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ORIGINAL RESEARCH

Characteristics of Bone Marrow in Patients Presenting with Pancytopenia at a Tertiary Care Centre in Northern India

Dr. Neha Ahuja[1], Dr. Himashree Nath[2], Dr. Parul Ahuja[3], Dr. Poonam Mehrotra[4], Dr. Sangharsh Rao[5]

[1]Associate Professor, Department of Pathology, Rama Medical College, Hospital & Research Centre, Kanpur U.P., India
[2]Post Graduate Student, Department of Pathology, Rama Medical College, Hospital & Research Centre, Kanpur U.P., India
[3]Associate Professor, Department of Oral Maxillofacial Surgery, Dr. B.S. Kushwah Institute of Medical Sciences, Kanpur U.P., India
[4]Associate Professor, Department of Radiodiagnosis, Dr. B.S. Kushwah Institute of Medical Sciences, Kanpur U.P., India
[5]Assistant Professor, Department of Anatomy, Rama Medical College, Hospital & Research Centre, Kanpur, U.P., India

Corresponding Author
Dr. Neha Ahuja
Associate Professor, Department of Pathology, Rama Medical College, Hospital & Research Centre, Kanpur U.P., India

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ABSTRACT

Background: Pancytopenia refers to the concurrent presence of anemia, leukopenia, and thrombocytopenia. It may be classified as either primary or secondary. The examination of bone marrow is of significant importance in elucidating the etiology of pancytopenia. The objective of this study is to ascertain the etiology of pancytopenia, to determine the prevalence of various diseases contributing to pancytopenia, and to evaluate the significance of bone marrow examination in such cases. **Materials and Methods:** This research was undertaken in the vicinity of Kanpur, Uttar Pradesh, over a span of three years across various healthcare centers. Patients exhibited a range of symptoms. A bone marrow aspiration and biopsy were conducted on the patients, specifically from the posterior superior iliac crest. Aspiration smears were subjected to staining using the Leishman stain for microscopic examination. Prior to the placement of the tissue in 10% neutral buffered formalin fixative, touch imprints of the bone marrow biopsy were prepared and subsequently analyzed. **Results:** A total of 150 cases were studied during a period of three years. Age of patients range from 1 year to 60 years. 69 cases were female and 81 were male. The commonest cause of pancytopenia was megaloblastic anemia seen in 23 cases (46%) followed by nutritional anemia seen in 7 cases (14%), 5 cases (10%) were Aplastic anemia, 4 cases (8 %)were acute myeloid leukemia, 3 cases (6%) were acute lymphoblastic leukemia, 3 cases(6%) were lymphoma, 3 cases (6 %) were multiple myeloma, 1case (2%) was chediak higashi syndrome and 1 case (2%) was malaria. Conclusion: Bone marrow study helps in the diagnosis of cause of pancytopenia and also helps in planning for further investigations and management.

Keywords: Bone Marrow, Chediak Higashi Syndrome, Megaloblastic Anemia And Pancytopenia

INTRODUCTION

Pancytopenia is a condition that encompasses anemia, leucopenia, and thrombocytopenia respectively.[1] It has the potential to be either primary or secondary. The failure of the bone marrow is the main cause of this condition.[2] The replacement of bone marrow by toxins, malignant cells, as well as abnormal cells, ineffective hematopoiesis, or the entrapment of normal cells in a hyperplastic and overactive reticuloendothelial system, is all factors that contribute to secondary causes.[3] Pancytopenia constitutes a significant clinico-hematological condition frequently encountered in contemporary clinical practice.[4] The clinical manifestation, therapeutic approaches, and prognosis of the condition exhibit diverse trends. This condition is characterized by a reduction in the quantities of all three primary cellular components of the blood: erythrocytes, leukocytes, and thrombocytes.[5] It does not constitute a distinct disease entity but rather represents a triad of

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clinical findings that can arise from various pathological processes, either directly or indirectly affecting the bone marrow.[6] The treatment and prognosis of patients are determined by the severity of pancytopenia as well as the underlying pathology that causes it.[7] The current study has been done to investigate the numerous causes of pancytopenia and to correlate the peripheral blood findings with bone marrow aspirate because the causes of pancytopenia in India are not well defined.[7,8] Aetiology varies from region to region. As a result, this information will be useful in the preparation of the diagnostic and treatment strategy for patients presenting with pancytopenia.

