Patterns of pancytopenia in Yemen

Yemen'de pansitopeni nedenleri

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Abstract

Objective: The aim of this study was to determine the incidence of pancytopenia in relation to sex and age and to become aware of the clinical manifestations of pancytopenic patients according to the causes of pancytopenia.
Materials and Methods: This was a prospective descriptive study that included all patients with pancytopenia admitted to or attending the Hematology-Oncology Department in Al-Gamhouria Teaching Hospital, Aden, during the period 1 January–31 December 2005.
Results: The most common causes of pancytopenia were malaria and hypersplenism in > 45% of patients, followed by megaloblastic anemia in 14.7%, and aplastic anemia and acute leukemia in 13.3% each. The other causes as determined in the present study were myelodysplasia in 8.0%, myelofibrosis in 4.0% and iron deficiency anemia in 1.3%. The most common symptom was fever in 86.7% of patients. Pallor and splenomegaly were the most common physical findings.
Conclusions: Hypersplenism and malaria were the most common causes of pancytopenia followed by megaloblastic anemia, aplastic anemia and acute leukemia. *(Turk J Hematol 2008; 25: 71-4)*
Key words: Pancytopenia, hypersplenism, bone marrow.

Özet

Amaç: Bu çalışmanın amacı, pansitopeninin cinsiyet ve yaşa bağlı insidansını belirlemek ve pansitopenik hastalarda pansitopeninin nedenlerine göre gelişen klinik belirtilerin anlaşılmasıydı.
Yöntemler: Bu çalışma, 1 Ocak–31 Aralık 2005 tarihleri arasında Aden'deki Al-Gamhouria Eğitim Hastanesi Hematoloji-Onkoloji polikliniğine kabul edilen veya tedavi görmekte olan pansitopenili tüm hastaların dahil edildiği prospektif tanımlayıcı bir çalışmadır.
Bulgular: Pansitopeninin en sık görülen nedeni, hastaların %45'inden fazlasında görülen sıtma ve hipersplenizm olarak belirlendi. Bunları, %14.7'lik oranla megaloblastik anemi ve her birinin %13.3'lük görülme sıklığı ile aplastik anemi ve akut lösemi izledi. Mevcut çalışmada belirlendiği üzere pansitopeninin diğer nedenleri, %8'lik oranla myelodisplazi, %4'lük oranla miyelofibroz, ve %1.3 oranla demir eksikliği idi. En yaygın bulgu, hastaların %86.7'sinde görülen yüksek ateşti. Solukluk ve splenomegali en yaygın fiziksel bulgulardı.
Sonuç: Hipersplenizm ve sıtmanın, pansitopeninin en yaygın nedenleri olduğu gözlendi. Bunu megaloblastik anemi, aplastik anemi ve akut lösemi izledi. *(Turk J Hematol 2008; 25: 71-4)*
Anahtar kelimeler: Pansitopeni, hipersplenizm, kemik iliği

Introduction

Pancytopenia refers to a reduction in all three formed elements of blood -- erythrocytes, leukocytes, and platelets. Pancytopenia can be due to decrease in hemopoietic cell production in 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. in ineffective hematopoiesis and dysplasia, maturation arrest of all cell lines and peripheral sequestration of blood cells [1-3]. The

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incidence of various disorders causing pancytopenia varies according to geographical distribution and genetic disturbances. [4-6] Pancytopenia is a common hematological problem with an extensive differential diagnosis, and the optimal diagnostic approach to pancytopenia remains undefined. [7-9] In Yemen, the incidence of pancytopenia is largely unknown.

Materials and Methods

Pancytopenia was diagnosed in the presence of anemia (hemoglobin <11 g/dl), leukopenia (total leukocyte count [TLC] <4,000/mm^3), and thrombocytopenia (platelet count <150,000/mm^3). [10] A total of 75 patients were studied at Al-Gamhouria Teaching Hospital in Aden from 1 January to 31 December 2005. Patients with cancer chemotherapy were excluded. A questionnaire including a detailed relevant history and physical examination were applied in all patients. Complete blood counts and bone marrow aspiration were performed in all patients, using standard methods. Bone marrow trephine biopsy was done in 22 patients (29.3%) for the evaluation of bone marrow in insufficient cells, dry tap or hypoplastic bone marrow. A complete blood count obtained from venous blood was counted by an automated blood counter (PCE-170N).

Statistical methods include descriptive statistics (mean, median, SD). Analysis was done on SPSS and Epi info v 3.3.

Results

During the period 1 January to 31 December 2005, 75 patients fulfilled the criteria of pancytopenia according to the study protocol at Al-Gamhouria Teaching Hospital. Age range was 3-85 years, with a male to female ratio of 1.03:1. The largest number of cases was found in the age group of 16-30 years (37.3%) followed by the age groups of <15 years (22.7%) and 46-60 years (20%).

The most common causes of pancytopenia were malaria, hypersplenism, megaloblastic anemia, aplastic anemia, and acute leukemia (Tables 1 and 2).

