ORIGINAL PROF-1501

AETIOLOGY OF PANCYTOPENIA

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Article Citation:
Tariq M, Khan N, Basri R, Amin S. Aetiology of pancytopenia. Professional Med J Jun 2010;17(2):252-256.

ABSTRACT... Background: Pancytopenia is a reduction in the number of each type of peripheral blood cell. Therefore the role of bone marrow examintion in diagnosis of pancytopenia is important to know etiology of pancytopenia. The objective of the study was to know the aetiology of pancytopenia. **Methods:** This descriptive (Cross sectional) study was carried out in Khyber teaching hospital. Fifty patients with pancytopenia were included in the study from 1st January 2008 to 30th October 2008. Full blood counts, bone marrow examinations and trephine biopsies were performed according to standard methods. Statistical packages for social science (SPSS.11) was used to analyze data. **Results:** Out of 50 patients, 36% were of aplastic anaemia, 16% megaloblastic anaemia, 14% myelodysplastic syndrome and 12% acute lymphoblastic leukemia (ALL), Hypersplenism in 10%, 4% non Hodgkin lymphoma (NHL) and 4% multiple myeloma, 2% each of acute myeloblastic leukemia and chronic myelocytic leukemia. All of these disorders were common in male as compared to female. **Conclusions:** Aplastic anaemia was the commonest cause of pancytopenia followed by megaloblastic anemia and myelodysplastic syndrome in our study.

Key words: Pancytopenia, Megaloblastic Anemia, Aplastic Anemia

INTRODUCTION

Pancytopenia is defined as a reduction in all three types of cellular components in peripheral blood and this involves anaemia, neutropenia, and thrombocytopenia[1]. It presents with symptoms of marrow failure such as pallor, dyspenoea, bleeding, bruising and increased propensity to infections. The causes of this condition are many and varied[2]. The incidence of various disorders causing pancytopenia varies due to geographical distribution and genetic disturbances. The management and prognosis of pancytopenia depends on the underlying pathology[3,4]. Pancytopenia can be due to decrease in hemaopoietic cell production in the bone marrow e.g. by infections, toxins, malignant cell infiltration or suppression or can have normocellular or even hypercellular marrow, without any abnormal cells, e.g. ineffective hematopoiesis and dysplasia, maturation arrest of all cell lines and peripheral sequestration of blood cells[5].

Bone marrow biopsy plays a significant role in understanding the aetiology of pancytopenia, in patients who need a laboratory work up[6]. Commonly, it is done for the evaluation of unexplained cytopenias and malignant conditions like leukemia. Bone marrow examination is

Article received: 31/03/2009
Accepted for Publication: 29/01/2010
Received after proof reading: 29/03/2010
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.also at times done for the diagnosis or staging of a neoplasm and storage disorders. Trephine biopsy is usually performed when there is hypoplasia or aplasia on aspiration[7]. Pancytopenia is an important clinicohaematological entity encountered in our day-to-day clinical practice. There are varying trends in its clinical pattern, treatment modalities, and outcome. The aim of this study was to evaluate the etiological spectrum of pancytopenias on the basis of bone marrow examination.

PATIENTS AND METHODS

We conducted a cross sectional,, single center (Medicine Department, Khyber Teaching Hospital, Peshawar) study from 1st January 2008 to 30th October 2008 on 50 cases of pancytopenia. Patients with pancytopenia above 14 years of age, and of either sex were included. Those who were already diagnosed by bone marrow examination, those who received blood transfusion and patients on cancer chemotherapy were not included in this study.

Pancytopenia was diagnosed in the presence of anemia (hematocrit value <0.35 in women, <0.40 in men), leucopenia (WBC$\leq$3.5x10^9/L) and thrombocytopenia (platelets < 150 x 10^9/L).

In all patients, a detailed relevant history including the treatment history, history of drug intake, radiation exposure. Meticulous clinical examination of every patient was done for pallor, jaundice, hepatomegaly, splenomegaly and lymphadenopathy. After history and examination basic investigations were performed for each patient including Haemoglobin, hematocrit value, Total leukocyte count, Platelet count, Reticulocyte count. Absolute values including packed cell volume (MCV), mean corpuscular haemoglobin (MCH) and mean corpuscular haemoglobin concentration (MCHC) were calculated for every patient, Blood film examination after staining with giemsa's stain for red cell morphology and malarial parasite(MP) was performed, Chest radiograph and abdominal ultrasonography was done in selected patients. Bone marrow examination was done in all patients and wherever required, a trephine biopsy were also performed. Statistical packages for social science (SPSS.11) was used to analyze data.

RESULTS

This was a hospital based prospective study conducted on 50 indoor patients of pancytopenia at Khyber teaching hospital, Peshawar from 1st January 2008 to 30th October 2008. Some important observations were made from this study as under. Majority of the patients (64%) were male and 36% were female. Male to female ratio were 1.7:1. Sex wise distribution is given in table-I. This study showed that majority of the patients (54%) had malignant disorders of bone marrow which causes pancytopenia..