AIM AND OBJECTIVES

1. To find out the cause of pancytopenia.
2. To ascertain the prevalence rates of various diseases that result in pancytopenia.
3. To elucidate the significance of bone marrow research.

MATERIALS AND METHODS

This investigation was conducted as a prospective study. The present study was carried out in the vicinity of Kurnool over a span of four years, encompassing various healthcare facilities. Individuals of all age categories and both genders were included in the study. Within the scope of the study, a total of 100 bone marrow aspirations and 100 biopsies were conducted. Bone marrow aspiration and biopsy were performed under aseptic conditions. The area was infiltrated with xylocaine. The most frequently utilized anatomical sites were the posterior superior iliac crest and the sternum. Sterilized Salah's needles of varying sizes are employed for aspiration, contingent upon the patient's age. A 10cc syringe was employed for the purpose of aspiration. The aspirated material was disseminated on clean slides in a manner consistent with a smear preparation. Concurrently, a bone marrow biopsy, imprint smears, a complete blood count, and a peripheral smear were conducted. Leishman stain was employed to stain the peripheral smear, bone marrow aspiration smear, and touch imprint smears. Touch imprint smears are instrumental in enhancing the identification of morphological characteristics. Bone marrow smears underwent evaluation concerning cellularity, the ratio of myeloid to erythroid cells, erythropoiesis, myelopoiesis, and megakaryopoiesis. A bone marrow biopsy was conducted utilizing a Jamshidi needle. Prior to immersion in 10% neutral buffered formalin fixative, touch imprints were prepared on clean glass slides.

Inclusion Criteria: The study encompassed cases exhibiting hemoglobin levels below 10 g/dL, total leukocyte counts below 4,000 cells/mm³, and platelet counts lower than 150,000 cells/mm³.

Exclusion Criteria: Instances of chemotherapy-induced pancytopenia were omitted from consideration.

RESULTS

A comprehensive study was conducted on a total of 100 cases of pancytopenia. Among these, 57 were male and 43 were female, as detailed in Chart No. 1. The age range of the patients extended from 1 year to 70 years, as depicted in Table 2. Patients exhibited a variety of clinical features. The hematological profile was primarily characterized by macrocytic anemia, accounting for 47 of cases, followed by nutritional anemia. Leucopenia and thrombocytopenia were observed in all clinical cases. Among the 100 analyzed cases, 44 were diagnosed as megaloblastic anemia, 16 as nutritional anemia, 10 as acute myeloid leukemia, 9 as aplastic anemia, 7 as acute lymphoblastic leukemia, 6 as multiple myeloma, 4 as lymphoma, 3 as Chediak-Higashi syndrome, and 1 as malaria (refer to Table 3). In our study, the most prevalent etiology of pancytopenia is identified as megaloblastic anemia, accounting for 44 of cases, followed by nutritional anemia, which constitutes 16. Upon conducting a bone marrow aspiration, one observes megaloblasts characterized by a sieve-like nuclear chromatin pattern, alongside asynchronous maturation between the nucleus and the basophilic cytoplasm. Granulopoiesis exhibits a small number of giant metamyelocytes.

