

**CASE REPORT**DOI: <https://doi.org/10.3329/mediscope.v8i1.52206>**Bone Marrow Granuloma with Miliary Mottling presenting as Pancytopenia- A rare finding in Tuberculosis - A Case report****MAB Momin¹, RD Singh², U Bhattu³, KM Reddy⁴****Abstract**

Bone marrow granuloma and miliary mottling presenting as pancytopenia together is a rare finding in disseminated form of tuberculosis. Here we report a case of a 52-year, old male patient presented with generalized weakness, loss of appetite, decreased physical activity for one month. Initial lab hematological investigations revealed pancytopenia and high Erythrocyte sedimentation rate. Bone marrow biopsy was performed to determine the cause of pancytopenia which showed caseating granulomas with positive acid fast bacilli on Ziehl-Neelsen staining (Z-N). In chest X-ray miliary mottling and bone marrow biopsy findings together confirmed the case of disseminated tuberculosis. This unusual presentation highlights the considerable diagnostic challenge and importance of bone marrow biopsy for early diagnosis and initiation of treatment.

Key words: Tuberculosis, Bone marrow granuloma, Miliary mottling, Pancytopenia.

Introduction

Tuberculosis (TB) is still world's largest public health problem. In India, accounts for about a quarter of the Global TB burden.¹ Extrapulmonary tuberculosis involves 11-16% of all patients of tuberculosis out of which Granulomas in bone marrow biopsy was rare, found in 0.5-2.0% and miliary mottling accounts for 1-2 % of patients with tuberculosis. Extrapulmonary tuberculosis can present with various hematological manifestations, include anemia of different types, leukemoid reaction, and rarely pancytopenia.²

Bone marrow examination play crucial role in etiological diagnosis of pancytopenia. Bone marrow granulomas associated with variety of infections, connective tissue disorders, hematological and non-hematological malignancies.³

Here we describe the case of an immunocompetent patient who presented with non specific symptoms and pancytopenia. This case emphasizes importance of bone marrow biopsy with Z-N staining for timely diagnosis and rapid initiation of treatment as radiographic findings are not specific for disseminated form of tuberculosis.

1. Dr. Majed Abdul Basit Momin, Consultant pathologist, Department of Laboratory Medicine, Yashoda Hospital, Hyderabad, India. Email: majedmomin878@yahoo.co.in

2. Dr. Rahul Dev Singh, Consultant pathologist, Yashoda Hospital, Yashoda Hospital, Hyderabad, India.

3. Dr. Ugandhar Bhattu C, Consultant pulmonologist, Yashoda Hospital, Hyderabad, India.

4. Dr. Krishna Mohan Reddy G, Consultant Physician, Yashoda Hospital, Yashoda Hospital, Hyderabad, India.

Case Report

A case of 52-year-old male patient presented with generalized weakness, loss of appetite, decreased physical activity for four weeks. He had lost 14 kg of weight over the course of month. He denied history of fever, cough and alteration of bowel habit. He is a known diabetic for the past three years and on medication. There was no past history or contact history of tuberculosis. On clinical examination he had pallor, was afebrile, his pulse rate and respiratory rate were normal. He had no icterus and no lymphadenopathy. Systemic examination was unremarkable except bilateral crepitation in both lower zones. A complete hemogram revealed Pancytopenia with Hemoglobin 8.7g/dl (13.5-16.5gm/dl), total white blood cell count 1300cells/cumm (4000-11000/cumm) and platelets 90,000/cumm (1.5-4.5lakhs/cumm). Peripheral blood smears showed normocytic normochromic RBCs, mild anisopoikilocytosis and normal differential and morphology of white blood cells. Erythrocyte sedimentation rate was 90 mm in the first hr. He had low serum protein 5.6gm/dl (6.3-8.5 gm/dl) with low serum albumin 2.1gm/dl (3.5-5gm/dl) and globulin 3.5gm/dl (2.3-3.5gm/dl), increase Alkaline phosphatase level 145U/ L (38-126U/L) and normal bilirubin and normal aminotransferases enzyme level. Random plasma glucose level was 148mg/dl. His renal function test was normal. Routine urine examination was normal. Viral serology for HIV, HBsAg and HCV was non reactive. The result of his Mantoux test was negative. Chest radiograph showed diffuse reticulonodular lung lesions and mass like consolidation in right mid and lower zone (Figure 1). An ultrasound abdomen scan showed no organomegaly or lymphadenopathy.

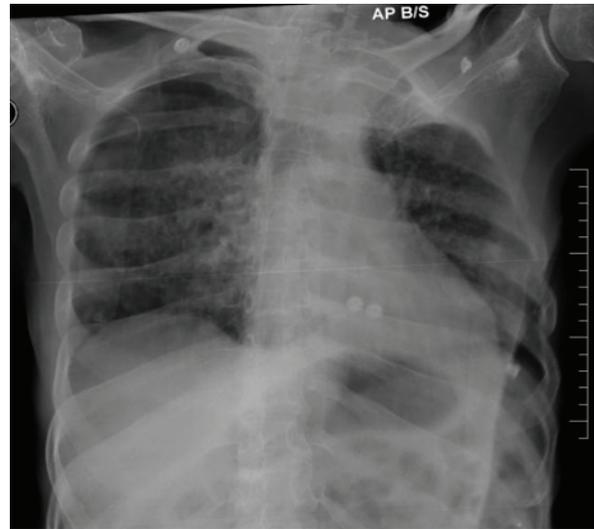


Figure 01: Chest X ray (P-A view) Diffuse reticulonodular lung lesions and mass like consolidation in right mid and lower zone

Bone marrow aspiration and biopsy was performed. Bone marrow aspiration was diluted, however histological examination of bone marrow biopsy section showed few caseating granulomas composed of epithelioid cells and necrosis was seen in interstitial and paratrabeular loci (Figure 2a, 2b & 2c). Acid Fast stain (Ziehl-Neelsen stain) came positive for Acid Fast bacillus (Figure 2d), suggestive of tuberculous granulomatous inflammation.

