

Original Article

Diagnostic Utility of Bone Marrow Examination in Chronic Liver Disease Patients Referred For Evaluation of Hematological Derangements

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Abstract:

Objective: To see the diagnostic utility of bone marrow examination in patients of chronic liver disease referred for evaluation of hematological derangements.

Material and methods: The study was conducted from July 2009 to July 2011 at the Department of Pathology, Pakistan Institute of Medical Sciences (P.I.M.S), Islamabad. A total of 75 diagnosed cases of Hepatitis C induced chronic liver disease, referred from different departments of PIMS with various indications for bone marrow examination were included in the study. All these cases were qualitative PCR-positive for HCV-RNA. Patient who had already received or were on anti-viral therapy were excluded. Routine blood cell counts were done and later all the patients were subjected to bone marrow examination. Data was entered on SPSS version 16 and statistically analyzed.

Results: In a total of 75 patients of chronic liver disease age ranged from 15 years to 76 years with a mean age of 43 years. The male to female ratio was 0.92:1. The main indications of bone marrow examination in the current study were cytopenias. Hypersplenism was the commonest finding in our patients, observed in 34.7% cases followed by Idiopathic Thrombocytopenic Purpura (22.6%), anemia of chronic disease (13.3%), hypoplastic bone marrow (5.3%), bone marrow aplasia (4%) and megaloblastic marrow (5.3%). Iron deficiency was the main diagnosis in 2 cases but it was observed in association with many other conditions like hypersplenism, Idiopathic Thrombocytopenic Purpura, reactive bone marrow, hypoplastic bone marrow and when combined, iron deficiency was found in 28(37.3%) cases. Similarly megaloblastic change was also found in association with other factors and in total was observed in 8 (10.7%) cases.

Conclusion: Bone marrow examination in Hepatitis C Virus infected patients can be a valid test for hematologic evaluation, especially for patients with severe pancytopenia and /or sudden alterations in peripheral cell counts.

Key words: Chronic liver disease, HCV, pancytopenia, cytopenias

Introduction

According to World Health Organization estimates, about 3% of the world population has been infected with HCV. There are about 170 million patients with HCV infection in the world and 3 to 4 million are diagnosed annually. In Pakistan about 10 million patients are infected with HCV.¹

HCV is a single-stranded RNA virus that is transmitted primarily by parenteral routes and most commonly presents as a chronic hepatitis in infected patients. Its presence in hepatocytes affects innate and

adaptive immune responses to fully clear virion and leads to known liver diseases associated with HCV such as chronic hepatitis, progressive fibrosis, cirrhosis and hepatocellular carcinoma. ² Patients with HCV infection also develop abnormalities in peripheral cell counts like neutropenia, thrombocytopenia and anemia. Hypersplenism, autoimmune processes, antiviral therapy, folate deficiency, decreased thrombopoietin levels and many unknown factors contribute in their pathogenesis. Main mechanism leading to cytopenias during antiviral therapy is bone marrow suppression and hemolysis. The patients are commonly presented for bone marrow biopsy due to these cytopenias.³

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The progression of Hepatitis C in the body may take several years or even decades to come to chronic stage or to a stage where severe liver damage is evident. HCV infection has a well-documented association with a number of extra hepatic manifestations such as cytopenias, mixed cryoglobulinemia and non-Hodgkin's lymphoma (NHL).⁴ Anemia may present as a significant complication. It may be due to chronic illness, bone marrow suppression, folate or B12 deficiency, antiviral drugs and bleeding. Thrombocytopenia is a common complication in patients with HCV. The etiology is multifactorial like bone marrow suppression, auto antibodies, hypersplenism, antiviral therapy and decreased thrombopoietin levels.⁵ The presentation of NHL associated with HCV is quite different from standard presentation of NHL and more commonly presents as primary extra nodal lymphomas, especially liver spleen and salivary glands.⁶ Bone marrow biopsy in HCV infected patients can be a diagnostic tool in evaluating degree and nature of unexplained cytopenias. Additionally, it may be an essential procedure for the diagnosis of bone marrow hypoplasia and various associated hematological malignancies. We report a spectrum of bone marrow findings in chronic liver disease patients due to HCV.

Materials and Methods

The study was conducted at Pathology Department, Pakistan Institute of Medical sciences Islamabad. The study was conducted in 2 years time period (July 2009 to July 2011). A total of 75 diagnosed cases of Hepatitis C induced chronic liver disease, referred from different departments of PIMS with various indications for bone marrow biopsy were included in the study. All these cases were qualitative PCR-positive for HCV-RNA. Patients who were on antiviral therapy, co infection with HIV and diagnosed cases of malignancies were excluded.

Clinical history along with physical findings was entered on specially designed proforma. In every patient about 2.5 ml of blood was collected in an EDTA containing tube by a clean venepuncture, using a 5 ml disposable syringe. Peripheral blood smears were freshly prepared. All the patients were subjected to bone marrow aspiration using disposable Lumbar puncture needle size 16 gauge. Results were entered on SPSS version 16 and statistically analyzed.

