

Etiology of Pancytopenia and its Bone Marrow Picture

Sayyad Nikhat Anjum¹, Aman M Naikwadi²

ABSTRACT

Introduction: Pancytopenia is an important clinical-hematological entity encountered in our day-to-day clinical practice. Pancytopenia may be a presentation of a wide variety of disorders, which primarily or secondarily affect the bone marrow. Study aimed to identify the etiology and bone marrow morphology of pancytopenia patients.

Material and methods: Total 30 non-malignant patients who had pancytopenia were included in the study. Based on clinical findings bone marrow aspiration and trephine biopsy were carried out. All the bone marrow aspirate smears were stained with May-Grunwald Giemsa and trephine biopsies were stained with hematoxylin and eosin.

Results: The majority of patients were from age group 29-38 years (9 cases). Male to female ratio was 1.5:1. Commonest complaint presented was weakness in 28 cases followed by fever in 21 cases. Other presenting complaints were fatigue, breathlessness, icterus. Severe acute malnutrition was present in 6 patients followed by malaria and dengue (5 cases each), Enteric fever in 2 patients. The most common cause of Pancytopenia was megaloblastic anaemia and was seen in 13 cases. Bone marrow was hypercellular in all cases.

Conclusion: Detailed physical examination; hematological investigations along with bone marrow aspiration and bone marrow biopsy wherever necessary in Pancytopenic patients are helpful to diagnose or to rule out the causes of Pancytopenia.

Keywords: Etiology, Pancytopenia, Bone Marrow Picture

INTRODUCTION

Pancytopenia is an important clinical-hematological disorder observed in our day-to-day clinical practice. In pancytopenia all three major formed elements of blood (red blood cells, white blood cells and platelets) are decreased in number.¹ It is not a disease but numerous findings that may result from a number of disease processes.² The severity and the underlying pathology determine the management and prognosis of the patients with pancytopenia.³ Although various studies carried in India had shown the association of pancytopenia with different etiology,^{3,4} still causes of pancytopenia are not well defined.

Pancytopenia may be a presentation of a wide variety of disorders, which primarily or secondarily affect the bone marrow.⁵ This may be due to ineffective red cell production, decreased cell production, increased utilization of cells and increased destruction without an adequately matching compensatory increase in the cell production. The cause of pancytopenia may be thus lies in the bone marrow, periphery or both. Various factors such as geographic distribution and genetic disturbances may cause variation in the incidence of disorders causing pancytopenia.⁶⁻⁸ Prognosis in pancytopenia

depends upon the underlying pathology and determines the management in line with it.

The bone marrow picture in each individual may vary depending on the etiology, from non-specific changes to be replaced completely by malignant cells. According to underlying cause, degree and duration of the disorder, clinically pancytopenia can lead to fever, pallor, infection, or serious illness and sometimes death. Knowing the exact etiology behind it is important for prompt treatment and prognosis assessment. While published literature is available on the hematological diagnosis of pancytopenia on basis of bone marrow morphology, few investigators have attempted to find out the underlying etiology and clinical course of the disorders leading to this condition. In this study, we evaluated the various disorders which cause pancytopenia and necessary investigations for diagnosis of this condition in our patients. The aim of this study is to identify the etiology and bone marrow morphology of pancytopenia patients. The study focused on identifying treatable and reversible causes of pancytopenia.

MATERIAL AND METHODS

The study was conducted in the Department of Medicine in collaboration with the Department of Pathology, SMBT Medical College and Hospital, Igatpuri, Nasik (Maharashtra). Source of data:

Patient's age group between 18 years to 68 years from 1st January 2018 to 31st December 2018 admitted in medicine ward of SMBT Medical College and Hospital, Nasik. Pancytopenia was reported by automated cell counter. Hemoglobin, <9 g/dL; total leukocyte count (TLC), <4,000 / μ L; platelet count, <100,000/ μ L.⁴were taken as criteria for pancytopenia. Platelet count was confirmed by PBF manually.

Inclusion criteria

Patients of either sex from 18 years to 68 years of age. Patients satisfying the criteria for pancytopenia.

