CLINICOHAEMATOLOGICAL SPECTRUM OF PANCYTOPENIA IN A TERTIARY CARE HOSPITAL

Taj Ali Khan[1], Irfan Ali Khan[2], Khalid Mahmood[3]

ABSTRACT

***Objective**: To determine the frequency, clinical presentation and underlying causes of pancytopenia in patients presenting to a tertiary care hospital in Peshawar.*

***Methodology**: This cross-sectional, observational study was conducted at Department of Pathology, Lady Reading Hospital Peshawar from January to December 2011. Patients of all ages having pancytopenia on blood film examination (TLC < 4000/ul, Hb < 10 gm/dl and Platelets < 150000/ul) were included in the study. Already diagnosed patients of Aplastic Anemia, Acute Leukemia receiving treatment and those not willing for bone marrow examination were excluded from the study. History, General Physical and systemic examination were recorded at presentation. The peripheral blood counts were performed with sysmex – automated hematology analyzer. Bone marrow aspiration and trephine biopsy were performed according to the standard protocol and examined microscopically to find the underlying cause of pancytopenia. Other relevant investigations were also done.*

***Results**: During the study period, we received 600 patients for bone marrow examination from various units. Out of these, 160 (26.7 %) patients had pancytopenia. Common clinical presentations were Pallor (95%, n=150), followed by generalized weakness (75%, n=120), fever (52%, n=83), bleeding manifestation (37.5%, n=60), gastrointestinal symptoms (32.5%, n=52) and splenomegaly (23.5%, n=38). The common causes of pancytopenia were aplastic anemia (37.5%, n=60) followed by magaloblastic anemia (13.75 %, n=22), Acute Leukemia (13.75%, n=22) and hypersplenism (10%, n=16).*

***Conclusion**: Pancytopenia is a common occurrence. Aplastic Anemia and Magaloblastic Anemia are the commonest causes of Pancytopenia followed by Acute Leukemia. Common clinical presentations were Pallor, fever, weakness, bleeding manifestation and Splenomegaly.*

***Key Words:** Pancytopenia, Aplastic Anemia, Megaloblastic Anemia, Leukemia.*

This article may be cited as: Khan TA, Khan IA, Mahmood K. Clinicohaematological spectrum of pancytopenia in a tertiary care hospital. J Postgrad Med Inst 2013; 27(2):143-7.

INTRODUCTION

Pancytopenia means a disorder in which all 3 blood elements (red blood cells, white blood cells and platelets) are decreased than normal. It refers to a combination of Anemia, leucopenia and thrombocytopenia (Hb < 10 g/dl, TLC < 4000/ul, Platelets < 150000/ul) [1]. It is a common clinical problem with an extensive differential diagnosis. The severity of Pancytopenia and the underlying pathology determine the management and prognosis of the patient[1]. The causes of Pancytopenia are many and the frequency of different disorders causing Pancytopenia varies according to geographical distribution. It may be due to ineffective hematopoiesis with cell death in the marrow; defective cell production which are rapidly removed from circulation, sequestration and destruction of cells by the action of the antibodies or trapping of normal cells in a hypertrophied or over reactive reticulo-endothelial system[2].

Though few clear recommendations can be found as to the optimal investigative approach to a patient with pancytopenia but still Bone marrow biopsy plays a significant role in understanding the etiology of pancytopenia. Some experts suggest that marrow examination is essential to the diagnosis, but it has not been established whether the procedure is necessary in all pancytopenic

[1,2]Department of Pathology, Lady Reading Hospital, Peshawar - Pakistan

[3]Department of Medicine, Lady Reading Hospital, Peshawar - Pakistan

Address for Correspondence:
Dr. Taj Ali Khan,
Department of Pathology,
Lady Reading Hospital, Peshawar - Pakistan
E-mail: khan.tajali@aku.edu

Date Received: May 28, 2012
Date Revised: November 26, 2012
Date Accepted: December 9, 2012

patients[3].

Common questions that a healthcare professional asks are: 1) what are the most common causes of pancytopenia?; and 2) what is the best diagnostic approach to the pancytopenic patient? Thorough evaluation of Pancytopenic patient including bone marrow examination and trephine biopsy is necessary for most patients to reach at early diagnosis and institute timely treatment. Early diagnosis on the basis of clinical suspicion is necessary for timely treatment and to avoid the occurrence of complication. Patients usually present with either symptoms of Anemia, neutropenia or thrombocytopenia[1, 4]. The purpose of our study is to find the bone marrow aspiration / trephine biopsy findings in cases of Pancytopenia and to identify its clinical presentations.