Table-I. Sex distribution of patients.

Sex	Frequency	%age
Male	32	64%
Female	18	36%

Minimum age for patient with pancytopenia was 15 years and maximum age was 70 years. Age wise distribution is given in table-II.

Table-II. Age distribution of patients.

Age	Frequency	% age
15-20	10	20.0%
21-30	06	12.0%
31-40	10	20.0%
41-50	15	30.0%
51-60	04	8.0%
61-70	05	10.0%

Among clinical features pallor was present in all patients. Clinical features of patients with pancytopenia are listed in table-III. Majority of the patients (50%) were having haemoglobin 4-8gm/dl, 28% patients were with haemoglobin less than 4gm/dl and 22% patients were with haemoglobin between 9-10gm/dl. Sex to Hemoglobin distribution is given in table-IV.

Table-III. Clinical features of patients presenting with pancytopenia.		
Clinical Features	**Frequency**	**% age**
Pallor	50	100%
Fatigue	15	30%
Splenomegaly	12	24%
Lymphadenopathy	11	22%
Fever	9	18%
Bleeding	5	10%
Weight Loss	4	8%
Hepatomegaly	4	8%
Jaundice	2	4%

Table-IV. Distribution of sex and haemoglobin level			
Hemoglobin gm/dl	**No of male Patients**	**No of female patients**	**Total**
1-4	8(16%)	3(6%)	22%
4-8	16(32%)	9(18%)	50%
9-10	8(16%)	6(12%)	28%
Total	64%	36%	100%

Out of 50 patients, 36% were of aplastic anaemia, 16% megaloblastic anaemia, 14% myelodysplastic syndrome and 12% acute lymphoblastic leukemia (ALL), Hypersplenism in 10%, 4% non Hodgkin lymphoma (NHL) and 4% multiple myeloma, 2% each of acute myeloblastic leukemia and chronic myelocytic leukemia. All of these disorders were common in males as compared to female. The results are listed in the table-V.

DISCUSSION

Pancytopenia is a serious haematological problem, which makes the patient prone to anaemic manifestations, infections and bleeding tendency. Underlying it are many diseases, which are diagnosed by bone marrow aspiration and trephine biopsy[8].

Table-V. Causes of pancytopenia		
Disease	**Frequency**	**% age**
Aplastic anaemia	18	36%
Megaloblastic	8	16%
Myelodysplastic syndrome	7	14%
Acute lymphoblastic leukemia	6	12%
Hypersplenism	5	10%
Non Hodgkin lymphoma	2	4%
Multiple myeloma	2	4%
Acute myeloblastic leukemia	1	2%
Chronic myelocytic leukemia	1	2%

Pancytopenia is not an uncommon hematological problem encountered in our clinical practice and should be suspected on clinical grounds when a patient presents with unexplained anemia, prolonged fever and tendency to bleed. In our study aplastic anemia constituted the largest group (36%) which is consistent with the study by Niazi M[9], who showed it in 38.3 %. Epidemiologically, aplastic anemia has a pattern of geographic variation opposite to that of leukemia, with higher frequency in the developing world than in the industrialized West[10]. Large prospective studies indicate an annual incidence of two new cases per million populations in Europe and Israel[11]. Megaloblastic anemia is the 2nd most common disorder in our patients. In other similar studies its frequency ranges from as low as 13.04%[12] to as higher as 68%[13]. Megaloblastic anemia due to vitamin B12 or folic acid deficiency is now a well-recognized and established cause of cytopenias[14]. Though we were unable to determine the underlying cause of megaloblastic anemia, but folate deficiency is more common in children, while B12 deficiency is more common in adults[15]. It is a common problem in the developing countries. A possible explanation of folates deficiency in our country could be the various chronic inflammatory disorders of the gut like chronic diarrheas and malabsorptive states apart from poor nutrition. Hypersplenism was present in 10%, which is found to be present in 14.4% cases in a study by Iqbal

W[5]. In this study leukemias were noted, with acute lymphoblastic leukemia as the commonest malignancy in our patients (12%). Approximately 2500 cases per annum are diagnosed in the United States, accounting for about one third of all the cases of childhood cancers. Eighty percent of these are acute lymphoblastic leukemia (ALL), 17% are acute myeloid leukemia (AML) and the rest are cases of chronic myeloid leukemias[16]. The incidence of ALL in our country is lower as compared to the developed countries, as is the case in India and China[17,18]. Common clinical presentations were pallor, visceromegaly, fatigue, fever, and bleeding from nose and gastrointestinal tract.

CONCLUSIONS

Aplastic anemia was the commonest and most serious non-malignant disorder found in this study. Amongst the non-malignant hematological disorders, megaloblastic anemia was the most common disorder found on bone marrow examination in this study. Myelodysplastic syndrome and acute lymphoblastic leukemia was the most common amongst the malignant hematological disorders. Bone marrow aspiration and trephine biopsy were found to be useful diagnostic tools in evaluating the aetiology of pancytopenia.

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