Results

In present study 39 (52%) of the patients were females, 36 (47.4%) were males with male to female ratio of 0.92:1. Clinical features included fever (50.7%), bleeding manifestations (45.3%), feeling of weakness

(28.9%), abdominal pain (29.3%), shortness of breath (12.0%), vomiting (5.3%) and joint pain (4.0%). Pallor was observed in majority (89.5%) of patients and jaundice was observed in 33.3% cases. Hepatomegaly was observed in 49(54.4%) of cases and spleen was enlarged in 53(58.9%) of cases.

As shown in table 1 the main indications for bone marrow biopsy were cytopenias, i.e. pancytopenia in 40 (53.3%) cases, bicytopenia in 14 (18.6%) cases thrombocytopenia 16 (21.3%). Bone marrow biopsy due to anemia was done in 5 (6.6%) cases. The bone marrow smears were hypocellular in 11 (14.7%) cases, hypercellular in 41 (54.6%) cases and moderately cellular in 23 (30.7%) cases.

Indications	N (%)
Pancytopenia	40 (53.3)
Bicytopenia	14 (18.6)
Thrombocytopenia	16 (21.3)
Anemia	5 (6.6)

Diagnosis	N (%)
Hypersplenism	26 (34.7)
Excessive peripheral platelet destruction (ITP)	17 (22.7)
Reactive bone marrow hyperplasia	09 (12)
Anemia of chronic disease	10 (13.3)
Hypoplastic bone marrow	04 (5.3)
Megaloblastic anemia	04 (5.3)
Aplastic anemia	03 (4)
Iron deficiency	02 (2.7)

Table 2 shows the breakup of diagnoses made on bone marrow aspiration smears. As shown in the table, hypersplenism was the commonest diagnosis in these patients comprising 26 (34.7%) cases. Spleen was enlarged in 20(76.9%) patients, in 6(23.0%) cases it was enlarged but was not clinically palpable. Majority of

these patients 15(57.6%) were referred due to pancytopenia. Immune thrombocytopenic purpura was the second common finding observed in 17 (22.7%) patients. Majority of cases were presented with bleeding manifestations and history of fever. Anemia of chronic disorder was observed in 10(13.3%) patients, megaloblastic change in 4 (5.3%) cases, hypoplastic bone marrow in 4 (5.3%) cases and aplastic anemia in 3(4%) cases. Iron deficiency was the main diagnosis in 2 cases but it was observed in association with many other conditions like hypersplenism, ITP, reactive bone marrow, hypoplastic bone marrow, reactive bone and when combined, iron deficiency was found in 28(37.3%) cases. Similarly iron staining pattern of chronic disease was observed in association with other conditions like hypersplenism, ITP, reactive bone marrow, in hypoplastic bone marrow and when combined was observed in total in 22 (29.3%) cases. Megaloblastic change likewise was also found in association with hypersplenism and reactive bone marrow hyperplasia and in total was observed in observed in 8 (10.7%) cases.

Discussion

Patients with HCV infection can develop peripheral blood count abnormalities which are due to hypersplenism, antiviral therapy, decreased thrombopoietin levels, and/or autoimmune mechanisms.⁴ In the present study, most of the patients presented with fever and bleeding manifestations and these findings are comparable with other studies.^{7,8}

Hematological abnormalities of wide range have been noted in these patients. Anemia is a frequent presentation in patients with chronic liver disease and various factors contribute to it. These include iron deficiency, folic acid deficiency, vitamin B12 deficiency and anemia of chronic disease. Iron deficiency anemia was the commonly observed finding in our cases, in total observed in 28 cases (2 cases isolated iron deficiency and 26 cases in association with other conditions). Our results are comparable to the study done in Thai patients by Intragumtornchai et al.⁹ Blood loss is frequent in CLD patients due to portal hypertension and thrombocytopenia, which leads to iron deficiency. Anemia of chronic disorder (assessed by iron stain in fragments) was observed in 22(29.3%). The frequency of megaloblastic change in our study is comparable to data reported by Kimber C et al,¹⁰ Some other studies however have reported a higher frequency.¹¹ Aplastic bone marrow was found in 4% cases which is comparable to other studies.^{12,13}

Hypersplenism being the most frequent finding (34.7%) in our patients leading to pancytopenia that is one of the consequences of chronic liver disease. Others have observed findings comparable to our results as hypersplenism has been reported in 40%, 25%, and 24% respectively in different studies.^{14,15,16} A higher frequency of hypersplenism (64%,68%) however was reported by Fadi N and Ashraf S. et al^{17,11}.

In our study excessive peripheral platelet destruction was observed in 17(22.7%) cases. Out of those, ITP was diagnosed in 15 (16.4%) patients, in 2 (2.2%) cases excessive peripheral platelet destruction was due to infection. Qamar U and colleagues reported 20% while Wang CS found out 10.2% of their cases having ITP.¹⁸ Previous studies suggest that prevalence of HCV positive ITP patients is greater than would be expected by chance and it should be considered in patients of chronic liver disease with unexplained thrombocytopenia. This has been reported by other cross-sectional studies showing 22%, 14%, 13% and 30% cases of ITP respectively.^{20,21,22,23}

Conclusion

The results of this study suggest that bone marrow biopsy in HCV-infected patients can be a valid test for hematologic evaluation, especially for patients with severe pancytopenia and /or sudden alterations in peripheral cell counts.

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