METHODOLOGY

This study was conducted at Hematology section, department of Pathology, Lady Reading Hospital Peshawar from January to December 2011. Patients of all ages and both sexes having Pancytopenia on peripheral blood examination i.e. patient having TLC <4000/ul, Hb <10g/dl Platelets <150000/ul, were included in the study. Patients of aplastic anemia, Acute Leukemia and those not willing for bone marrow examination were excluded from the study. Already diagnosed patients as to the cause of peripheral blood cytopenias and those who were on treatment were also excluded. Clinical details of the patients like age, sex, symptoms and signs were recorded in Performa.

Three milliliter of blood was taken from one of the anticubital vein in EDTA tube aseptically and peripheral blood counts were performed with sysmex XS-1000i automated hematology analyzer. Peripheral smear was stained by May-Granwald-Geisma stain for all cases and examined in detail. Patient found to have pancytopenia on blood smear examination underwent bone marrow examination. The procedure was explained to the patients in detail and written informed consent was taken. Bone marrow aspiration and bone trephine biopsy were performed according to the standard methods and examined microscopically to make the diagnosis. Trephine biopsy was performed in most of these cases except in very sick children. Other relevant investigation like ultrasound abdomen, blood culture, serum vitamin B12 and folate were also done when indicated.

The data was statistically analyzed for various parameters like age incidence, presenting symptoms and clinical findings and underlying etiology as to the causes of pancytopenia.

RESULT

During the study period, we received 600 patients for bone marrow examination from various units. Out of 600, a total of 160 patients presented with pancytopenia including 96 male and 64 female patients with male to female ratio of 1.5:1. Age of the patients ranged from 09 months to 75 years with a mean age of 35 years. Pancytopenia was observed in 53 (33%) Pediatric Patients i.e. Age <15 years, 63 (39.5%) patients were of the age group of 16 – 40 years and 44 (27.5%) were > 40 years of age.

Generalized weakness was the commonest symptoms present in 75% (n=120) of the pancytopenia patients followed by fever (52%, n=83), bleeding manifestation (37.5%, n=60) gastrointestinal symptoms (32.5%, n=52), generalized body aches (18%, n=29) and respiratory symptoms (12.5%, n=20) {Table 1}.

Table 1: Presenting complaints and physical finding in Pancytopenia patients

Symptoms and signs	Frequency	% age
Pallor	150	95 %
Generalized weakness	120	75 %
Fever	83	52 %
Bleeding manifestation	60	37.5 %
GIT Symptoms	52	32.5 %
Splenomegaly	38	23.5 %
Generalized body aches	29	18 %
Respiratory symptoms	20	12.5 %
Lymphadenopathy	07	4.4 %
Jaundice	05	3.2 %

Table 2: Distribution of causes of Pancytopenia

S. No	Cause of pancytopenia	No. of cases	% age
1	Hypoplastic/Aplastic marrow	60	37.5
2	Megaloblastic Anemia	22	13.75
3	Acute Leukemia	22	13.75
4	Hypersplenism	16	10
5	Non Hodgkins Lymphoma	11	6.9
6	Myelodysplastic syndrome	09	5.6
7	Mixed Deficiency Anemia	06	3.75
8	Visceral Leishmaniasis	06	3.75
9	Infection/Sepsis	04	2.5
10	Multiple myeloma	02	1.25

Pallor was noted in 95% (n=150) of cases followed by splenomegaly (23.5%, n=38), Lymphadenopathy (4.4%, n=7) and jaundice (3.2%, n=5) {Table 1}.

The commonest cause of pancytopenia in this study was aplastic/ hypoplastic marrow diagnosed in 60 (37.5%) patients. The next common cause was magaloblastic Anemia found in 22 (13.75%) patients. Acute Leukemia was also diagnosed in 22 (13.75%) patients; out of which Acute lymphoblastic Leukemia accounted for 16 (10%) and Acute Myeloid Leukemia for 6 (3.75%) patients. Hypersplenism due to various causes was found in 16 (10%) cases. Non Hodgkins Lymphoma (6.9%, n=11), myelodysplastic syndrome (5.6%, n=9), mixed deficiency anemia (3.75%, n=6), visceral leishmaniasis (3.75%, n=6), infections/sepsis (2.75%, n=4) and multiple myeloma (1.25%, n=2) accounted for the remaining causes of pancytopenia (Table 2).

