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Blood and bone marrow findings in tuberculosis in adults -A cross sectional study

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Abstract: *Background:* Tuberculosis is a major public health problem in India. Hematolgical changes have been studied with variable results. *Aims and objectives:* The present study was undertaken to know the prevalence of blood and bone marrow changes in tuberculosis. *Methods:* The peripheral blood and bone marrow changes were evaluated in hundred adult patients with tuberculosis, admitted at District Hospital, Belgaum and KLES Hospital and MRC were. *Results:* The peripheral blood findings seen were anemia, raised ESR, leukocytosis, neutrophilia, lymphocytosis, eosinophilia, leucopenia, thrombocytosis and thrombocytopenia. The bone marrow changes seen were hypercellularity , myeloid hyperplasia , erythroid hyperplasia with megaloblastic changes and reactive plasmacytosis. Another interesting finding in bonemarrow was presence of granulomas which were seen in 5% of cases of which 1 case showed positivity for acid fast bacilli on Zeihl – Neelsen stain. *Conclusion:* The varied hematological findings observed in tuberculosis should prompt us to consider tuberculosis as one of the differential diagnosis in patients with hematological findings.
Keywords: Tuberculosis; Blood, Bone marrow; Granuloma., Acid fast bacilli

Introduction

Tuberculosis is a chronic bacterial infection caused by Mycobacterium tuberculosis. This ancient infection has plagued humans through ages. Its elimination has remained extremely difficult as long as poverty, over population, HIV infection exists in large portions of earth [1]. It is an index of social organization and standard of living in the community [2]. Tuberculosis can affect any organ. Lung is usual site involved. The extra pulmonary sites involved are lymph nodes, pleura, genitourinary tract, bones, joints, meninges, peritoneum[3]. Today as a result of hematogenous dissemination in HIV infection, extra pulmonary is seen more commonly than in the past.

Hematopoietic system is another organ seriously affected by tuberculosis. It exerts a dazzling variety of hematological effects involving both cell lines and plasma components. The hematological changes sometimes act as useful factors providing a clue to diagnosis, assessing the prognosis, indicating the complication of underlying infection as well as therapy and response to therapy [1]. The ease of availability of blood investigations, simplicity and relative safety of procedures, the relative low cost factors in these investigations prompted us to study the blood and bone marrow changes, which may help in diagnosis and follow up of patients with tuberculosis.

Material and Methods

This prospective study was conducted in the department of pathology, Jawaharlal Nehru medical college, Belgaum. The study included 100 patients more than 16years of age admitted with the diagnosis of District hospital and KLE society's Hospital & Medical Research centre Belgaum from April 1st 2004 to March 31st 2005. Patients, less than 16years, with signs and symptoms of drug toxicity due to antitubercular drugs and having primary hematological diseases were excluded from the study. Pertinent information regarding the history of illness was collected according to the questionnaire by personal interview. A thorough clinical examination was done and the findings were complemented by findings in case records. The peripheral blood was evaluated for

hemoglobin, total white blood cell count, differential count, platelet count, reticulocyte count, peripheral smear examination and erythrocyte sedimentation rate. Bone marrow aspiration and trephine biopsy was performed on all the patients. Bone marrow aspiration smears were stained with Wright's stain and trephine biopsy slides were stained with H&E stain. The bone marrow aspiration and trephine biopsy slides were also stained with Zeihl-Neelsen (ZN) stain and screened for acid fast bacilli. For evaluation of peripheral blood and bone marrow findings criteria outlined by Dacie and Lewis were used. Ethical clearance was obtained from the institutional Ethical committee and informed consent was obtained from all patients participating in the study.

Results

The hundred cases were evaluated out to know the prevalence of blood and bone marrow changes in tuberculosis. Out of the 100 cases, 83(83%) cases presented with pulmonary manifestations and 17(17%) presented with extra pulmonary manifestations. 28(28%) cases were HIV seropositive. The peak incidence was seen in the age group of 26 to 35years (32%). Anemia was seen in most of the patients ie in 96(96%) cases. Majority of them mild anemia of normocytic hypochromic type. The WBC abnormalities included leucocytosis in 34(34%) cases, leucopenia in 3(3%) cases, neutrophilia in 35 (35%) cases, lymphocytosis in 6(6%) cases, lymphocytopenia in 2(2%) cases and eosinophilia in 5(5%) cases. Platelet count was normal in majority ie in 89(89%) cases. 8(8%) cases showed thrombocytosis and 3(3%) cases showed thrombocytopenia. ESR was raised in all the cases. An ESR of greater than 100mm\1hour was seen in 23(23%) cases. [Table1].

Table-1: Peripheral Blood Findings in Tuberculosis

Peripheral Blood Findings	No. of Cases	%
Red Blood cells		
No anemia(Normal Hb ie >135g/L in males &>125g/L in females)	04	04.00
Mild anemia(Hb<Normal≥100g/L)	50	50.00
Moderate anemia(<100g/L & >70g/L)	37	37.00
Severe anemia(≤ 70g/L)	09	09.00
White Blood Cells		
Normal count	63	63.00
Leukocytosis	34	34.00
Leukopenia	03	03.00
Neutrophilia	35	35.00
Lymphocytosis	06	06.00
Lymphocytopenia	02	02.00
Eosinophilia	05	05.00
Platelets		
Normal	89	89.00
Thrombocytosis	08	08.00
Thrombocytopenia	03	03.00
Erythrocyte Sedimentation rate		
Increased	100	100.00
<100 mm/1hour	77	77.00
>100mm/1hour	23	23.00