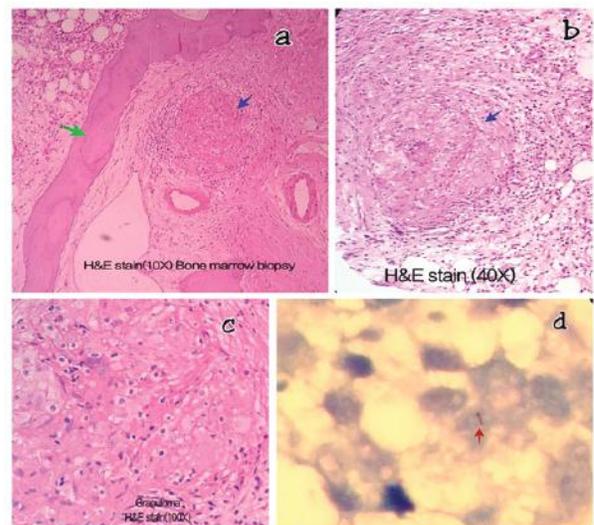


Figure 02: 2a 2b 2c: Bone marrow biopsy histology section (H&E stained)

show bone marrow granulomas with epithelioid cells. Figure 2d: Positive Acid -Fast-Bacillus (Z-N stain slide)

Based on radiological and bone marrow biopsy findings, the patient was diagnosed and treated as disseminated tuberculosis with Antitubercular chemotherapy in the form of isoniazid, rifampicin, pyrazinamide, and ethambutol with intravenous steroids.

During his initial follow up after three weeks, his blood count improved without alteration in liver enzymes. On further follow up after three months with continuous antitubercular drugs his count stabilized (hemoglobin 11.2gm/dl, WBCs count 4200/cumm and platelets count 1.6 lakhs/cumm) to normal level with weight gain by five kg. His antitubercular treatment continued for nine months.

Discussion

Bone marrow granulomatous inflammation is a type of chronic inflammation resulting from persistent antigenic stimulation. It is characterized by aggregates of epithelioid cells, giant cells surrounded by mononuclear cells with or without caseation necrosis. Bone marrow granuloma (BMG) is not a frequent finding in bone marrow biopsy. The incidence of BMG ranges from 0.3% to 2.2% and can be caused by a spectrum of underlying infectious, noninfectious disorder to hemato-lymphoid malignancy, commonest being tuberculosis in developing country like India.⁴

Hematological manifestation varies from anemia, bicytopenia to thrombocytopenia. Anemia is most common in pulmonary tuberculosis while pancytopenia is commonly encountered in extrapulmonary or disseminated form of tuberculosis. Pancytopenia in such case is due to infiltration of the bone marrow by caseating or non-caseating

granulomas causing reversible or irreversible fibrosis. It can be due to hypersplenism, secondary hemophagocytic lymphohistocytosis (HLH) or maturation arrest. Bone marrow trephine biopsy plays an important role in the diagnosis of bone marrow granulomatous inflammation as granulomas are not commonly seen in aspiration cytology, probably because of fibrosis in an around the granulomas.⁵

Miliary mottling consist of numerous pulmonary opacities with size of less than 3 mm, scattered throughout the lungs on chest X- ray. It takes weeks between the time of dissemination and the radiographic appearance of disease. The most common etiology of miliary mottling is infectious, such as miliary tuberculosis and histoplasmosis, but can be seen in sarcoidosis, pneumoconiosis and secondary metastasis to the lungs from malignancy of thyroid, kidney and lungs. High-resolution CT can help to narrow down the differential diagnoses by distributing the micronodules into centri-lobular, perilymphatic, and random patterns.⁶ Definitive diagnosis of suspected miliary tuberculosis includes clinical and laboratory workup for extrapulmonary involvement.

This case has limitation as HRCT scan, bronchoscopy, culture and GeneXpert examination could not done due to patients refusal because of financial constraints. In our case Bone marrow biopsy showed granulomas with positive acid fast bacillus gives us enough evidence to diagnosed and treat as disseminated tuberculosis.

The treatment of disseminated tuberculosis includes a six to nine month regimen (initial two months of isoniazid, rifampin, pyrazinamide and ethambutol followed by four to seven months of isoniazid and rifampin). Adjunctive corticosteroids may be useful in patients with miliary tuberculosis, tuberculous

meningitis or tuberculous pericarditis with refractory hypoxemia.⁷ Compared to pulmonary tuberculosis, disseminated tuberculosis carries poor prognosis and high mortality rate (50%). Other factor related to high mortality is severity of disease, time of diagnosis, immunocompetent status of patient.⁸ Our patient showed early improvement without complications probably because of initial stage of disease, early diagnosis with good compliance and close follow up.

Conclusion

To conclude, bone marrow granulomas with positive acid fast bacilli presenting as pancytopenia is a rare finding. Miliary mottling, though suggestive of infective etiology but is not definitive. Clinical and laboratory workup especially bone marrow trephine biopsy with special Z-N staining in such cases helps in early diagnosis and also to avoid unnecessary investigations.

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