ORIGINAL ARTICLE

A STUDY OF PANCYTOPENIA IN ADULT PATIENTS MORE THAN 12 YEARS OF AGE IN NORTH WEST REGION OF SAURASHTRA

Bhaskar B Thakkar [1], Ukti N Bhavsar[2], N J Trivedi[3], A S Agnihotri[4]

[1]Associate Professor, Department of Pathology, GCS Medical College & Hospital, Ahmedabad; [2]Second year Resident; [3]Professor; [4]Professor & Head, Department of Pathology, CU Shah Medical College, Surendranagar, Gujarat

Correspondence: Dr. Bhaskar B Thakkar, Email: Drbhaskar_9@yahoo.com

ABSTRACT

Introduction: Pancytopenia is a manifestation of many serious & life threatening diseases with an extensive differential diagnosis. Major causes of pancytopenia in developing countries are megaloblastic anemia, parasitic infection, hypersplenism and aplastic anemia.

Methodology: In this study total 100 cases were studied by examining Peripheral smears of blood samples obtained by routine phlebotomy procedure and stained by Romanowsky stains. Bone marrow sampleswere obtained by routine bone marrow aspiration and biopsy procedures if indicated. Biochemical and other special investigations were done to confirm the diagnosis.

Results: Among the 100 cases studied, age of the patients ranged from 13 to 86 years with a mean age of 42.9 years and slight male predominance. Most of the patients presented with generalized weakness and fever. The commonest physical finding was pallor, followed by splenomegaly and hepatomegaly. The commonest marrow finding was hypercellularity with megaloblastic erythropoiesis. The commonest cause for pancytopenia was megaloblastic anemia followed by malaria.

Conclusion: The present study concludes that detailed primary hematological investigations along with other supportive tests are helpful to diagnose or to rule out the causes of pancytopenia. Megloblatic anemia is commnest cause of pancytopenia in most Indian and subcontinent studies. Present study also shows that invasive procedures like bone marrow aspiration and biopsy is avoided in most cases of pancytopenia.

Keywords: Pancytopenia, Pallor, Hypercellular Bone Marrow, Megaloblastic Anaemia, Malaria

BACKGROUND

Pancytopenia refers to a reduction in all the three formed elements of blood: red blood cells, white blood cells and platelets[1]. It is an important clinico-hematological entity encountered in our day to day clinical practice.

There are varying trends in its clinical pattern, hematological change, treatment modalities and outcome.[2]

It is a manifestation of many serious & life threatening diseases with an extensive differential diagnosis.It should be suspected on clinical grounds when a patient presents with pallor, prolonged feverand a tendency to bleed.

The aetiology of pancytopenia varies in different populations depending on the differences in age patterns, nutritional status, climate and the prevalence of infections. It is not a disease entity but a triad of findings that may result from a number of disease processes - primarily or secondarily involving the bone marrow[3]. The severity of pancytopenia and underlying pathology determine the management and prognosis of the patients[4].

Major causes of pancytopenia in developing countries are megaloblastic anemia, parasitic infection, hypersplenism and aplastic anemia. The presenting symptoms are often attributable to anemia or thrombocytopenia. Leucopenia is an uncommon cause of initial presentation but can become the most serious threat to life during the course of disorder.

Haematological investigation forms the bedrock in the management of patients with pancytopenia and therefore needs detailed study.developed.

OBJECTIVES

The present prospective study was done from July 2011 to August 2012, at Department of pathology, C.U. Shah medical college, Surendranagar. Aims and objectives of the present study are as follows:

- To find out the common causes of pancytopenia in our region (North-west Region of Saurashtra).
- To identify the specific causes of pancytopenia in which invasive procedures like bone marrow examination (aspiration & biopsy) and other special investigations are required.
- To determine the spectrum of pancytopenia with its frequency and common clinical presentation in our set up.

METHODS & MATERIALS

The present Prospective study was done on patients of more than 12 years of age from July 2011 to August 2012. Patients of both sexes were included. Case selection was based on clinical features and supported by laboratory evidence, which included peripheral blood counts for haemoglobin, leukocytes and platelets.

Source of Data

Patients from the department of medicine, surgery, obstetrics and gynecology and from periphery were included in the study.