Exclusion criteria

Patients on Chemotherapy, radiotherapy for malignancies

¹Assistant Professor, Department of Pathology, ²Assistant Professor, Department of General Medicine, SMBT Medical College and Hospital, Igatpuri, Nasik, Maharashtra, India

Corresponding author: Dr. Aman M Naikwadi, Assistant Professor, Department of General Medicine, SMBT Medical College and Hospital, Igatpuri, Nasik, Maharashtra, India

How to cite this article: Sayyad Nikhat Anjum, Aman M Naikwadi. Etiology of pancytopenia and its bone marrow picture. International Journal of Contemporary Medical Research 2019;6(7):G45-G48.

DOI: <http://dx.doi.org/10.21276/ijcmr.2019.6.7.44>

and known cases of hematological malignancy.

Patients were not ready to participate in the study.

A systematic detailed history, clinical examination and laboratory findings for etiology causing pancytopenia were recorded in proforma. Hematological profile included hemoglobin, red cell indices, TLC and DLC, platelet count, PBS morphology and bone marrow aspiration or biopsy were done. Relative tests were done to establish diagnosis of various diseases.

PBF was prepared with standard staining method and seen and counter checked by pathologist. Based on the clinical indication bone marrow aspiration and trephine biopsy were carried out. After obtaining written consent from the patient or guardian, bone marrow aspiration was carried out under aseptic precaution. The bone marrow procedure and further staining were carried out by standard methods.⁷⁻⁹ All the bone marrow aspirate smears were stained with May-Grunwald Giemsa and trephine biopsies were stained with hematoxylin and eosin. When indicated, special staining techniques such as myeloperoxidase, Sudan black B, periodic acid Schiff and Perl's stain on aspirate smears and reticulin stain on biopsy were done.

RESULTS

Total 30 non-malignant patients who had pancytopenia were included in the study. The present study showed the majority of patients were from age group 29-38 years (9 cases) and least common age group was 59-68 years where only 2 patients were found. In age groups 18-28 years, 39-48 years and 49-58 years 8, 6 and 5 cases were observed. The study showed male preponderance with male to female ratio 1.5:1. Patients with Pancytopenia presented with different clinical signs and symptoms, but some common features were identified. Commonest complaint presented was weakness

Clinical findings	
Pallor	30
Fever	21
Weakness	28
Bleeding	11
Dyspnea	9
Icterus	9
Splenomegaly	8
Hepatomegaly	6
Lymphadenopathy	3
Bone pain	2

Table-1: Clinical presentation of pancytopenia.

Bone Marrow Findings	
Megaloblastic anemia	13
Hypoplastic marrow	7
Acute lymphoid leukemia	2
Normal marrow	3
Storage disorder	2
Myelodysplastic syndrome	1
Microcytic erythropoiesis	2

Table-2: Bone marrow findings in cases of pancytopenia.

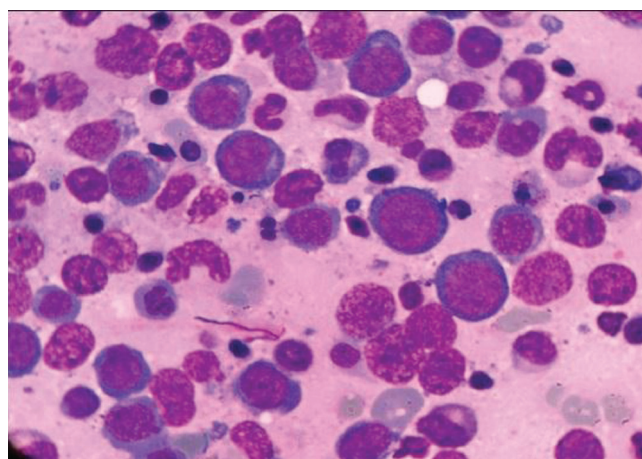


Figure-1: Bone marrow showing megaloblasts, with royal blue cytoplasm and sieve-like chromatin (Leishman, $\times 1000$)

in 28 cases followed by fever in 21 cases. Other presenting complaints were fatigue, breathlessness, icterus. Pallor was the most common clinical finding and it was found in almost all cases. Icterus was seen in 9 cases. Bleeding manifestations like epistaxis, gum bleeding and petechial rashes were seen in 11 cases. Splenomegaly was seen in 8 cases and hepatomegaly in 6 cases (Table – 1). In cases of megaloblastic anemia, enteric fever and malaria, splenomegaly and hepatomegaly were seen. Lymphadenopathy was noted in leukemia cases. Our results show the distribution of cases according to etiology. Severe acute malnutrition was present in 6 patients followed by malaria and dengue (5 cases each), Enteric fever in 2 patients. Myelodysplastic syndrome, systemic lupus erythematous and measles were seen in one patient each. Chronic kidney disease/ liver disease were seen in 3 patients. 2 cases of each were seen of leukemia and aplastic anemia. Multiple myeloma was diagnosed in 2 cases.