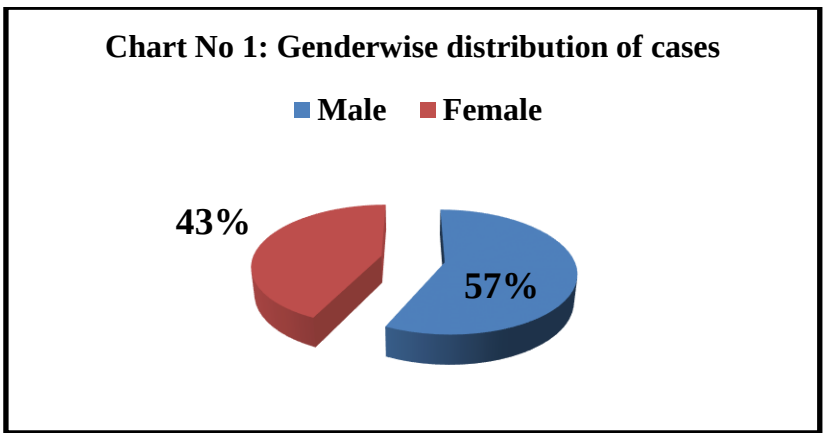

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Table No. 1: Age wise distribution of cases	
Age	**No. of cases**
1-10	3
11-20	5
21-30	17
31-40	24
41-50	26
51-60	19
>60	6

Table No.2: Causes of Pancytopenia	
Diagnosis	**No. of cases**
Megaloblastic anemia	44
Nutritional	16
Acute megaloblastic leukemia	10
Aplastic anemia	9
Acute Lymphoblastic leukemia	7
Multiple myloma	6
Lymphoma	4
Chediak higashi syndrome	3
Malaria	1

Table No.3: Comparison of findings between Bone Marrow Aspiration and Bone Marrow Biopsy		
Diagnosis	**No. of BMB cases**	**No. of case same as BMA**
Megaloblastic anemia	44	44
Nutritional	16	16
Acute megaloblastic leukemia	10	9
Aplastic anemia	9	9
Acute Lymphoblastic leukemia	7	7
Multiple myloma	6	6
Lymphoma	4	4
Chediak higashi syndrome	3	2
Malaria	1	1

Five instances were identified as cases of aplastic anemia. The aspiration smears demonstrate a cellularity level that is suboptimal for the patient's age. The nucleated cells remaining predominantly encompass lymphocytes, plasma cells, mast cells, and macrophages. A limited number of normoblastic erythroid precursors are observed. Myelopoiesis is diminished and demonstrates a leftward shift, with only a few segmented forms observed. A sparse distribution of megakaryocytes is observed (refer to Fig.2). In reference to the second set of cases, all five bone marrow biopsies exhibited hypocellular marrow with a relative increase in adipose tissue, yet no infiltrates or fibrosis were observed. In four instances of acute myeloid leukemia, the biopsies revealed the presence of greater than 20 myeloblasts, alongside hypercellular marrow with diminished trilineage hematopoietic elements. Three cases exhibited acute lymphoblastic lymphoma, characterized by diminished erythropoiesis, myelopoiesis, and megakaryopoiesis, with the entire bone marrow being supplanted by lymphoblasts comprising more than 80. Three cases were diagnosed as lymphoma. In these patients, bone marrow analysis indicated a severe reduction in all three hematopoietic lineages alongside the presence of medium-sized lymphoid cells. In such cases, the potential presence of a lymphoproliferative disorder was contemplated, and this was subsequently substantiated in two instances as low-grade non-Hodgkin's lymphoma and in one instance as high-grade non-Hodgkin's lymphoma through immunohistochemical analysis of bone marrow biopsy specimens. Three instances of plasma cell myeloma exhibited an elevated quantity of lymphoid cells as well as the presence of atypical plasma cells, accompanied by hypocellular to normocellular marrow. A single incidence of malaria was identified, characterized by the presence of malarial pigment within the aspiration smears. A single instance of Chediak-Higashi syndrome was identified, characterized by the presence of abnormal giant inclusion bodies within leukocyte precursor cells observed in aspiration smears. Observation of giant granules in lymphocytes in a peripheral blood smear. Among the 100 instances of pancytopenia examined, a correlation between bone marrow aspiration and

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bone marrow biopsy was observed in 48 cases. In two instances, the bone marrow biopsy was deemed inadequate (refer to Table 4).