Method of Collection of Data

A detail clinical history and physical examination to be performed in each case. Complete blood count(Hb, TC, DC, Platelet count) by automated blood counters, peripheral smear study , reticulocyte count and bone marrow aspiration/biopsy to be performed in needed cases.

Inclusion criteria in our study were: Hemoglobin <10 gm/dl; Total leukocyte count (TLC) < 4000/microL and Platelet count <1,40,000/microL

Exclusion criteria in our study were: Patients who have already been diagnosed with pancytopenia; Patients who have recently received blood transfusions; or Patients who do not give consent for bone marrow aspiration and biopsy.

Blood samples of patients were obtained by routine phlebotomy procedure.2 ml of EDTA (ethelenediamine tetra-acetic acid) anticoagulated blood was collected and processed through automated hematology analyser; and 9 hematological parameters were obtained, which included haemoglobin, red blood cell count, total leukocyte count, differential count, platelet count, mean corpuscular haemoglobin (MCH), mean corpuscular hemoglobin concentration(MCHC), packed cell volume (PCV). In cases of very low counts and abnormal cells, a manual review of the instrument's results was

performed using the improved Neubauer counting chamber Peripheral smear was stained by Leishman stain for all the cases and examined in detail. Bone marrow aspiration was done in needed cases after obtaining written consent from the patient or guardian.bone marrow sample obtained by routine bone marrow aspiration procedures by salah's needle. Staining of peripheral smear and bone marrow aspirate with Romanowasky stain. A detailed relevant history, including drug intake,was obtained and a meticulous physical examination was conducted for all patients. Anaemia was defined as mild (Hb 9–10 gm%), moderate (Hb 5–9 gm%) and severe (Hb< 5 gm%). Leucopenia was defined as mild(leucocyte count 3,000-4000/mm3), moderate (leucocyte count 1,000–3,000/mm3) and severe (leucocyte count< 1,000/mm3). Thrombocytopenia was defined as mild(platelet count 50,000-140000/mm3), moderate (platelet count 20,000–50,000/mm3) and severe (platelet count< 20,000/mm3). Other investigations were performed in selected cases according to their provisional diagnosis, including malarial parasite and antigen, serological tests for enteric fever, blood culture, liver function test, assay of vitamin B12 and folic acid, enzyme-linked immunosorbent assay for the humanimmunodeficiency virus (HIV) I and II, and the hepatitis B surface antigen (HBsAg). The patients' history, physical examination results and haematological parameters were recorded on the study proforma and the data was tabulated. The data was expressed as number and percentage.

RESULTS

Out of a total of 100 patients who were recruited in the study, 52 were male and 48 were female (male-to-female ratio 1.08:1) (table 2). The mean age of the patients was 42.9 (range 13–86) years. Seventy percent of the patients were from the rural areas.

In terms of the socioeconomic status, 57% the patients were from the middle income group, 30% were from the lower income group and 13% were from the higher income group.

Table 1: Sex Distribution of Different Cases of Pancytopenia

Diagnosis	Male (%)	Female (%)	Total (%)
Megaloblasticanemia	23 (44.23)	14 (29.17)	37 (37.00)
Malaria	10 (19.23)	9 (18.75)	19 (19.00)
Hypersplenism	6 (11.54)	8 (16.67)	14 (14.00)
Aplastic anemia	2 (3.85)	4 (8.33)	6 (6.00)
Tuberculosis	2 (3.85)	3 (6.25)	5 (5.00)
Alcoholism	4 (7.69)	0 (0.00)	4 (4.00)
Typhoid fever	1 (1.92)	2 (4.17)	3 (3.00)
Drug induced	1 (1.92)	2 (4.17)	3 (3.00)
ITP	0 (0.00)	2 (4.17)	2 (2.00)
Viral infection	0 (0.00)	1 (2.08)	1 (1.00)
Microfilaria	1 (1.92)	0 (0.00)	1 (1.00)
Leukemia	1 (1.92)	0 (0.00)	1 (1.00)
HIV	0 (0.00)	1 (2.08)	1 (1.00)
Undiagnosed	1 (1.92)	2 (4.17)	3 (3.00)
Total	52 (100)	48 (100)	100 (100)

The most common clinical feature in our study was pallor (100%), followed by weakness (97%). Bleeding

from various sites was encountered by 20% of the patients. Other common features were fever (70%),and respiratory distress (32%). Splenomegaly (23%), hepatomegaly (17%) and lymphadenopathy (03%) were also noted.

