

**Case report**

**Pleural fluid smear AFB positivity: To search for underlying immunosuppression**

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**Abstract:**

Tubercular pleural effusion may cause a diagnostic dilemma as mycobacterium could not be detected in most cases due to paucibacillary nature of effusion. Pleural fluid AFB smear is positive in less than ten percent cases except in patients with tubercular empyema. However, percentage of AFB positivity in smear increases significantly if there is underlying immunodeficiency disorder. We hereby report a case of unilateral pleural effusion which was diagnosed to be of tubercular origin based on biochemical and cytological parameters along with plenty of AFB in pleural fluid smear. The patient was subsequently evaluated for any associated immunosuppression and he was found to have non-Hodgkin lymphoma.

**Keywords:** pleural tuberculosis; Non-Hodgkin lymphoma; immunosuppression; Mycobacterium tuberculosis

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**Introduction:**

Tubercular pleural effusion remains a diagnostic challenge in spite of recent advances in the field of microbiology and biochemistry. Due to paucibacillary nature of the disease, very often a definite microbiological proof can't be obtained despite extensive investigation; and we have to rely on clinico-radiological features and other surrogate markers of tuberculosis before starting anti-tubercular therapy. This is also not an uncommon practice to start antitubercular therapy empirically in undiagnosed cases of pleural effusion in countries with high prevalence of tuberculosis; and tubercular aetiology can be confirmed in such cases retrospectively with improvement of the patient during treatment. Pleural fluid Acid fast bacilli (AFB) smear is positive in less than 10% of tubercular pleural effusion as concluded by majority of studies.<sup>1,2</sup> However, mycobacterial burden in pleural cavity is higher in immunocompromised

patients and they are more likely to have a positive result from pleural fluid analysis for Mycobacterium tuberculosis.<sup>3</sup> We hereby report a case of pleural tuberculosis which was found to have plenty of AFB in pleural fluid; and subsequent search for immunosuppressive illness revealed underlying non-Hodgkin lymphoma (NHL).

**Case Report:**

A twenty year male patient presented to our department with complaints of dry cough and right sided chest pain since five weeks. He also had low grade intermittent fever since four weeks along with gradually progressive breathlessness. There was no history of haemoptysis or wheeze; but a positive history of loss of appetite and easy fatigability was present. There was no significant past medical or surgical illness. He was a non-smoker, non-alcoholic and no contact history with tuberculosis was found. On examination, there was pallor without any icterus, oedema or clubbing;

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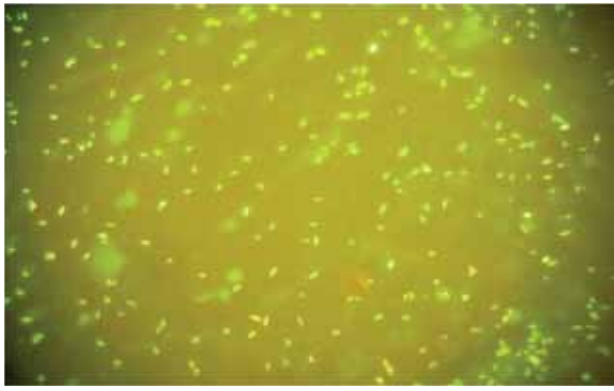


Figure 1: Pleural fluid smear shows plenty of AFB on Auramine-Rhodamine staining under fluorescent microscopy

but bilateral non-tender multiple supraclavicular lymphadenopathy was noted. Respiratory system examination finding was consistent with massive right sided pleural effusion with contralateral mediastinal shift. Chest X-ray (postero-anterior view) confirmed right sided pleural effusion without any parenchymal lesion. Thereby, a provisional diagnosis of tubercular pleural effusion was made and pleural fluid analysis was advised.

Aspirated pleural fluid was straw coloured, exudative (as per Light's criteria), predominantly lymphocytic and adenosine deaminase (ADA) was highly elevated (143U/L). Pleural fluid smear for AFB was positive with presence of plenty of bacilli (Figure 1).

Sputum for AFB was negative. So, a tubercular aetiology of the effusion was confirmed and patient was put on conventional antitubercular therapy. However, he was further evaluated for any underlying immunodeficiency disorder because of pleural fluid AFB positivity.

