Miliary Tuberculosis With Bone Marrow Aspirate Granulomas Presenting As Obstructive Jaundice- Rare Presentation And Rare Findings In Common Disease- A Case Report

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Abstract : Miliary tuberculosis (MTB) is a disseminated form of tuberculosis which may involve the lungs and other organs. Granulomas in bone marrow aspirate are an infrequent finding. Obstructive jaundice as the sole presentation of miliary tuberculosis is a rare entity. We report a case of 64-year old male presented with complaints of jaundice, pedal edema, anorexia and nausea for 5 days. A provisional diagnosis of obstructive jaundice with anemia was made. Lab investigations reveal increased bilirubin and alkaline phosphatase levels, anemia and high ESR. Bone marrow aspiration cytology show many granulomas. Chest X ray show diffuse miliary mottling in both lungs and HRCT show features suggestive of MTB. Based on bone marrow aspirate granulomas and radiological findings, a possibility of the tuberculous etiology suggested and empirical treatment with a four-drug anti-tuberculous regimen initiated and treated successfully with complete resolution of symptoms before confirmation of aspirate sample by radiometric culture.

Key words : Miliary tuberculosis;Bone marrow granulomas; obstructive jaundice.

Introduction : Miliary tuberculosis (MTB) is a type of disseminated and active tuberculosis (TB) accounts for 1 to 2% of all TB cases and about 8% of all forms of extrapulmonary tuberculosis in immunocompetent individuals. Also, MTB is often under-diagnosed in the elderly, resulting in diagnosis of disseminated TB upon autopsy.[1] Granulomas in bone marrow aspiration cytology is rare , found in 0.5 to 2.2% of trephine biopsies. Bone marrow granulomas include a variety of infections, connective tissue disorders, lymphoma and metastatic Carcinoma.[2]

Obstructive jaundice as the sole presentation of MTB is a rare entity and only a few cases reported in the literature so far. Jaundice occur secondary to compression of bile ducts by enlarged lymph nodes in the porta hepatis.[3] Here, we present a case of miliary tuberculosis without pulmonary and major hematological manifestion diagnosed on radiological and bone marrow examination, which was confronted by administration of regressive treatment before the establishment of the definite diagnosis.

Case report : A 64-year-old male presented with a history of jaundice associated with nausea and edema over feet for fifteen days duration. There was no history of fever, haematemesis, malena, pruritus or clay-coloured stools, no haemoptysis or breathlessness. Physical examination showed a elderly aged adult male of normal build and nourishment with a body weight of 58 kg. He was pale, icteric with bilateral pitting pedal oedema. Vitals were stable. Cardiovascular & central nervous system examinations were within normal limits. Respiratory examination reveal bilateral basal crepts. Abdominal examination showed a non-tender hepatomegaly 3 cm below the costal margin with a smooth surface. There was no shifting dullness.

Lab Investigations revealed hyperbilirubinaemia with total bilirubin 4 mg/dl (0.2-1.3mg/dl) and direct 1.8 mg/dl. Alkaline phosphatase 385 (38-126 U/L) and gammaglutamyl Transferase222 (12-43 U/L) levels were raised. AST and ALT levels were normal. Serum total protein was low 6.0 (6.3-8.5 gm/dl) with albumin of 2.3 gm/dl and globulin 3.7 gm/dl.Coagulation study was normal. Blood urea,Creatinine and electrolytes were normal. Haemogram showed Hb 9.8 gm/dl with neutophilia (92%) on peripheral smear. Platelet count was normal (1.6 lakhs/cumm) and ESR was elevated 70 mm at the end of 1 hour. Serum electrolytes were normal. Urine

examination was positive for bile salts and bile pigments and urobilinogen levels were not raised. Viral serology for HIV, HBV and HCV were negative. Mantoux (15 mm) were positive. Weil-felix, Paul-Bunnel and Brucella serologies were negative.

