The Role of the Bone Marrow Study in Typhoid Fever with Pancytopenia

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ABSTRACT

Background and Objectives: Typhoid fever is an endemic infectious disease in Sulaimanyia city in Kurdistan region of Iraq. Last years we observe there are remarkable haematological changes associated with this disease. Pancytopenia was one of these changes. The aim of this study was to evaluate the role of bone marrow study in typhoid fever with pancytopenia.

Methods: In this prospective study only culture positive enteric fever patients were taken. For all patients CBC and blood Film were done. Bone marrow study including aspirate and biopsy was done for all patients with peripheral blood pancytopenia.

Results: Two thousands culture positive enteric fever patients were taken into this study. Presenting symptoms included mainly fever and rigor. The peripheral blood of these patients revealed different haematological changes, like normocytic anaemia, leucopenia, bicytopenia and pancytopenia. Pancytopenia was in 127 (6.3%) patients. Bone marrow was active in all patients. Histiocytes are increased in activity in 55 (43%) cases; only in 17 (13%) cases haemophagocytosis was seen. No granuloma seen in all cases. Majority of the patients regain the normal blood parameters values within two to eight weeks.

Conclusions : Bone marrow study has no clear role for explanation the peripheral blood pancytopenia in typhoid fever. There is no indication for bone marrow study for culture positive typhoid fever with pancytopenia, unless the pancytopenia is persistent. Most probably the pancytopenia is caused by peripheral blood factor.

Key words: Typhoid fever; pancytopenia; Bone marrow.

INTRODUCTION:

Typhoid fever is a systemic infection caused by Salmonella typhi. The clinical profile, laboratory features, antibiotic sensitivity pattern of the organism and the clinical response of the illness to the antibiotics differ from country to country and within the same country.[1] The definite diagnosis of typhoid fever is achieved by culture of blood and bone marrow. Positive blood cultures are seen in 60-80% of the cases. Possibility of blood culture positivity decreases after the first week and becomes negative in the fourth week. [2,3] Clinical presentation and severity of the disease is varied. Fever, headache, flu-like symptoms, fatigue, nonproductive cough, lack of appetite, nausea, and myalgia are the most frequent symptoms [4,5]. Classical disease duration is 4 weeks and high fever, toxemia, and constipation occur in the first week, diarrhea in the second week, and splenomegaly, bone marrow findings as well as complications such as encephalopathy, intestinal hemorrhage and perforation are typical findings seen in the third week [5,6] Leucopenia and relatively normal leucocyte count is common in typhoid fever while the bone marrow depression in the form of pancytopenia is less common and was seen in 5%only.[7] Many cases of typhoid fever have peripheral blood cytopenias that were not

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concurrent bone marrow suppression, suggesting a peripheral mechanism responsible for the blood dyscrasia in those cases.[8] However, in other studies the patients suffering from typhoid fever with pancytopenia, bone marrow examination revealed extensive haemophagocytosis which possibly contributed to the pancytopenia.[9] The term haemophagocytosis describes the pathological finding of activated macrophages and engulfing erythrocytes, leucocytes, platelets, and their precursors cells.[10] Pancytopenia is a deficiency of all three cellular elements of blood (red blood cells, white blood cells and platelets) resulting in anaemia, leucopenia and thrombocytopenia. Depending on the degree and duration of the impairment it can lead to serious illness and death. While bone marrow failure syndromes and malignancies are important causes, certain non-malignant conditions such as infection and nutritional anaemia are equally important causes. [11]

MATERIAL AND METHODS

This prospective study was carried out in the General Teaching Hospital of Sulaimanyia city, Department of Hematology, from June 2007 to September 2009 over a period of 28 months. Age of the patients is ranged from 9 to 45 years. All the patients was diagnosed as typhoid fever by blood culture, some of them bone marrow culture was also done. CBC and blood film were done for all patients. Pancytopenia was defined as haemoglobin (Hb) <11 g/dL, absolute neutrophils count (ANC) <2x 10^9/L, platelet count <150 x 10^9/L. Haematological parameters at presentation were recorded. Haematological parameters included Hb, total and differential leukocyte count, ANC, red cell indices and examination of peripheral smear. Bone marrow aspiration and trephine biopsies were carried out in all the cases with pancytopenia. There are many cases were diagnosed and treated In the other hand there are cases presented with bicytopenia with blood culture positive, again these cases were not included in this study. Majority of the bone marrow studies were done before we get the results of blood culture, especially if the bone marrow culture was also required.

RESULT:

Two thousands culture positive enteric fever patients were taken into this study. Presenting symptoms included mainly fever and rigor. The peripheral blood of these patients revealed different haematological changes, like normocytic anaemia, leucopenia, bicytopenia and pancytopenia. Pancytopenia was in 127 (6.3%) patients. Bone marrow was active in all patients. Histiocytes are increased in activity in 55 (43%) cases; only in 17 (13%) cases haemophagocytosis was seen. No granuloma seen in all cases. Majority of the patients regain the normal blood parameters values within two to eight weeks.

Table: Distribution of the cases according to the bone marrow findings.

Bone marrow cellular activity and histiocytes activity	No of cases	%
Total number of cases with pancytopenia and active marrow regardless histiocytes activity	127	100
Cases with active marrow with increased histiocytes activity , but without evidence of haemophagocytosis	55	43
Cases with active marrow with increased histiocytes activity and haemophagocytosis	17	13

DISCUSSION :

General teaching Hospital of Sulaimanyia is a large centre receiving the typhoid patients in Sulaimanyia city. The age profile in this study was that of a dominantly young population. In this study we concentrate on the role of the bone marrow examination for explaining the peripheral blood pancytopenia which was present in 6.3% of this study. There is an agreement with other studies like Wg Cdr S Gupta 5% [7] and findings of Dutta et al 8% [12]. Since the Widal test is not reliable as a diagnostic method for this disease, the blood and bone marrow culture is the only available method for the diagnosis. The bone marrow suppression is believed to be due to a maturity arrest of the myeloid series, erythroblasts and megakaryocytes with excessive phagocytic activity of the histiocytes in the marrow [13].In this study the histiocytes activity is increased in 43% of cases, but only 17% of all cases haemophagocytosis was observed. The marrow in all cases is active in all lineages and without evidence of maturation arrest. However, the pancytopenia still one of the complications needs to be investigated by physicians and bone marrow examination is the available choice for this aim. The bone marrow is invasive and discomfortable procedure and in some think that we can postponed the bone marrow examination for cases suspected typhoid fever with pancytopenia until we get blood culture result, if it is positive no need for this procedure, unless the pancytopenia is persistent. The close follow up of the blood parameters during the treatment is the best choice as an alternative to the bone marrow examination. However, persistent of pancytopenia is indicate bone marrow examination to exclude other possibility, like bone marrow aplasia.

CONCLUSION:

Bone marrow study has no clear role for explanation the peripheral blood pancytopenia in typhoid fever. There is no indication for bone marrow study for culture positive typhoid fever with pancytopenia, unless the pancytopenia is persistent. Most probably the pancytopenia is caused by peripheral blood factor.

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