Routine blood investigation revealed only mild

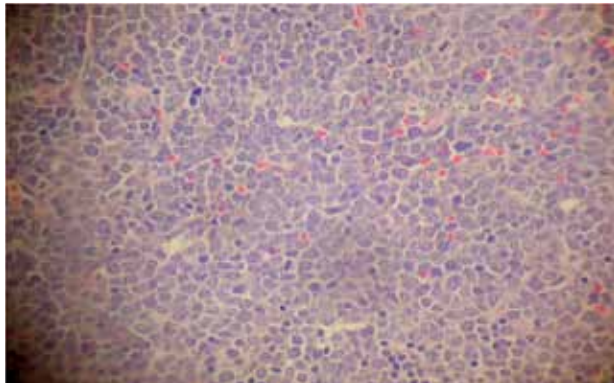


Figure 2: Histopathological examination from lymph node biopsy showing sheets of atypical large lymphoid cells with presence of mitotic figure suggestive of high grade NHL

anaemia (Hb-11.3 gm/dl) with normal renal and hepatic profile. Plasma glucose level was normal and he was non-reactive for both HIV 1 and 2. But an excision biopsy from right cervical lymph node revealed sheets of atypical large lymphoid cells which was consistent with high grade diffuse NHL of large cell type (Figure 2).

Immunohistochemistry was done to confirm the diagnosis and positivity for CD-20, CD-10 and CD79a was reported. Ultrasonography of whole abdomen revealed mild hepatosplenomegaly and multiple retroperitoneal lymph nodes without any ascites.

Patient was subsequently put on chemotherapy with cyclophosphamide, doxorubicin, vincristine and prednisolone (CHOP regimen) although rituximab could not be administered due to financial reason. Pleural effusion gradually subsided with antitubercular therapy and he clinically improved with above chemotherapeutic regimen. Currently he is being treated under the department of haematology with regular follow-up at our department.

#### **Discussion:**

Tubercular pleural effusion occurs in immunocompetent individual by an immunologically mediated hypersensitivity response to mycobacterial antigen following rupture of subpleural caseous focus into pleural space (Sibley 1950; Stead et al 1955) and due to this pathogenetic mechanism, number of organism is very low in pleural fluid. Mycobacterium tuberculosis has been cultured from pleural fluid in less than 30% cases of tuberculous pleurisy.<sup>3</sup> But, in contrast, increased frequency of positive smears for AFB in pleural fluid or tissue has been demonstrated by a number of studies in HIV-infected patients and probably this reflects greater burden of microorganism and more poorly formed granulomata.<sup>4</sup> So, pathogenesis of HIV-associated pleural TB might involve direct, bacterial invasion of pleural space, rather than an active cell-mediated immune response, although the exact mechanism for generation of such effusion remains uncertain. However, tubercular pleural effusion in immunocompromised hosts has mostly been studied among HIV-infected individuals. And there is not enough data to suggest whether the above mentioned pathogenesis of tubercular pleural effusion can be applied for other immunodeficiency disorders (IDD). The mechanisms of immunosuppression are different in HIV and NHL. The hallmark of HIV is a profound immunodeficiency resulting primarily from a progressive qualitative and quantitative

deficiency of helper T-cells occurring in a setting of polyclonal immune activation. On the other hand, systemic immunosuppression may be found in NHL due to an altered monocyte phenotype which can affect immunity through various pathways.<sup>5</sup> But we may assume that the mechanism of direct pleural invasion by mycobacteria remains the same in similar disorders where systemic immunity is eventually impaired.

Therefore, even if there is no history suggestive of an IDD, it should be searched for whenever pleural fluid shows positivity for AFB. As yield of pleural fluid smear for AFB is very low, it is usually not recommended for routine pleural fluid analysis except for a tubercular empyema where the positivity is often high.<sup>6</sup> However, recent observations have stressed the importance of looking for AFB positive smears by collecting a large amount of pleural fluid and centrifugation.<sup>2</sup> It has also been suggested to obtain smear for AFB in all known immunocompromised hosts as it is positive in upto 20% of HIV-infected individuals with tuberculous effusion.<sup>6</sup> This recommendation may

be used in reverse direction to identify underlying immune disorder as happened in our case. Also, we have to keep in mind that dual pathology involving malignancy and tuberculosis is not uncommon in clinical practice where a TB patient is often found to have a co-existent malignancy. Patients should also be evaluated for other immunodeficiency states like primary IDD (e.g. hypo-gammaglobulinemia), leukaemia, lymphoma, multiple myeloma, diabetes, chronic kidney or liver disease etc.

Different studies concluded that combination of pleural fluid and sputum culture may be used as an alternative approach to diagnose tuberculous pleurisy in areas where pleural biopsy or thoracoscopy and other novel diagnostic tests are unavailable.<sup>7</sup> But in rural settings of developing countries, where even the liquid culture for Mycobacterium is not available and in such resource limited situation, pleural fluid smears for AFB is often advised. And any positivity of smear for AFB in such cases should be carefully searched for an underlying IDD.

**Conflicts of interest:** None declared

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