA - 25, LDH- 502. Fluid was transudate in nature according to Modified Light's Criteria. Pleural fluid Cytology showed dense collection of neutrophils admixed with few lymphocytes, macrophages and mesothelial cells in background of degenerated cell. There were no atypical cells.

Sputum for AFB, Montoux test, HIV and HBsAg were negative. Diagnostic ascitic tapping was done on day 4 which was again transudative in nature. Ascitic fluid routine microscopy was suggestive of transudate fluid. Both Pleural fluid and ascitic fluid were sterile on culture and sensitivity. Both were negative on CBNAAT for tuberculosis bacilli and negative for ANA, CEA, CA-125 and AFP were normal. For persistent hypoproteinaemia,

protein replacement was done by intravenous Albumin. Due to recurrent massive pleural effusion, intercostal drainage tube was inserted in right 5<sup>th</sup> intercostal space.



**Figure 2: Thoracoscopic view of pleural nodule.**

Since no clear diagnosis was made, Thoracoscopy was performed, which revealed presence of a pleural nodule (Figure 2). Biopsy followed by histopathology showed strips of fibro-collagenous tissue along with adipose tissue showing mixed inflammatory cell infiltrate. No evidence of malignancy. CECT chest could not be performed due to poor general condition of the patient. On 10<sup>th</sup> day of admission a 1cm x 2cm size left apical axillary lymph node was palpated which was not present earlier, USG guided FNAC of lymph node done which showed mainly dense necrosis, admixed with scattered histiocytes and few epithelioid granuloma in the background of mixed inflammatory cells, no atypical cells were seen. FNAC was suggestive of tubercular abscess.

On this basis of above work up and with no evidence of malignant tissue on pleural biopsy; anti-tubercular therapy under DOTS category 1 was started along with fluoroquinolones. Patient's general condition was gradually deteriorating due to delay diagnosis of tuberculosis. Due to persistent hypoxia on ABG and fall in oxygen saturation, emergency intubation was done and she was put on mechanical ventilation on AC-VC mode. ET culture and sensitivity was sent which shows *Klebsiella* growth, sensitive to Colistin only. Despite of higher antibiotics (Doripenem, Colistin, Tobramycin), patient went into Sepsis and MODS and started developing hypotension, for which inotropic support was started. On day 16, patient suddenly developed cardiorespiratory arrest and despite of CPR couldn't be revived.

## DISCUSSION

The miliary tuberculosis is 'overt' if the typical miliary infiltrate is seen on the chest radiograph, whereas it is called 'cryptic' miliary tuberculosis where the typical radiology and clinical features are absent.<sup>2</sup> The diagnosis of cryptic miliary tuberculosis is difficult. Proud foot AT,

et al suggested the term “cryptic miliary TB” for this presentation.<sup>3</sup> Cryptic tuberculosis an atypical clinical presentation of tuberculosis and it differs in many respects from classical miliary tuberculosis. It was most often found in patients, particularly women, over the age of 60 years, usually with a normal chest radiograph, fever rarely present, with only few localising signs, negative tuberculin skin test or QFT Gold, negative smear for AFB in up to 50% cases, meningitis although rare until terminal stage, lymphadenopathy which is rarely present, thrombocytopenia and hypoalbuminemia.

Bacteriological investigation helps little in diagnosis.<sup>4</sup> Anaemia of chronic disease, leucocytosis, leucopenia, leukaemoid reaction, thrombocytopenia and disseminated intravascular coagulation are known to occur in disseminated tuberculosis.<sup>5</sup> In present case report, patient was 62 year. old female with anaemia, thrombocytopenia, normal chest roentogram negative tuberculin test and negative smear for AFB supported above evidence. This form of tuberculosis is difficult to diagnose and most common in older people and those with underlying diseases such as malignancy or blood dyscrasias.

HIV infection, chronic renal disease, diabetes, immunosuppression, endocrine disorder may alter the typical presentation and atypical presentations often delay or even can lead to missed diagnosis of cryptic tuberculosis.<sup>4,5</sup> Mycobacterium tuberculosis isolation from sputum, body fluids or biopsy specimens, histopathological examination of tissue biopsy specimens, and application of molecular methods such as PCR, can be useful for the confirmation of diagnosis.<sup>6</sup> In our case report, there was late presentation of axillary lymphadenopathy and their histopathological report was suggestive of tuberculosis.

In Extra-pulmonary locations; Ultra-sonography, CT, and MRI are useful in diagnosing the extent of organ involvement by lesions of disseminated TB. Recently, Positron-emission tomographic CT has been investigating tool for evaluation of suspected TB.<sup>7</sup> Confirmation of diagnosis is usually made at autopsy.<sup>2</sup> Delay in treatment is independent factor for mortality. A prompt and early

institution of adequate therapeutic trial with anti-tubercular treatment even in the absence of definite diagnosis of tuberculosis can be lifesaving.

## CONCLUSION

Tuberculosis should be in the differential diagnosis of an elderly patient presenting with vague respiratory symptoms or unexplained fever, anorexia, weight loss, change in behaviour or mental status or multiple organ dysfunction in the endemic area. Physical findings are often nonspecific. Abnormal chest radiograph, anaemia, thrombocytopenia, pyuria etc., without a definite diagnosis should prompt a search for tuberculosis.

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