ORIGINAL ARTICLE

FREQUENCY AND CHARACTERISATION OF PANCYTOPENIA IN MEGALOBLASTIC ANAEMIA

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Background: A wide variety of clinical conditions, that primarily or secondarily affect the bone-marrow may present with pancytopenia, one of such conditions is megaloblastic anaemia. The purpose of this study was to determine the frequency and nature of pancytopenia in megaloblastic anaemia. **Methods:** This was a prospective, cross-sectional descriptive study conducted in Medical Units, Ayub Teaching Hospital, Abbottabad, Pakistan during July 2010–January 2011. Total 90 patients were included in this study. Data were collected including history, clinical examination, haemoglobin level, mean cell volume, bone marrow examination and peripheral smear examination. **Results:** Of total 90 patients, 54 were male and 36 were female. Mean age was 28±15.84 years. Common presenting features were weakness, fever and bleeding manifestations. Pancytopenia was present in 63 (70%) patients. Most common presenting feature related to anaemia was weakness (80%). Bleeding manifestations, related to low platelet count were found in 35 (39%) patients. Physical Examination findings were: pallor (100%), splenomegaly (33%), bleeding manifestations (25%), hepatomegaly (17%), and hepatosplenomegaly (19%). Mean peripheral blood findings of the study population included haemoglobin level (6.25 g/dL), total leukocyte count (2818.7/μL), platelet count (44040/uL), and reticulocyte count (1.7%). Mean values for red cells indices included red blood cells count (2.6 million/uL), mean corpuscular volume (114.3 fL), mean corpuscular haemoglobin (27.3 ρg) and mean corpuscular haemoglobin concentration (31.8 g/dL). **Conclusions:** In megaloblastic anaemia, pancytopenia is a common and important clinical and haematological problem. Patients should be properly investigated for pancytopenia and its causes because many of them are completely curable while others are manageable. This will help to reduce patients' suffering, improve quality of life and prolong survival.

Keywords: Pancytopenia, megaloblastic anaemia, bone marrow aspiration, acute leukaemia, aplastic anaemia, hypersplenism

INTRODUCTION

Pancytopenia is the combination of anaemia, leucopoenia and thrombocytopenia. A vast majority of diseases may present with pancytopenia. In this disorder, all the three blood components (red blood cells, white blood cells and platelets) are decreased in blood. It is a common problem in clinical and haematological practice. It may be due to reduced production of blood cells as a consequence of bone marrow suppression or infiltration, or there may be peripheral destruction or splenic pooling of mature cells. Its common clinical manifestations include pallor, infections or bleeding problems.[1–5]

Various haemopoietic and non-haemopoietic conditions manifest with features of pancytopenia. The underlying mechanisms are decrease in haemopoietic cell production, marrow replacement by abnormal cells, suppression of marrow growth and differentiation, ineffective haematopoiesis with cell death, defective cell formation which are removed from circulation, antibody mediated sequestration or destruction of cells and trapping of cells in the hypertrophied and overactive reticulo-endothelial system.[3,5]

A wide variety of clinical conditions, that primarily or secondarily affect the bone-marrow may present with pancytopenia. One of such conditions is megaloblastic anaemia which is a heterogeneous group of disorders that share, common morphological characteristics.[6–9] The aetiology of megaloblastic anaemia is diverse but a common basis is impaired DNA synthesis. The most common causes of megaloblastosis are vitamin B_{12} and folate deficiencies. Cobalamin metabolism and folate metabolism are intricately related, and abnormalities in these pathways are believed to lead to the attenuated production of DNA. The bone marrow is hypercellular and there is accumulation of primitive cells due to selective death of more mature forms leading to pancytopenia.[7,8,10–14]

As some causes of pancytopenia are completely curable while others can be managed to reduce morbidity, therefore studies are warranted to explore nature of pancytopenia. Such work will be helpful to reduce patients' suffering, improve quality of life, and prolong survival. The purpose of this study was to determine the frequency and nature of pancytopenia in megaloblastic anaemia.

MATERIAL AND METHODS

This was a prospective, cross-sectional descriptive study conducted in Medical Units, Ayub Teaching Hospital, Abbottabad, Pakistan during a 6-month period from July 2010 to January 2011.

Pancytopenia was defined as reduction in the number of each type of peripheral blood cells, i.e., red blood cell count less than 4×10^{12}/L, white blood cells count less than 4×10^{9}/L and platelet count less than 150×10^{9}/L. Megaloblastic anaemia was defined as haemoglobin level of 9 mg/dl or less with a mean cell volume of more than 100 μm^3 and a hypercellular marrow with pro-megaloblasts, giant metamyelocytes, hyper-segmented neutrophils and multi-nucleate giant megakaryocytes on bone marrow examination.

Following formula was used to calculate sample size: $n=Z^2\times p(100-P)/d^2$, where n is sample size, p is anticipated prevalence of pancytopenia in megaloblastic anaemia (62%), d is acceptable margin of error, i.e., 10%, z is 1.96 at 95% confidence interval. Non-probability, consecutive sampling technique was used in this study.

All patients with megaloblastic anaemia, age between 15–60 years were included. Already diagnosed patients of pancytopenia taking replacement therapy or patients with hyperthyroidism detected on thyroid function tests or taking methotrexate detected on drug history were excluded.