The haematological parameters revealed a mean haemoglobin concentration of 6.2 g/dl. Anaemia was severe in 24%, moderate in 51% and mild in 25% of the cases. The leucocyte count was 600–3,900/mm3 of blood (mean 2,450/mm3). 52% of the patients had moderate leucopenia, while 46% and 2% had mild and severe leucopenia, respectively.

The platelet count was 5000–1,39,000 (mean 43,500× 10^3)/mm3 of blood. 66% of the patients had a mild degree of thrombocytopenia, 26% had moderate and 08% had severe thrombocytopenia.

Megaloblasticanemia (37%) was the commenest haematological disorder encountered during present study followed by malaria (19%), hypersplenism (14%), Aplastic anemia (6%) and Tuberculosis (5%)

Male to female ratio was 1.08:1 in study participants. Megaloblasticanemia was the commonest anemia in both male and female patients in present study.

Most common clinical presentation was weakness followed by fever. Least common presentation was bleeding.

Table 2: Age Incidence in Different Causes of Pancytopenia

Diagnosis	13-20 (%) (n=11)	21-30 (%) (n=18)	31-40 (%) (n=24)	41-50 (%) (n=13)	51-60 (%) (n=16)	>60 (%) (n=18)
MegaloblasticAnemia	0	5 (27.78)	7 (29.17)	4 (30.77)	7 (43.75)	14 (77.78)
Malaria	6 (54.55)	3 (16.67)	4 (16.67)	3 (23.08)	2 (12.50)	1 (5.56)
Hypersplenism	2 (18.18)	2 (11.11)	3 (12.50)	3 (23.08)	3 (18.75)	1 (5.56)
Tuberculosis	0	1 (5.56)	4 (16.67)	0	0	0
Aplastic anemia	1 (9.09)	2 (11.11)	0	0	2 (12.50)	1 (5.56)
Alcoholism	1 (9.09)	0	1 (4.17)	1 (7.69)	0	1 (5.56)
Typhoid fever	0	1 (5.56)	1 (4.17)	1 (7.69)	0	0
Drug induced	0	1 (5.56)	0	1 (7.69)	1 (6.25)	0
ITP	0	0	1 (4.17)	0	1 (6.25)	0
Viral infection	0	1 (5.56)	0	0	0	0
Microfilaria	0	1 (5.56)	0	0	0	0
Leukemia	0	0	0	0	0	1 (5.56)
HIV	0	1 (5.56)	0	0	0	0
Undiagnosed	1 (9.09)	0	2 (8.33)	0	0	0

Table 3: Clinical Presentations of Patients of Pancytopenia

Presenting complaints	Patients
fever	70
Weakness	97
Wt loss	38
Dyspnoea	32
Bleeding	20

Table 4: Physical Findings in Cases of Pancytopenia

Physical finding	Patients
Pallor	100
Icterus	11
Hepatomegaly	17
Splenomegaly	23
lymphadenopathy	03

Most common physical finding was pallor which was present in all the patients. Least common physical finding was lymphadenopathy.

DISCUSSION

Pancytopenia is not an uncommon hematological problem in clinical practice. However there are limited number of studies available from Indian subcontinent on the frequency of various causes of pancytopenia. The variation in the frequency of various conditions causing pancytopenia has been attributed to difference in methodology and diagnostic criteria employed, geographic area, period of observation, genetic differences and varying exposure to myelotoxic agents etc.

The commonest cause of pancytopenia in the present study was megaloblastic anemia, accounting for 37% of the cases. In most of the sub continental studies megaloblastic anemia was found to be either the commenst or the second most common cause of pancytopenia.

In one study each from India, Bangladesh and Pakistan the commonest cause of pancytopenia was aplastic anemia. One international study also found aplastic anemia as commonest cause of pancytopenia.