The commonest presenting complaint (Table 3) was fever in 86.7% (65/75) followed by fatigue in 76% (57/75) and dizziness in 64% (48/75) of the cases. Pallor was a physical sign seen in all patients (100%). Splenomegaly was seen in 48% (36/75) and hepatomegaly in 21.3% (16/75) of the cases.

Hematological parameters of patients with pancytopenia (Table 4) revealed that the mean hemoglobin concentration in patients with pancytopenia was 5.9±1.9 g/dl, which was very low (4.7±2.4 g/dl) in myelodysplastic syndrome. The mean absolute neutrophil count (ANC) was 705.4±530.1/mm^3, being lowest in both acute leukemia (244.2±354.0/mm^3) and aplastic anaemia (468.4±584.5/mm^3). The mean platelet count was 55.2±28.6/mm^3 and lowest mean value for platelets (38.6±26.1/mm^3) was seen in acute leukemia. The mean corpuscular volume (MCV) for patients with pancytopenia was 87.2±11.9 fl, and this was more significantly increased in megaloblastic anemia.

Discussion

Pancytopenia has multiple causes and the prognosis is dependent on the cause. The frequency of these causes has been reported in a limited number of studies [9,10]. Malaria was considered the most common cause of pancytopenia in this study. However, in this study, malaria caused pancytopenia not related to hypersplenism in 17.3% and related to hypersplenism in 13.3% of patients. In the study of Shishir et al. [11], malaria represented the fourth most frequent cause, with a percentage of 3.7%, in pancytopenic patients. Arya et al.[12] and Hemmer [13] reported that malaria due to Plasmodium falciparum has been implicated as a cause of pancytopenia. The second commonest cause of pancytopenia in the present study was hypersplenism in 28.0%, whereas in other similar studies this rate varied from 4.9% to 19% [5,8,9,14].

The increase in the incidence of hypersplenism in our study may be related to the increased prevalence of malaria, kala azar and other infectious diseases in Yemen [15]. The incidence of

Table 1. Causes of pancytopenia according to age group

Cause	Age group (years)					Total		Mean ± SD
	≤15	16-30	31-45	46-60	>60			
	No	No	No	No	No	No	%	
HS	12	7	0	2	0	21	28.0	16.6±15.7
Malaria	0	10	2	1	0	13	17.3	28.7±10.9
MA	0	2	3	6	0	11	14.7	44.6±12.3
AA	3	2	0	2	3	10	13.3	39.4±29.9
AL	2	5	0	2	1	10	13.3	33.4±19.5
MDS	0	2	1	1	2	6	8.0	46.2±22.8
MF	0	0	2	1	0	3	4.0	37.7±10.7
I D A	0	0	0	0	1	1	1.3	60.0
Total	17	28	8	15	7	75	99.9	31.9±20.7

AA: Aplastic anemia. AL: Acute leukemia. ANC: Absolute neutrophil count.
Hb: Hemoglobin. HS: Hypersplenism. IDA: Iron deficiency anemia. MA: Megaloblastic anemia. MCV: Mean corpuscular volume. MDS: Myelodysplastic syndrome.
MF: Myelofibrosis. SD: Standard deviation. TLC: Total leukocyte count No: Number of patients

hypersplenism as a cause of pancytopenia is subject to enormous geographical variation. In tropical countries, the incidence is as high as the frequency of splenic enlargement caused by tropical parasitic infections: malaria, leishmaniasis, brucellosis, and schistosomiasis [16-18]. Pancytopenia in hypersplenism and malaria patients in this study was transient, and resolved on treatment of the parasitic infection. The third most common cause of pancytopenia in this study was megaloblastic anemia in 14.7% of patients, while in other studies this rate varied from 1%-60% [19,20]. In contrast, other studies showed that megaloblastic anemia was the first cause of pancytopenia. Increased incidence of megaloblastic anemia in those studies correlates with the high prevalence of nutritional anemias in the nonindustrialized world [9,16]. Diagnosis of megaloblastic anemia in this study was established by bone marrow findings and responded well to the appropriate vitamin B12 therapy. The other most common causes were aplastic anemia and acute leukemia (13.3% for each). Similar findings with aplastic anemia were reported by Kishor et al. in India. 4 In contrast, a higher incidence of aplastic anemia (54%) was reported in the Philippines [21] and in Nepal (29.5%) [11]. In those studies, males were affected with aplastic anemia much more frequently than females, which might be a result of a higher incidence of occupational exposure to chemicals and of pesticide exposure as a common etiological agent for aplastic anemia in these countries. This contradicts results of our study, in which a female preponderance for aplastic anemia was determined. This can be explained in part by the fact that, in nonindustrialized countries, females use insecticides and chemicals more than males.

The most common clinical presentation was progressive pallor, which was universal in all patients, followed by fever in 86.7% of patients, which is more often observed in hypersplenism and malaria. Other non-specific features were also observed, like easy fatigability in 76.0%, dizziness in 64%, and weight loss in 45.3% of patients. These were observed more in hypersplenism, malaria, megaloblastic anemia, and acute leukemia. We found a correlation between pancytopenia and pallor, fever, and easy fatigability; this is in accordance with other studies [5,9,11]. In this study, we found a correlation between splenomegaly, hypersplenism and positivity of malaria and kala azar. Almost similar results were seen in other studies [4,7,9].