This study was approved by Ethical Committee of the Hospital. Patients presenting with anaemia admitted to medical units of Ayub Teaching Hospital through Emergency Department, Outdoor Department and consultants' private clinics were enrolled for initial workup. Complete clinical history was taken from each patient and detail clinical examination was performed. Patients having megaloblastic anaemia according to the operational definition on the basis of haemoglobin, mean cell volume and bone marrow examination was included in the study. A written informed consent was obtained from the patients or their attendants. Among these selected patients of megaloblastic anaemia, peripheral smear examination was done to detect pancytopenia. Already diagnosed patients of pancytopenia were not included in the study.

Mean and standard deviation was calculated for continuous variables such as age, haemoglobin, red cell count, total leucocyte count and platelet count. Frequency and percentage were computed for categorical variables like gender and pancytopenia. SPSS-10 was used for statistical analyses.

RESULTS

Of total 90 patients, 54 were male and 36 were female. Mean age was 28±15.84 years. Common presenting features were weakness, fever and bleeding manifestations.

Among total 90 patients of megaloblastic anaemia, pancytopenia was present in 63 (70%). Most common presenting feature was weakness (80%). Half of the patients presented with fever. Urinary tract infection, respiratory tract infection and diarrhoea were the common infections found in our patients. Bleeding manifestations were found in 35 (39%) patients (Table-1).

Clinically, the most common finding was pallor (100%), splenomegaly (33%), bleeding manifestations (25%), hepatomegaly (17%) and hepato-splenomegaly (19%). Mean peripheral blood findings of the study population included haemoglobin level (6.25 g/dL), total leukocyte count (2,818.7/uL), platelet count (44,040/uL), and reticulocyte count (1.7%) (Table-3). Mean values for red cells indices included red blood cells count (2.6 million/uL), mean corpuscular volume (114.3 fL), mean corpuscular haemoglobin (27.3 ρg) and mean corpuscular haemoglobin concentration (31.8 g/dL) (Table-4).

Table-1: General Characteristics

Characteristic	Frequency	Percentage
Gender		
Male	54	60
Female	36	40
Age (years)		
≤ 20	15	16.67
21–30	25	27.78
31–40	32	35.55
≥41	18	20
Mean±SD	28±15.84	
Range	15–60	
Main Presenting Features		
Weakness	72	80
Fever	45	50
Bleeding manifestations	35	39

Table-2: Findings on Physical Examination

Physical Examination	Frequency	Percentage
Pallor	90	100
Splenomegaly	30	33
Bleeding manifestations	25	28
Hepatomegaly	15	17
Hepatosplenomegaly	17	19

Table-3: Peripheral Blood Findings

Blood Findings	Minimum	Maximum	Mean±SD
Haemoglobin level	2.70	9	6.25±1.24
Total Leukocyte count	100	4000	2818.7±3746.9
Platelet count	1000	147000	44040.0±43318.8
Reticulocyte count	0.00	10	1.768±1.981

Table-4: Red Cell Indices

Red Cell indices	Minimum	Maximum	Mean±SD
Red blood cells count	0.83	5.0	2.6176±0.89
Mean corpuscular volume	101.00	125.65	114.31±18.26
Mean corpuscular haemoglobin	13.50	36.20	27.32±4.26
Mean corpuscular haemoglobin concentration	0.30	49.40	31.82±4.42

DISCUSSION

Pancytopenia is not an uncommon haematological problem encountered in clinical practice and should be suspected on clinical grounds when a patient presents with unexplained pallor, prolonged fever and tendency to bleed. Bone-marrow examination for the evaluation of pancytopenia is a frequently requested investigation. It is one of the most frequent and safe invasive procedures, with little or no risk of bleeding even in the

presence of severe thrombocytopenia.[15] In our study frequency of pancytopenia in megaloblastic anaemia was 63 (70%). Similar findings (68% to 72%) have been reported by other studies.[16,17] The most common presenting feature was weakness found in 72 (80%) patients. In other studies symptoms related to anaemia, e.g., weakness and fatigue were found in 78.2% patients.[18] The symptoms related to neutropenia, e.g., fever were the second most common encountered in our study found in 45 (50%) cases. In other studies, it varies from 40% to 50%.[3,17,18] The third common feature was related to bleeding manifestation which was recorded in 39% patients. In other studies it has been found in 37%.[3,18]

Physical examination of patients in our study showed pallor present in all 90 patients (100%). Other studies found 98.8% to 100% patients presenting with pallor.[5,17,18] Splenomegaly was found in 30 (33%) cases, which is slightly higher then the results of other report i.e., 24%.[18] A possible explanation may be the decreased frequency of bone-marrow aplasia 21% and increased frequency of visceral leishmaniasis 8%.[18] In this study, hypersplenism was found in 17% patients, Hepatosplenomegaly in 19% patients and bleeding manifestations in 28% which are comparable with other studies.[16,18] Mean peripheral blood findings of the study population included haemoglobin level (6.25 g/dL), total leukocyte count (2,818.7/uL), platelet count (44,040/uL), and reticulocyte count (1.7%). Whereas, mean values for red cells indices included red blood cells count (2.6 million/µL), mean corpuscular volume (114.3 fL), mean corpuscular haemoglobin (27.3 ρg) and mean corpuscular haemoglobin concentration (31.8 g/dL). Such results are in agreement with other published reports.[3,16,19–21]

CONCLUSION

In megaloblastic anaemia, pancytopenia is a common and important clinical and haematological problem. Patients should be properly investigated for pancytopenia and its causes because many of them are completely curable while others are manageable.

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