Hence findings of the present study correlates well with other reports from india and other subcontinent. The incidence of megaloblastic anemia in our study was 37% whereas in other studies it varies from 0.8%-68%.[4,10,11,20,21]

Table 5: Comparison of Cases of Pancytopenia with Other Studies

Study	Country	Year	Cases	Cause of pancytopenia	
				Commonest	Second common
International Agranulocytosis & Aplastic Anemia Study[20]	Israel & Europe	1987	319	Aplastic anemia (52.7%)	MDS (4.5%)
Keisu M[5]	Israel & Europe	1990	100	Neoplastic diseases, radiation (32%)	Aplastic anemia (19%)
Hossain et[10]	Bangladesh	1992	50	Aplastic anemia	Malaria and kalaazar
Vermal et al[11]	India	1992	202	Megaloblastic anemia (68%)	Aplastic anemia (7.7%)
Tilak et al[4]	India	1999	77	Megaloblastic anemia (68%)	Aplastic anemia (7.7%)
MussaarratNiazi et al[21]	Pakistan	2000	89	Aplastic anemia (38.3)	Megaloblastic anemia
Kumar R et al[22]	India	2001	166	Aplastic anemia	Megaloblastic anemia
Khunger JM et al[23]	India	2002	200	Megaloblastic anemia	Aplastic anemia
Dodhy et al	Pakistan	2005	100	Megaloblasticanemia(24.9%)	Hypersplenism (16.3%)
Recent study	India	2011-12	100	Megaloblastic anemia(37%)	Malaria (19%)

The high incidence of megaloblastic anemia correlates with high prevalence of nutritional anemia in the subcontinent[12]. This group of patients respond very well to the appropriate therapy. Most of the patients presented with history of weakness and fever.

Pallor is the most common finding in all patients with megaloblastic anemia. All cases of megaloblastic anemia in the present study showed presence of macrocytes and macroovalocytes on peripheral smear. Hypersegmented neutrophils were also noted in majority of smears. Circulating megaloblast is also seen in few cases.

Bone marrow aspiration and biopsy were hypercellular in all cases of megaloblastic anemia. Marked erythroid hyperplasia is present in almost all cases of megaloblastic anemia.

Malaria was the second most common cause of pancytopenia in our study. Malaria accounts for 19% of cases in our study which is also one of the commonest causes in subcontinent countries. As malaria is endemic in our part world, once the diagnosis of malaria is established the clinician treat the acute illness without advising bone marrow examination.

Kala azar as a cause of pancytopenia has been reported in some Indian studies, as they had patients from Bihar in their study. However, present study did not encounter any case of kalaazar. Hypersplenism was the third most common cause in present study.

Aplstic anemia was the fourth common cause in our study as was the majority of other indian studies.Aplastic anemia accounts for 6% of cases of pancytopenia in the present series, while range of 10 to 25% was reported in most western studies.[4,10,11,20,24]

Present study found 3 cases of drug induced pancytopenia. Present study also found a case of acute lymphoid leukemia. Pancytopenia can be seen in approximately 30% cases of acute leukemia at time of presentation. Immature cells can be seen in the peripheral smears or smears made from buffy coat. Bone marrow aspiration establishes the diagnosis however if the tap is dry then bone marrow biopsy becomes mandatory for diagnosis.[12] Myelodysplastic syndrome was not found in present study may be due to small sample size.

CONCLUSION

The present study concludes that detailed primary hematological investigations are helpful to diagnose or to rule out the causes of pancytopenia and also to avoid invasive procedures like bone marrow biopsy and aspiration with the help of other supportive investigations.

Megaloblastic anaemia is the commonest can be of pancytopenia in present study correlated well with other Indian and sub continent studies. Pallor is most common finding in all patients with Megaloblastic anaemia. Malaria is second most common cause of pancytopenia in our study as it is endemic in our region. Invasive procedures like bone marrow aspiration and Biopsy is avoided in most cases.