Of the nine cases of myelodysplastic syndrome, four were refractory anemia (RA), one was refractory anemia with ring sideroblast (RARS), two were refractory cytopenia with multi-lineage dysplasia and two had refractory Anemia with excess blast (RAEB).

DISCUSSION

Pancytopenia is a common and serious clinical and hematological problem. Pancytopenia is a common finding in clinical practice. It is not a disease in itself but there are various causes of this clinical triad of Anemia, neutropenia and thrombocytopenia. The early diagnosis of the causation of Pancytopenia is important because most of these causes are treatable[5]. In our study out of total of 600 patients referred to Pathology department for hematological evaluation and bone marrow examination, 160 (2.6%) cases had pancytopenia.

All these 160 cases of pancytopenia were studied, Age gender wise distribution, clinical features, bone marrow aspiration / trephine biopsy and various causes of pancytopenia were evaluated and observations compared to those in studies published in the literature.

In the present study generalized weakness (75%) was the commonest symptoms followed by fever (52%) bleeding manifestation (37.5%) GIT Symptoms (32.5%), Body Aches (18%) and respiratory symptoms (12.5%). Similarly, in a study by Niazi M et al[6], generalized weakness (68.2%) was the commonest symptoms followed by fever (47.7%) and bleeding manifestation (33.33%).

Pallor (95%) was the comments clinical finding followed by splenomegaly (23.75%), Lymphadenopathy (4.4%) and jaundice (3.2%). Pallor and splenomegaly were also the commonest signs observed by Niazi M et al[6] and Khodke K et al[7].

In the present study the commonest cause of pancytopenia is aplastic anemia (37.5%) Niazi M et al reported the same incidence of aplastic anemia (38.27%) in their study[6]. The incidence of aplastic anemia in a western study was reported to be 15%[8]. The incidence of aplastic anemia has been reported between 7.7% and 43% in different studies of the subcontinent[7,9,10].

Megaloblastic anemia was the cause of Pancytopenia in 22 (13.75 %) cases in our study.

The incidence of megaloblastic anemia has been reported from 10 % to 74 % in different studies conducted in the subcontinent[11, 12]. This wide variation in the incidence of megaloblastic anemia is probably due to variation in the nutritional status of that particular region where the study is done.

We also found mixed deficiency anemia as the cause of pancytopenia in 06 patients (3.75%). In these cases there was peripheral pancytopenia, hypercellular marrow, megaloblastic erythropoiesis and absent iron stores. Hyperplenism was found to be the cause of pancytopenia in 11.25% of cases. Iqbal W et al[12] reported hypersplenism in 14.4% case, where as Niazi M et al[6] reported its incidence to be 18.75% in patients of pancytopenia. In locally conducted studies, the rate of hypersplenism varied from 4.9 % to 28 %[12,13]. Incidence, as high as 45% has been reported in a study from Yemen[14]. This may be related to the increased incidence of tropical parasitic infections like recurrent malaria, leishmaniasis, brucellosis and also cirrhosis liver.

We encountered acute leukemia in 13.75 % of cases, most of which were patient of acute lymphoblastic leukemia (10 %). Acute myeloid leukemia presented as pancytopenia only in 2.75 % of the patients. It is in concordance with the study by Menon S et al[15] who reported the frequency as 13.05 %. Its incidence has been reported form 5 % to 25 % in different studies[8,11,16-18]. Most of our patients of acute leukemia presenting as pancytopenia were of paediatric age group.

Non hodgkin lymphoma was diagnosed in 6.9 % cases, which correlates with the findings in the study by Iqbal W et al[12]. Myelodysplastic syndrome was the cause of peripheral pancytopenia in 09 patients (5.6 %). Of the nine cases of myelodysplastic syndrome four were refractory anemia, two were refractory cytopenia with multilineage dysplasia, one was refractory Anemia with Ring sideroblast and two cases of refractory Anemia with excess blasts which compares with the similar study conducted in India[4].

We encountered 6 cases of visceral leishmaniasis (kala-azar) constituting 3.75% of the total case. Their ages ranged from 09 months to 02 years who belonged to Afghanistan, Chitral and Parachinar which is similar to the study by Iqbal et al[12] who reported the incidence of kala-azar as 4.8%. A study from India reported higher prevalence of kala-azar[19].