DISCUSSION

Pancytopenia is characteristic of numerous life-threatening conditions. Adverse circumstances, several of which include Amenable to treatment. Thus, the study of bone marrow significantly contributes to the advancement of therapeutic treatments. Such circumstances. The current research examines megaloblastic anemia.Anemia, affecting 46% of individuals, constituted the most prevalent cause of Pancytopenia (refer to Table 3), succeeded by nutritional factors. The prevalence of anemia is observed at 14%, while aplastic anemia accounts for 10%.Diseases account for 26% of the total, while other factors constitute 4%. According to the literature, aplastic anemia is identified as the most prevalent cause of pancytopenia. The present study identified megaloblastic anemia as the most prevalent cause, a finding that aligns with the research conducted by Metikurke et al.[4], BN Gayathri and Kadam[5], and Pereira A et al.[6]. Specifically, the incidence of megaloblastic anemia was reported as 74%, 72%, and 68% in the studies by BN Gayathri and Kadam[5], Khungar et al.[7], and Tilak et al.[8], respectively. In certain instances, the diagnosis of megaloblastic anemia via peripheral smears proves challenging due to the patient's utilization of over-the-counter treatments. Therefore, in these cases, a bone marrow study becomes instrumental in facilitating accurate diagnosis and subsequent treatment of the patients. In the present study, the second most prevalent cause of pancytopenia was identified as severe malnutrition, observed in seven instances. The condition of multiple micronutrient and protein-energy malnutrition results in the depletion of bone marrow. These results demonstrated a correlation with the findings of Metikurke et al.[4], Chandra et al.[9], and Borelli et al.[10]. In our study, aplastic anemia was identified as the third most common cause of pancytopenia. The incidence observed in the present study aligns with the findings reported by Metikurke et al., which documented a rate of 13%. Aplastic anemia can be attributed to environmental determinants, which may include exposure to pesticides, pharmaceuticals, chemicals, and infections. Bone marrow smears from seven cases of acute leukemia exhibited hypercellularity, accompanied by a reduction in trilineage hematopoietic cells and the presence of greater than 20% blast cells. The findings were identified by Pathak R et al.[11] and Das R et al. Reference [12]. Acute myeloid leukemia exhibits a higher prevalence in the adult population, whereas acute lymphoblastic leukemia is more frequently observed in the pediatric demographic. In contrast to the aforementioned cases, one of our pediatric female patients exhibited clinical features consistent with acute myeloid leukemia. Within this study, three cases were identified as lymphoid neoplasia. The examination of bone marrow in these cases reveals the presence of extensive sheets of atypical lymphoid cells. These findings are comparable to those observed in the studies conducted by Panigrahi R et al.[13], Horvath F et al.[14], and Desalphina M et al.[15]. In the course of our study, three instances were identified as plasma cell myeloma. The bone marrow exhibited a hypocellular to normocellular composition, characterized by an increased presence of lymphocytes and atypical plasma cells. The findings of this study were consistent with those reported in other research works.[11,12,13,16] The variability in the frequency of disorders can be attributed to differences in geographic locations, duration, and exposure to chemical agents.

CONCLUSION

Pancytopenia necessitates comprehensive evaluation, as it constitutes a prevalent hematological issue encountered in clinical practice. The examination of bone marrow constitutes a significant method for assessing the etiology of pancytopenia. The current research determined that the examination of bone marrow in instances of pancytopenia assists in identifying the underlying cause. Additionally, it provides insight into the prevalence of various diseases responsible for pancytopenia, thereby facilitating improved patient management. Bone marrow aspiration and biopsy represent straightforward, safe, and minimally invasive outpatient procedures for the assessment of the underlying causes of pancytopenia.

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