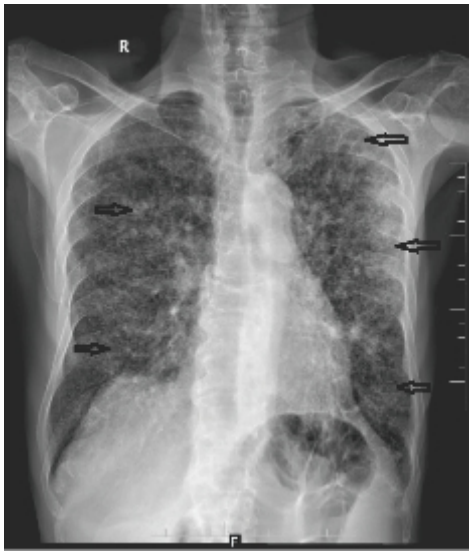
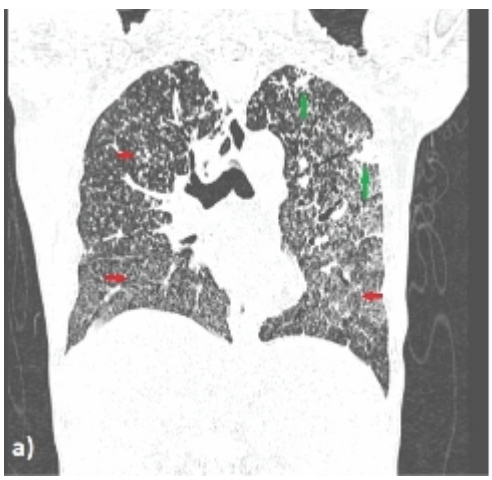


Fig:1 Chest X ray (PA view) Diffuse miliary mottling in both lungs

Chest x ray Diffuse miliary mottling in both lungs(figure 1 black arrows).There is no evidence of effusion. Ultrasonography of abdomen reveal coarsened echotexture of Liver, mild Splenomegaly and mild ascites. No focal lesions. No IHBD. CBD measures 7mm. HRCT Chest done without contrast showed (Figure2) Bilateral diffusely, scattered randomly distributed centrilobular nodules with peripheral areas of consolidation and associated fibroparenchymal changes suggestive of Milliary Tuberculosis and Hepatosplenomegaly. Calcified periportal nodes, mediastinal and hilar nodes seen.



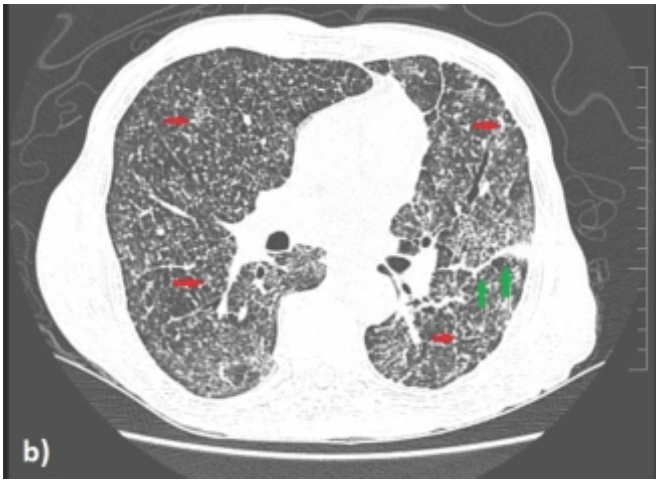


Figure 2 : CT chest noncontrast coronal (a) axial (b) sections showing Bilateral diffusely, scattered randomly distributed centrilobular nodules (red arrows) with peripheral areas of consolidation and associated fibroparenchymal changes (green arrows).

Bone marrow aspiration cytology smears show cellular marrow with presence of many granulomas consisting epithelioid cell (figure 3). There was no caseation necrosis. Consistency of bone appears hard for age. Bone marrow apsirate sample processed for TB culture for radiometry.

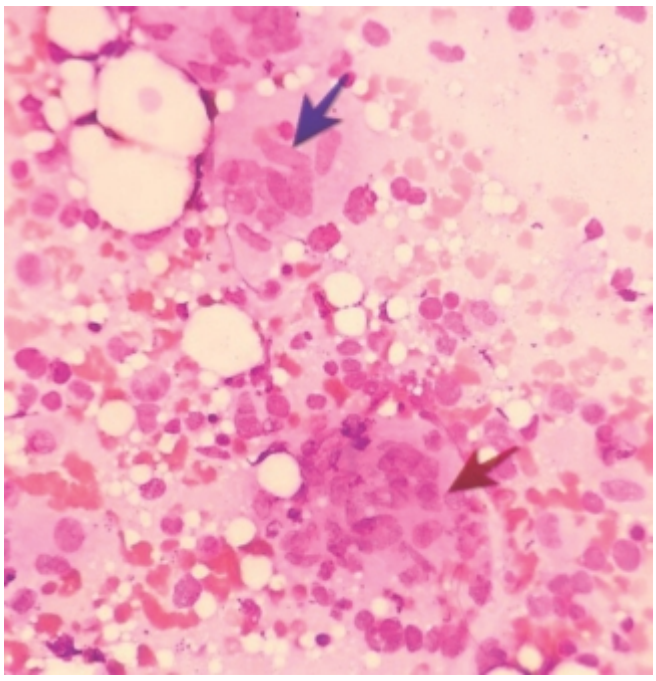


Figure 3 ; Bone marrow aspiration cytology smears show granulomas (red arrow) & epithelioid cells (blue arrow)

Based on clinical, hematological, radilogical and bone marrow cytology findings, patient was started on four-drug anti-tuberculous therapy (ATT). He became asymptomatic on ATT with regression of jaundice and constitutional symptoms.

