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Original Article

Usefulness of Bone Marrow and Pattern of Morphological lesions in Patients of Chronic Renal Disease

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Abstract

Objective: Bone marrow examinations provide useful insight into various etiological features of altered haematology and pattern of morphological lesions in patients of Chronic Renal Disease.

Materials and Methods: A total of 58 patients with documented Chronic Renal Disease, who underwent bone marrow biopsy for various indications, were included. Their clinical data, peripheral blood and bone marrow findings were analyzed.

Results: In a total of 58 cases studied, age ranged from 15-80 years. There were 74%males and 26% females. Male to female ratio was 2.8:1. The most common among the clinical features was pallor seen in 91% of cases. Bone marrow biopsy revealed Anemia of chronic disease in 44.8%,Bone marrow hypoplasia in 37.9%, Iron deficiency in 5.1%, Multiple myeloma in 6.9%, Excessive peripheral platelet destruction in 13.7%, Chronic renal disease with known NHL and hemolysis in 1.7% of cases.

Conclusion: Bone marrow aspiration and trephine biopsies were found useful in investigating various hematological abnormalities in patients presenting with Chronic Renal Disease.

Key Words: Bone marrow biopsy, chronic renal disease.

Introduction

Chronic renal disease (CRD) is defined as the presence of kidney damage usually with a marked reduction in glomerular filtration rate for more than 3 months.[1] It is an important cause of morbidity and mortality. [2] The prevalence of CRD is more than 2000 per million populations in Japan, 800 per million populations in the European Union, less than 100 per million populations in India and more than 600 per million populations in Saudi Arabia.[3] This problem is growing in developing as well as developed countries. In Pakistan roughly 15 to 20% persons of 40yrs or older have reduced estimated GFR.[4] Anemia is an important complication of CRD and is multifactorial. Apart from anemia, in CRD other haematological alterations include pancytopenia, thrombocytopenia and coagulopathies.[5] Many patients of CRD manifest haematological changes in addition to biochemical findings which make the bone marrow an essential investigation. Bone marrow examination reveals useful insight in to various etiological features of altered haematology in patients of CRD. The present study was to evaluate the usefulness of bone marrow biopsy and observe bone marrow morphological changes in chronic renal disease patients.

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Materials and Methods

It was a cross sectional descriptive study carried out at the department of Pathology, Pakistan Institute of Medical Sciences, Islamabad during the January 2009 to January 2010. A total of 58 patients with diagnosed CRD who underwent bone marrow aspiration/ trephine biopsy for various indications were included.

Their clinical features, detailed haematological profile, indications and results of marrow examination were recorded. Blood counts were performed using a fully automated haematology analyzer (system Kx-21). Bone marrow aspiration and trephine biopsies were carried out using 16 gauge lumbar puncture needle and Islam`s bone marrow biopsy needle respectively. The bone marrow smears were stained using Wrights and Prussian blue stains. Trephine sections were stained using H&E stains. The data were analyzed on SPSS version 14.

Results

In a total of 58 cases studied, age ranged from 15- 80 years with a mean age ± SD of 34.1 ± 18.16 years. There were 43 males and 15 females. Male to female ratio was 2.8:1. Various clinical features in patients of CRD referred for bone marrow biopsy are listed in Table-1. The most common among the clinical features was pallor seen in 91% of cases followed by fever seen in 39% of cases.

Table 1. Clinical presentation in Patients of Chronic Renal Disease.

Clinical features	No of Cases	Percentage (%)
Pallor	53	91.4
Fever	23	39.7
Easy fatiguability	15	25.9
Loss of appetite	12	20.7
Polyuria	05	8.6
Oliguria	04	6.9
Edema (Feet, periorbital, sacral and generalized)	14	24.1
Bone pains	06	10.3
Jaundice	03	5.2
Bleeding(Epistaxis, bleeding gums, haematemesis and haematuria)	07	12.1
Lymphadenopathy	04	6.9
Hepatomegaly	08	13.8
Splenomegaly	04	6.9

Haematological parameters are shown in Table 2 reveal Mean haemoglobin of 8.4 g/dl ± 2.14 with MCV of 83fl ± 9.03. White cell count ranged between 5- 31× 10^9/l. Mean platelet counts were 174× 10^9/l ± 192.5.

Various indications for performing bone marrow biopsies in patients of CRD are enumerated in Table 3. The most common indication for which the patients were referred for bone marrow biopsy was the presence of persistent unexplained cytopenias including pancytopenia, bicytopenia, thrombocytopenia and anemia together comprised 62% of all indications.