Multiple myeloma presented as pancytopenia in 02 Cases (1.25%) in our study compared to Gayathri BN et al[18] who reported the incidence of 0.86%, Khodke K et al[7] who reported the incidence of 04%[1], Tilak V et al[19] who reported the incidence of 1.3% and Khunger JM et al[9] as 1% in their studies.

CONCLUSIONS

Pancytopenia is a common haematological problem and should be suspected in patient presenting with unexplained anemia, weakness, fever or bleeding manifestation. Bone Marrow aspiration and Trephine biopsy are useful in diagnosis of the cause of pancytopenia. Aplastic anemia is the commonest cause of pancytopenia followed by megaloblastic anemia. Acute leukemia, myelodisplastic syndrome and non hodgkin lymphoma are amongst the malignant disorders presenting as pancytopenia.

REFERENCES

1. Incidence of aplastic anemia: the relevance of diagnostic criteria. By the international Agranulocytosis and Aplastic Anemia Study. Blood 1987;70:1718-21.
2. Hoffbrand AV, Lewis SM, Tuddenham EG. Postgraduate haematology. 4th ed. Oxfford: Butterworth-Heinemann; 1999.
3. Savage DG, Allen RH, Gangaidzo IT, Levy LM, Gwanzura C, Moyo A, et al. Pancytopenia in Zimbabwe. Am J Med Sci 1999;317:22-32.
4. Kumar DB, Raghupati AR. Clinicohematologic analysis of pancytopenia: study in a tertiary care hospital. Basic and Applied Pathology 2012;5:19-21.
5. Rehman HU, Fazil M, Khan FM. The etiology pattern of Pancytopenia in children upto 15 years. Pak Armed Forces Med J 2003;53:183-7.
6. Niazi M, Raziq F. The Incidence of underlying pathology in pancytopenia: an experience of 89 cases. J Postgrad Med Inst 2004;18:76-9.
7. Khodke K, Marwah S, Buxi G, Yadav RB, Chaturvedi NK. Bone marrow examination in cases of pancytopenia. J Indian Acad Clin Med 2001;2:55-9.
8. Pine M, Walter AW. Pancytopenia in hospitalized children: a five year review. J Pediatr Hematol Oncol 2010;32:e192-4.
9. Khunger JM, Arulselvi S, Sharma U, Ranga S, Talib VH. Pancytopenia: a clinico haematological study of 200 cases. Indian J Pathol Microbiol 2002;45:375-9.
10. Naseem S, Varma N, Das R, Ahluwalia J, Sachdeva MU. Marwaha RRK. Pediatric patients with bicytopenia/pancytopenia: review of etiologies and clinico-hematological profile

at a tertiary center. Indian J Pathol Microbiol 2011;54:75-80.

11. Bhatnagar SK, Chandra J, Narayn S, Sharma S, Sing V, Datta AK. Pancytopenia in children: etiological profile. J Trop Pediatr 2005;51;236-9.
12. Iqbal W, Hassan K, Ikram N, Nur S. Aetiological breakup in 208 cases of pancytopenia. J Rawal Med Coll 2001;5;7-9.
13. Rahman H, Fazil M, Mohammad F. Clinical presentation of pancytopenia in childrens under 15 yrs of age. J Postgrad Med Inst 2003;17;46-51.
14. Hamid GA, Safa A, Shukry R. Pattern of pancytopenia in Yemen. Turk J Hematol 2008;25;71-4.
15. Menon S, Shaikh S, Nizamani MA. Etiological spectrum of pancytopenia based on bone marrow examination in children. J Coll Physicians Surg Pak 2008;18;163-7.
16. Gupta V, Tripathi S, Tilak V, Bhatia BD. A study of clinico-haematological profiles of pancytopenia in children. Trop Doct 2008;38:241-3.
17. Santra G, Das BK. A cross-sectional study of the clinical profile and aetiological spectrum of pancytopenia in a tertiary care centre. Singapore Med J 2010;51:806-12.
18. Gayathri BN, Rao KS. Pancytopenia: a clinico hematological study. J Lab Physicians 2011; 3:15-20.
19. Tilak V, Jain R. Pancytopenia: a clinico-hematologic analysis of 77 cases. Indian J Pathol Microbiol 1999;42:399-404.

CONTRIBUTORS

TAK conceived the idea and planned the study. IAK did the data collection and analyzed the study. KM helped in the write up of the manuscript. All the authors contributed significantly to the research that resulted in the submitted manuscript.