Fig-1: Bone marrow biopsy – Granuloma showing aggregation epitheloid cells (H&E; x400)

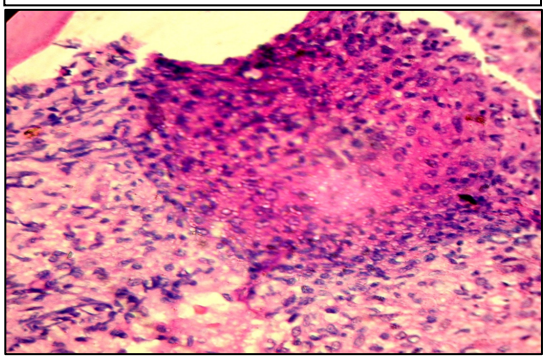
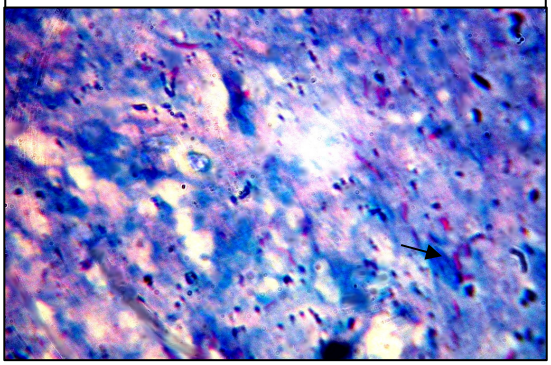


Fig-2: Bone marrow biopsy – Acid fast bacilli (arrow) in necrotic background. (ZN stain; x1000)



Bone marrow changes-Majority of the patients had normocellular bone marrow. Hypercellularity of the marrow was seen in 46 (46%) cases. 2(cases) showed hypocellularity. Myeloid and erythroid hyperplasia was seen in 14(14%)cases and 10(10%) cases respectively. Megaloblastic reaction was seen in 8(8%) cases. Megakaryocytes were normal in all the cases. Reactive plasmacytosis was seen in 46(46%) cases. Granulomas [Fig1] were seen in bone marrow biopsy in 5(5%) cases of which in 2(2%) cases they were illformed. ZN stain revealed positivity in only one case. [Fig2] Perls stain for iron revealed normal iron stores in 84(84%)cases, increased iron stores in 12(12%)cases and decreased iron stores in only 4(4%)cases.[Table2]

Table-2: Bone Marrow Findings in Tuberculosis

Bone Marrow Findings	No. of Cases	%
Cellularity		
Normocellular	52	52.00
Hypercellular	46	46.00
Hypocellular	02	02.00
M : E Ratio		
Normal	74	74.00
Myeloid hyperplasia	14	14.00
Erythroid hyperplasia	12	12.00
Erythroid Series		
Normoblastic	92	92.0
Megaloblastic	08	08.00
Myeloid Series		
Normal maturation	92	92.00
Giant Metamyelocytes	08	08.00
Megakaryocytes		
Normal	100	100.00
Increased	--	--
Depressed	--	--
Plasmacytosis	46	46.00
Granulomas	5	5.00
ZN Stain (AFB Positive)	1	1.00
Iron Stores		
Normal	84	84.00
Increased	12	12.00
Decreased	04	04.00

Discussion

Hematological studies have been studied by various authors in the past with varied results. The prevalence of anemia in our study was similar to that reported by previous studies [4-7]. A blunted erytropoietic response of the bone marrow, release of TNF-α and other cytokines by tuberculosis activated monocytes suppressing the erythropoietic production, block in the reticuloendotheial transfer of iron in to the nucleus of developing red cell are also postulated as cause for anemia [1,8-9]. The occurrence of leucocytosis, neutrophilia, lymphocytosis was similar to other studies and are thought to be the immune responses to tuberculosis [5,8,10-11]. The prevalence of cytopenias was seen in lesser percentage of cases as compared to studies done on patients with disseminated military tuberculosis [6,8,11]. The prevalence of thrombocytopenia and throbocytosis was similar to earlier studies [6,8,10]. Thrombocytosis is postulated to be due to increased thrombopoietic factors as a inflammatory response [1]. Varied mechanisms like drugs immune mechanisms, bone marrow fibrosis, granulomatous involvement of bone marrow and hypersplenism have all been put forward as possible causal factors for thrombocytopenia [1]. Raised ESR, which is one of the indicators of severity of disease and a prognostic tool, was in agreement with previous studies [5,12].

The bone marrow findings in our study were consistent with previous studies [6,8]. Involvement of bone marrow as suggested by finding of granuloma and\or of acid fast bacilli in the bone marrow were rare but interesting findings in our study, which is consistent with literature [13-14]. However bone marrow culture and other molecular techniques like polymerase chain reaction would have perhaps improved the yield. Though varied results have been shown in earlier studies regarding the bone marrow iron stores, normal or increased stores are seen in majority. Our study is in agreement with their results. However the other iron related measurements were not done in our study. Literature reveals decreased serum iron, total iron binding capacity, trasnferrin saturation and increase in serum ferritin in patients with tuberculosis. These abnormalities result from redistribution of iron as a acute phase reaction. Though the total iron stores are normal, iron is unavailable for normal hematopoiesis and excess non-hemic-iron is visible in the bone marrow [1].

Conclusion

Tuberculosis is one of the common infections in this part of country affecting the most productive age group. Hematological investigations are one of the commonly performed investigations in clinical practice. The varied hematological findings observed in tuberculosis should prompt us to consider tuberculosis as one of the differential diagnosis in patients with hematological findings.

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