Table 2: Haematological parameters in Patients of Chronic Renal Disease

Haematological parameters	Range	Mean ± SD
Haemoglobin (g/dl)	4.8 -13	8.4 ± 2.14
White cell count (x 10^9 / l)	5 - 31	7.63 ± 6.13
Platelet count (x 10^9/l)	10 - 995	174.2 ± 192.5
Red cell count (x 10^{12}/l)	1.7 - 5.5	3.079 ± 0 .85
PCV (%)	14.3 - 41.7	24.98 ± 6.44
Mean Corpuscular Volume (fl)	54- 102	83.10 ± 9.03
Mean Corpuscular Haemoglobin (pg)	18.1 -35.5	27.57 ± 3.26
Mean Corpuscular Haemoglobin Concentration (g/dl)	26 - 40	33.32 ± 2.46

Table 3. Indications of Bone marrow biopsy in 58 cases of Chronic renal disease

Indications	No. of Cases (n=58)	Percentage (%)
Pancytopenia	15	25.9
Bicytopenia	08	13.8
Anemia	08	13.8
Thrombocytopenia	05	8.6
Infiltrative Bone Marrow Diseases		
• Suspecting Multiple Myeloma	08	13.8
• Suspecting MPD	02	3.4
Persistent Leucocytosis	05	8.6
Fever of Uncertain Origin	04	6.9
Suspicion of Miliary TB	03	5.2

Bone marrow features of 58 patients of CRD are detailed in Table 4.

Table 4. Bone Marrow Examination Results of 58 Patients of CRD

Bone Marrow	No. of Cases	%
Anemia of chronic disease	26	44.8
Hypoplasia	22	37.9
Iron deficiency	03	5.1
Multiple myeloma	04	6.9
Excessive peripheral	08	13.7
Platelet destruction	01	1.7
Hemolysis	01	1.7
CRD with NHL		

Bone marrow findings in patients of CRD showed that Anemia of Chronic disease was most common followed by Hypoplasia. Table 5 reveals further distribution of 26 cases that had increased iron with absence of siderocytes and sideroblasts suggestive of Anemia of Chronic disease. There are 22 cases of bone marrow hypoplasia and its distribution is shown in Table 6. In this study only 3 cases had Iron deficiency. Out of which 2 cases had isolated Iron deficiency and 1 case had Iron deficiency with Megaloblastic anemia as shown in Table 7. Only 1 case had Excessive peripheral platelet destruction. Excessive peripheral platelet destruction was also seen in another 7 cases with Anemia of Chronic disease. In total we had 8 cases of excessive peripheral platelet destruction which formed almost 13.7% of studied marrow.

Table 5. Additional features in 26 Cases Showing Bone Marrow Consistent with Anemia of chronic disease.

Bone marrow	No of Cases (n=26)	%
Reactive Hyperplasia	15	62.5
Excessive peripheral platelet destruction	07	26.9
Patchy Hypoplasia	03	11.5
Granuloma	01	4.2

Table 6. Distribution of 22 cases of Bone Marrow Hypoplasia

Bone marrow	No. of Cases (n=22)	%
Mild	07	31.8
Moderate	08	36.3
Severe	01	4.8
Patchily hypoplastic marrow	06	27.2

Table 7. Distribution of 3 Cases of Bone Marrow Consistent with Iron deficiency

Bone marrow	No of Cases	%
Iron Deficiency	02	66.6
Megaloblastoid change	01	33.3

Discussion

Anemia is a common complication of CRD and is almost a universal abnormality.[6]In the present study mean haemoglobin was 8.4 ± 2.1 whereas Hassan et al [7] and Muhammad Luqman Butt et al [8] report haemoglobin of 7.45 ± 2.1 and 7.4 gm/dl respectively which is quite comparable. As the cause of anemia is multifactorial in CRD so its treatment is based on its cause.[9]

Anemia of Chronic disease is characterized by increase iron with absence of siderocytes and sideroblast in our patients. Chronic inflammation is a common feature of CRD. In CRD patients inflammation shut down iron release from the reticulo-endothelial storage pool therefore preventing iron delivery to the erythrocyte precursors.

Increased pro-inflammatory cytokines level such as IL-1, IL-6 and TNF- alpha have been proposed to cause anemia in CRD. In this regard various mechanisms have been proposed which include bone marrow suppression, reduced erythropoietin production, intestinal bleeding and impaired iron metabolism.[10] In our study the bone marrow hypoplasia is possibly due to marrow suppression by proinflammatory cytokines.

CRD patients with anemia are treated with Recombinant Human EPO (rHU EPO).[11] EPO mainly target the early normoblast but also effect the myeloid cells, lymphocytes and megakaryocytes.[12] Recombinent Human Erythropoietin has long term effects on marrow [13] such as increased cellularity, reduction in myeloid to erythroid ratio indicating expansion of erythroid pool, increase in megakaryocytes, reduction in fatty tissue and hemosiderin which is an indicator of mobilization of marrow iron stores.

Factors that causes resistance of patients to the effect of exogenous EPO thus complicating the treatment include decreased iron stores, blood loss, inflammation, malignancies, hemolysis or bone marrow fibrosis.[14] In our study Iron deficiency cases were low and this is because most of our cases were on maintenance dialysis and regular follow up. Beside this the control mechanism of iron absorption to body stores are intact in patients on maintenance dialysis and oral iron therapy is recommended.[15]

In our study 6.9% cases had evidence of Multiple myeloma based on presence of increased plasma cells and 1.7% cases of CRD with known NHL and hemolysis each. CRD patients are at high risk of developing malignancy.[16]In our study 13.7% cases had marrow examination suggestive of Excessive peripheral platelet destruction. Platelet count is reduced and mild thrombocytopenia is associated with CRD.[17] Factors like infections, ITP, DIC are responsible for platelet destruction in our study.

Conclusion

The bone marrow aspiration and trephine are useful tools in finding the etiology of anemia in CRD.

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