Hemoglobin concentration, TLC, platelet count and erythrocyte sedimentation rate were not different among pancytope-

Table 2. Causes of pancytopenia in relation to sex

	Sex				
Causes	Male		Female		Ratio (M:F)
	No.	%	No.	%	
HS*	12	16.0	9	12.0	1.3:1
Malaria	6	8.0	7	9.3	0.9:1
MA	6	8.0	5	6.7	1.2:1
AA	2	2.7	8	10.7	0.3:1
AL	5	6.7	5	6.7	1:1
MDS	3	4.0	3	4.0	1:1
MF	3	4.0	0	0.0	3:0
IDA	1	1.3	0	0.0	1:0
Total	38	50.7	37	49.3	1.03:1

*Causes of hypersplenism: Malaria (n: 10), kala azar (n: 6), brucellosis, schistosomiasis and Felty's syndrome (n: 1 for each), portal hypertension (n: 2).
AA: Aplastic anemia. AL: Acute leukemia. ANC: Absolute neutrophil count. Hb: Hemoglobin. HS:Hypersplenism. IDA: Iron deficiency anemia. MA: Megaloblastic anemia. MCV: Mean corpuscular volume. MDS: Myelodysplastic syndrome. No: Number of patients

Table 3. Clinical manifestations according to the causes of pancytopenia

	Causes of pancytopenia							
Clinical manifestations	**HS**	**Malaria**	**MA**	**AA**	**AL**	**Others**	**Total**	
	No.	**No.**	**No.**	**No.**	**No.**	**No.**	**No**	**%**
Symptoms								
Fever	21	12	6	7	9	10	65	86.7
Fatigue	12	10	10	7	10	9	57	76.0
Dizziness	8	9		9	6	9	7	4864.0
Weight loss	12	7		6	3	1	5	3445.3
Anorexia	6	7		5	2	3	5	2837.3
Night sweat	5	7		3	1	2	3	2128.0
Signs								
Pallor	21	13	11	10	10	10	75	100
Splenomegaly	21	3		4	0	5	3	3648.0
Bleeding	6	4	3	6	5	5	29	38.7
Hepatomegaly	10	1	1	0	2	2	16	21.3
Lymphadenopathy	3	1	0	2	4	1	11	14.7

AA: Aplastic anemia. AL: Acute leukemia. HS: Hypersplenism. IDA: Iron deficiency anemia. MA: Megaloblastic anemia. No: Number of patients

Table 4. Hematological parameters in pancytopenic patients

	Hb (g/dl)	TLC/mm3	ANC/mm3	Platelet1000 /mm3	MCV (fl)
Diagnosis	Mean±SD	Mean±SD	Mean±SD	Mean± SD	Mean±SD
HS	6.4±1.9	2154.8±712.4	673.9±448.4	61.8±25.8	83.5±7.7
Malaria	6.4±2.0	2030.8±808	757.6±401.4	60.3±30.7	80.8±15.4
MA	5.5±1.7	2318.2±686.8	1080.5±335.9	60.±31.9	101.2±11.9
AA	5.5±2.2	1805.0±968.5	468.4±584.5	46.4±33.0	88.4±3.9
AL	5.5±1.4	1795.0±1064.2	244.2±354.0	38.6±26.1	86.1±9.8
MDS	4.7±2.4	2558.5±586.9	946.5±788.1	53.7±16.8	94.0±7.2
MF	6.8±2.1	1766.7±1026.3	806.7±524.7	45.7±28.7	82.2±1.5
IDA	2.0±0.0	2800±0.0	1204±0.0	92.9±0.0	66.9±0.0
Total	5.4±1.9	2168.6±820.9	767.4±530.1	59.9±28.6	84.7±11.9
P-value*	0.3	0.4	0.002	0.3	0.0001

AA: Aplastic anemia. AL: Acute leukemia. ANC: Absolute neutrophil count.
Hb: Hemoglobin. HS: Hypersplenism. IDA: Iron deficiency anemia. MA: Megaloblastic anemia. MCV: Mean corpuscular volume. MDS: Myelodysplastic syndrome.
MF: Myelofibrosis. SD: Standard deviation. TLC: Total leukocyte count

nic patients, but differences were determined in reticulocyte count, ANC and MCV. This might be due to the different causes of pancytopenia and different characteristics of each cause [8,9,11].

The causes of pancytopenia were treatable in 56% of patients, who fully recovered from pancytopenia. Death occurred in 21.3%, which was due to severe pancytopenia and overwhelming infections.

In conclusion, the most common five causes of pancytopenia were malaria and hypersplenism malaria, megaloblastic anemia, aplastic anemia and acute leukemia. Infectious disease is considered the leading cause of pancytopenia and there is a strong relationship between parasitemia and hypersplenism. The most common clinical manifestations were progressive fever, fatigability, dizziness, and weight loss, whereas the common signs were pallor, splenomegaly, lymphadenopathy and bleeding. Aplastic anemia and acute leukemia were found to be the most serious causes of pancytopenia. Severe pancytopenia has significant relation with the clinical outcome and can be used as a prognostic indicator.

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