The commonest cause of Pancytopenia was megaloblastic anaemia and was observed in 13 cases followed by hypoplastic marrow 7 cases. 15 cases had iron deficiency along with megaloblastic anemia. On bone marrow aspiration, megaloblastic erythroid hyperplasia was seen along with micronormoblasts. The characteristic features of Megaloblasts seen were sieved nuclear chromatin, asynchronous maturation of nucleus, bluish cytoplasm and cytoplasmic blebs. (Figure-1) In granulocyte series giant meta-myelocytes and band forms were predominant.

2 cases were of ALL (acute lymphoblastic leukaemia) and one patient was diagnosed with myelodysplastic syndrome. Bone marrow was hypercellular in all cases. Erythroid and megakaryocytic series were reduced. In ALL, lymphoblasts formed the more than 40% marrow. 2 cases who presented with weakness and bony tenderness, were diagnosed as multiple myeloma. Bone marrow showed increased number of plasma cells. 2 cases of storage disorder were diagnosed. (Table-2) A 27-year-old male was presented with pallor and splenomegaly. Diagnosis of Gaucher's disease was considered based on bone marrow finding which showed large cells with eccentrically placed nucleus and abundant cytoplasm which was PAS (periodic acid Schiff) positive.

DISCUSSION

Pancytopenia can be due to reduction in hematopoietic cell production in the bone marrow (in aplastic anemia), due to infections or due to increased cell destruction either in bone marrow itself or in spleen.

In the present study, majority of the cases were in the age group 29-38 years which is similar to studies of Khodke, et al.⁹ with 40% cases in the age group of 12-30 and Pathak, et al.¹⁰ with 30% of cases in the age group of 15-30 years. In this study, males outnumbered female with male to female ratio of 1.5:1 similar to the studies of Khodke et al⁹ and Shah, et al.¹¹ males were more than females.

Pallor was seen in almost all cases. Fever and weakness were seen in 21 and 28 cases respectively. Poonam, et al¹² found fever (56%) as the most common symptom followed by generalized weakness (46%). In a study by Tilak, et al³ generalised weakness (51%) was the commonest symptom followed by fever (27%).

The most common cause of Pancytopenia, reported in literature has been aplastic anemia. While, the present study found megaloblastic anaemia as the commonest cause of Pancytopenia and it is seen in 13 cases. Our results were comparable to study done by B N Gayathri and Kadam¹³ where in most common cause for Pancytopenia is megaloblastic anemia (74.04%) followed by aplastic anemia (18.26%). Occurrence of megaloblastic anemia was 72% and 68% in the studies done by Khunger, et al.¹⁴ and Tilak, et al.³ respectively. All the above studies have been carried out in India, and they have shown the importance of megaloblastic anaemia being the major cause of Pancytopenia. It is a rapidly manageable disorder and should be promptly diagnosed.

Our results show that most important and common cause of pancytopenia was severe malnutrition in 6 cases. This multiple micronutrient and protein energy deficient state leads to depleted and changed bone marrow. These results are in line with study conducted by Chandra et al¹⁵ in 2002 in Delhi and Borelli et al¹⁶ in 2009 in Brazil. Second most common cause of pancytopenia in our study was dengue fever in 5 cases. In dengue there is hemo-concentration leucopenia and thrombocytopenia, which may be due to immunological suppression of bone marrow or hemo-phagocytic syndrome. Malaria was causative for pancytopenia in 5 cases there was 3 cases of Plasmodium falciparum and 2 cases of Plasmodium vivax. Study results are comparable with Khunger et al¹⁴ who reported an incidence of 1%, Tilak et al³ reported incidence of 3.9%.