REFERENCES

1. Ishtiaq O, Baqai HZ, AnwerF,Hussai N. Patterns of pancytopenia patients in a general medical ward and a proposed diagnostic approach. Available from:http://www.ayubmed.edu.pk/JAMC/PAST/16-1/osama.htm-206K-6/24/2007. [Last accessed on 2007].
2. Kar M,Ghosh A. Pancytopenia. Journal, Indian Academy of clinical Medicine 2002;Volume 3,No.1January-march 2002:29-34.
3. Guinan EC, Shimamura A. Acquired and inherited aplastic anemia syndromes In: Greer JP, Foerster J, Lukens JN, Rodgers GM, Paraskevas F, Glader B, editors. Wintrobe's Clinical Hematology. 11thed, Philadelphia: Lippincott Williams and Wilkins; 2004. P.1397-419.
4. Tilak N, Jain R. Pancytopenia- a clinical hematological analysis of 77 cases. Indian J PatholMicrobiol 1999;42(4):399-404.
5. Kishore Khadke, S. Maewah, G buxi, RB yadav, NK Chaturvedi, Bone Marrow Examination in cases of pancytopenia. Journal, Indian Academy of Clinical Medicine 2001;Volume 2, No.1 and 2,January-June2001;55-59.
6. Williams and Wilkins, Baltimore. Wintrobe's clinical haematology, 10thedn., USA, Black Well Science Limited,1999.2320-41.
7. Bain B. J., Clerk DM, Lampart IA and Wilkins BS. Bone marrow pathology, 3rdedn.Oxford, Blackwell science,2000,949-951.
8. Hennry JB. Clinical diagnosis and management by laboratory methods. 19th edn.Phildhelphia,W.B.Saunders,1999,718-755.
9. Reisner EH. The nature and significance of megaloblastic blood formation. Blood. 1958;13:313-332.
10. Hossain MA, Akond AK, Chowdhary MK et al. Pancytopenia- a study of 50 cases. Bangladesh Journal of pathology 1992;1:9-12.

11. Verma N, Dash S. reappraisal of underlying pathology in adult patient presenting with pancytopenia. Trop Geog Med 1992;44:322-7.
12. Kishore Khadke, S. Maewah, G buxi, RB yadav, NK Chaturvedi, Bone Marrow Examination in cases of pancytopenia. Journal, Indian Academy of Clinical Medicine 2001;Volume 2, No.1 and 2,January-June2001;55-59.
13. Mohler DN and Levell BS. Aplastic anemia an analysis of 50 cases. Ann intern Med. 1958;49:326-362.
14. De Planque MM, van Krieken JHJM, Kluin-Nelemans et al. Bone marrow histopathology of patients with severe aplastic anemia before treatment and at follow up.Br J Haematol. 1989;72:439-444.
15. Tichelli A, Gratwohi A, Wurch A, et al. Late haematological complication in severe aplstic anemia. Br J Haematol. 1988;69:413-418.
16. Abdalla SH. Haematopoiesis in human malaria. Blood cells. 1991;16:401-416.
17. Agrawal M.B. Hematology today, 10th edition, Bombay, M.B. Agrawal,2004, 67-68.
18. Bain B. J Classification of leukemia: the need to incorporate cytogenetic and molecular genetic information . J ClinPathol. 1998;51:420-423.
19. Harris NL, Jaffe ES, Diebold J, etal.world health organization classification of neoplastic diseases of the haemopoietic and lymphoid tissue. J ClinOncol 1999; 17:3835-3849.
20. International agranulocytosis& aplastic anemia study. Incidence of aplastic anemia , the prevelaence of diagnostic criteria. Blood 1987;70:1718-21.
21. Mussarafniazi, Fazl-i-Raziq, Incidence of underlying pathology in pancytopenia- an experience of 89 cases, journal of postgraduate medical institute,2004;Vol:18,:(1) 76-79.
22. Kumar R; Kalra SP; Kumar H; Anand AC; Madan H,Pancytopenia—a six year studyJournal of association of physicians of india,2001,vol:49, 1078-81.
23. Khunger JM; Arulselvi S; Sharma U; Ranga S; Talib VH, Pancytopenia a clinicohaematological study of 200 cases,Indian journal of pathology and microbiology,2002,Vol:45(3),375-9.
24. Wintrobe MM (ed).Clinical haematology. Eighth edition, philadelphia : Lea and Febiger 1981: pp699-915.