Discussion : Miliary TB is defined as widespread millet-like (1–5 mm) seeding of Mycobacterium bacilli in the lung and possibly in other organs of the body, mostly liver, spleen,lymph nodes, pleura, pericardium, meninges and bone marrow.[4] Miliary TB usually occurs in immunocompromised host, among immunocompetent adults, miliary TB accounts for less than 2% of all TB cases and 20% of all extra-pulmonary TB cases in clinical studies. The clinical presentation of miliary tuberculosis can be acute, subacute or chronic. The subacute or chronic presentations of miliary TB are more common than acute disease and patients may present with failure to thrive, fever of unknown origin, night sweats or dysfunction of one or more organ systems.[5] Obstructive jaundice presentation is a rare and cause of jaundice in miliary tuberculosis is multifactorial. Most case reports describe obstructive jaundice secondary to tuberculous involvement of the biliary tree, pancreas or ampulla of Vater and post-tubercular biliary stricture .[3]

The most common laboratory abnormalities include anemia, leukopenia, thrombocytopenia and lymphopenia, elevated ESR and C-reactive protein, hyponatremia, hypercalcemia and sterile pyuria. Advanced age (> 60 years), lymphopenia, thrombocytopenia, pancytopenia, hypoalbuminemia, elevated transaminase levels and delayed treatment have been identified as independent predictors of mortality.[6]

In granulomatous bone marrow disease, haematological parameters were altered almost in all the cases.Anemia is the commonest finding. Pancytopenia with leucoerythroblastic picture encountered in chronic cases. Granulomas in marrow aspiration cytology smears are difficult to identify probably because of the fibrosis in and around the granulomas. BMB (biopsy) is a better tool than BMA (aspiration) to demonstrate granulomas as the morphology is better preserved and more amount of tissue is available for study.[7] There are no distinguishing features in the morphology of bone marrow granuloma to permit a definitive diagnosis of the underlying conditions. Though the granulomas associated with caseous necrosis and Langhan type giant cells would be seen more frequently in tuberculosis, the diagnosis cannot be made solely on morphological criteria. Bone marrow can be collected at same time of BMA procedure for culture studies and is especially helpful in disseminated bacterial, fungal and tuberculous infection. The viable organism counts in the bone marrow are considerably less affected by antibiotic treatment than peripheral blood.[8]

The classic chest radiograph appearance is a faint, reticulonodular infiltrate distributed fairly uniformly throughout the lungs. This miliary pattern of infiltrates is seen in about 84% of cases. Other chest radiograph abnormalities include pleural effusion, hilar/mediastinal adenopathy, interstitial or alveolar infiltrates, or cavities. Chest CT scan is a more sensitive test for evaluating miliary TB.[6]

Acid-fast bacilli in microscopy and culture of body fluids, tissue or drainage from an infected focus establishes the diagnosis especially if organisms or caseating granulomas are seen. The tuberculin skin test (PPD) can be a supportive diagnostic tool if positive, but anergy is observed more frequently among patients with miliary TB (up to 68% of cases) than those with pulmonary or isolated extrapulmonary involvement. PPD conversion may often occur following treatment.[5]

Fiberoptic bronchoscopy is usually warranted if acid-fast bacilli are not detected at multiple sites (sputum, gastric aspirate, pleural fluid, ascites, urine, etc.) and there is evidence of pulmonary involvement on chest radiography.[9]

In present case ,high ESR ,bone marrow granulomas,chest X ray and HRCT Chest gives enough evidence to suspect tuberculosis and anti-tuberculus started empirically as TB culture take three weeks. There was complete resolution of symptoms after two weeks of treatment.

The approach to antimicrobial therapy for treatment of miliary TB is the same as for pulmonary TB.[10] Early empirical treatment for possible but not yet definitive miliary TB increases the likelihood of survival and should never be withheld while test results are pending.

Conclusion : Miliary tuberculosis is a potentially lethal form of tuberculosis and rarely presented with obstructive jaundice and bone marrow granulomas in aspirate cytosmears are rare . Though there are no morphological features which allow reliable differentiation between the causes of granulomas, but in correlation with chest X ray and HRCT findings provides high index of suspicion and to to start early antimycobacterial therapy to prevent an otherwise fatal outcome as confirmatory takes long time.

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