Enteric fever also contributed to 2 cases. This may be due to total or partial bone marrow suppression. James and Dutta¹⁷ in 1997 showed that in enteric fever 8.3% prevalence of pancytopenia was present. The present study states that in all the cases of Pancytopenia both bone marrow aspiration and bone marrow biopsy must be performed as a part of diagnosis.

Difference in the occurrence of disorders causing Pancytopenia has been due to study design variations, various diagnostic criteria, different geographic area, duration of observation,

genetic differences and varying exposure to cytotoxic/chemical agents.

CONCLUSION

Pancytopenia is a common hematological disorder encountered in clinical practice and should be evaluated completely and promptly. Bone marrow aspiration is an important diagnostic tool in haematology which helps to evaluate various cases of Pancytopenia.

The present study concluded that detailed physical examination; hematological investigations along with bone marrow aspiration and bone marrow biopsy wherever necessary in Pancytopenic patients are helpful to diagnose or to rule out the causes of Pancytopenia. These are also useful in planning further investigations and treatment.

REFERENCES

1. Ishtiaq O, Baqai HZ, Anwer F, Hussai N. Patterns of pancytopenia patients in a general medical ward and a proposed diagnostic approach. *J Ayub Med Coll Abbottabad* 2004; 16:8-13.
2. 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*. 11th ed, Philadelphia: Lippincott Williams and Wilkins; 2004; p1397-419.
3. Tilak V, Jain R. Pancytopenia-A Clinico-hematologic analysis of 77 cases. *Indian J Pathol Microbiol* 1992; 42:399-404.
4. Kumar R, Kabra SP, Kumar H, Anand AC, Madan H. Pancytopenia – a six year study. *J Assoc Phys India* 2001; 49:1078-81.
5. Williams WJ, Bentkr E, Erskv AJ. *Haematology – 3 edition*, Singapore, Mc Graw Hill Book Company 1986; 161-84.
6. International agranulocytosis and aplastic anemia study. Incidence of Aplastic anemia, relevance of diagnostic criteria. *Blood* 1987; 70:1718-21.
7. Wintrobe MM (ed). *Clinical Hematology*. Eighth edition, Philadelphia: Lea and Febiger 1981; 699-915.
8. Keiser M, Ost A. Diagnosis in patients with severe pancytopenia suspected of having aplastic anemia. *Eur J Haematol* 1990; 45:11-14.
9. Khodke K, Marwah S, Buxi G, Vadav RB, Chaturvedi NK. Bone marrow examination in cases of Pancytopenia. *J Academy Clin Med.*, 2001; 2: 55–9.
10. Pathak R, Jha A, Sayami G. Evaluation of bone marrow in patients with pancytopenia. *J Patho Nepal.*, 2012; 2: 265-71.
11. Shah P, et al. Bone marrow examination in case of pancytopenia. *Int J Res Med Sci.*, 2017; 5: 1494-1498.
12. Poonam, et al. Diagnosis of bone marrow aspiration. *Indian Journal of Basic and Applied Medical Research*, March 2016; 5: 723-732.
13. B N Gayathri, Kadam Satyanarayan Rao. Pancytopenia: A Clinico Hematological Study. *Journal of Laboratory Physicians*, 2011; 3: 15-20.
14. Khunger JM, Arculselvi S, Sharma U, Ranga S, Talib VH. Pancytopenia - A Clinicohaematological study of 200 cases. *Indian J Pathol Microbol.*, 2002; 45: 375-9.

15. Chandra J, Jain V, Narayan S, et al. Folate and cobalamine deficiency in megaloblastic anemia in children. *Indian Pediatr*, 2002; 39:453-7.
16. Borelli P, Barros FEV, Nakajima K, Blatt SL, Beutler B, Pereira J et al. Protein-energy malnutrition halts hemopoietic progenitor cells in the G0/G1 cell cycle stage, thereby altering cell production rates. *Brazilian J Med Boil Res* 2009; 42:523-530.
17. James J, Dutta TK, Jayanthi S. Correlation of clinical and hematologic profiles with bone marrow responses in typhoid fever. *Am J Trop Med Hyg.* 1997; 57:313-6.

Source of Support: Nil; **Conflict of Interest:** None

Submitted: 02-03-2019; **Accepted:** 26-03-2019; **Published:** 28-07-2019