Original Research Article

Evaluation of pancytopenia on bone marrow aspiration - study at a tertiary care center in Kashmir valley, India

Subuh Parvez Khan1*, Sajad Geelani2, Fiza Parvez Khan3, Noorjahan Ali1, Shazieya Akhter1, Sumayya Shah1, Nusrat Bashir4, Javid Rasool2

1Department of Haematopathology, 2Department of Clinical Haematology, Sher-e-Kashmir Institute of Medical Sciences, Srinagar, Jammu and Kashmir India
3Department of Haematology and Transfusion Medicine, 4Department of Pathology, Government Medical College, Srinagar, Jammu and Kashmir India

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*Correspondence:
Dr. Subuh Parvez Khan, E-mail: khansubuh@gmail.com

ABSTRACT

Background: Pancytopenia refers to combination of anaemia, leukopenia and thrombocytopenia. It may be a manifestation of a wide variety of disorders, which primarily or secondarily affect the bone marrow. However, aetiology of pancytopenia varies from one geographical region to another. Bone marrow aspiration plays an important role in identifying the cause of pancytopenia. This study was carried to identify the causes of pancytopenia and to find out the bone marrow morphology in cases of pancytopenia.

Methods: This study was conducted in the department of haematology in a tertiary care center in Kashmir valley for a period of 3 years. Inclusion criteria: cases with hemoglobin less than 10 gm/dl, total leucocyte count of less than 4000/mm³ and platelet count less than 100,000/mm³ were included in the study.
Exclusion criteria: Patients receiving chemotherapy/radiotherapy were excluded from the study. Bone marrow aspiration (BMA) was performed from posterior iliac crest of the patients. Bone marrow aspiration smears were stained with Leishman stain for microscopy.

Results: A total of 334 cases were studied during a period of 3 years. Age of patients ranged from 1 year to 85 years with mean of 43.59 years. 180 cases were male, and 154 cases were female with male:female ratio of 1.2 :1. The commonest cause of pancytopenia was megaloblastic anemia seen in 103 cases (30.8%) followed by dual deficiency anemia seen in 69 cases (20.7%). 37 cases (11%) were of acute leukaemia. Aplastic anemia was seen in 35 cases(10.5%). Other causes of pancytopenia were myelodysplastic syndrome, multiple myeloma, iron deficiency anemia and hypersplenism.

Conclusions: Bone marrow aspiration in patients of pancytopenia helps in the identification of the underlying cause in most of the cases. BMA is helpful for understanding the disease process; and in planning further investigations and management of cytopenia patients.

Keywords: Bone marrow aspiration, Megaloblastic, Pancytopenia

INTRODUCTION

Pancytopenia refers to combination of anaemia, leukopenia and thrombocytopenia. It may be a manifestation of a wide variety of disorders, which primarily or secondarily affect the bone marrow. It could be associated with decrease in hematopoietic cell production either due to destruction of marrow tissue by toxins or replacement by malignant or abnormal cells or suppression of normal growth and differentiation. Other
mechanism including ineffective haematopoiesis with cell death in the marrow, formation of defective cells which are rapidly removed from circulation, sequestration and/or destruction of cells by the action of antibodies or, trapping of normal cells in a hypertrophied and over-reactive reticuloendothelial system. Marrow cellularity depends on the cause of pancytopenia. Marrow is hypocellular in cases of primary production failure a or hypercellular as in cases of peripheral destruction of haematopoietic elements, ineffective erythropoiesis or infiltrative disorders of bone marrow. However, aetiology of pancytopenia varies from one geographical region to another. Common aetiologies in developing countries like India being megaloblastic anaemia, infection, drugs, hypersplenism and aplastic anaemia. The severity of pancytopenia and the underlying pathology determine the management and prognosis of the patients. This study was carried to identify the causes of pancytopenia and to find out the bone marrow morphology in cases of pancytopenia.

METHODS
This study was conducted in the department of haematology in a tertiary care center in Kashmir valley for a period of 3 years from January 2015 to December 2017.

Inclusion criteria

- Cases of pancytopenia with hemoglobin less than 10 gm/dl
- Total leucocyte count of less than 4000/mm³ and platelet count less than 100,000/mm³.

Exclusion criteria

- Patients receiving chemotherapy/radiotherapy were excluded from the study.

Written informed consent of all study subjects was obtained before undergoing the procedure. BMA was done from posterior superior iliac spine in all the patients with salah needle, the aspirate was drawn with a 20-ml plastic syringe. Bone marrow smears were prepared immediately following aspiration. After being air dried these smears where stained with Leishmann stain for morphological examination. Periodic Acid Schiff (PAS) stain, Sudan Black B(SBB) and Myeloperoxidase (MPO) stain was done wherever required. Statistical analysis was done using SPSS 16.0 software.

RESULTS
A total of 334 cases were studied during a period of 3 years. Age of the cases ranged from 1 year to 85 years with mean of 43.59 years,180 cases were male, and 154 cases were female with male:female ratio of 1.2 : 1. The commonest cause of pancytopenia was megaloblastic anaemia seen in 103 cases (30.8%) followed by dual deficiency anemia seen in 69 cases (20.7%). 37 cases (11%) were of acute leukaemia. Aplastic anemia was seen in 35 cases (10.5%). Other causes of pancytopenia were myelodysplastic syndrome, multiple myeloma, iron deficiency anemia and hypersplenism. Bone marrow aspiration findings are shown in Table 1.

Table 1: Bone marrow aspiration findings in cases of pancytopenia.

| Bone marrow findings | No. of cases | Percent |
|----------------------|--------------|---------|
| Acute leukaemia      | 37           | 1       |
| Aplastic anemia      | 35           | 10.5    |
| Dual deficiency anemia | 69          | 20.7    |
| Gauchers disease     | 01           | 0.3     |
| Hyperspleenism       | 06           | 1.8     |
| Iron deficiency anemia | 07         | 2.1     |
| Leishmaniasis        | 02           | 0.6     |
| Malaria              | 01           | 0.3     |
| Myelodysplastic       | 15           | 4.5     |
| syndrome             |               |         |
| Megaloblastic anemia  | 103          | 30.8    |
| Multiple myeloma     | 17           | 5.1     |
| Normoblastic erythroid| 29           | 8.7     |
| hyperplasia           |               |         |
| Non Hodgkins lymphoma | 07           | 2.1     |
| Secondaries          | 05           | 1.5     |

DISCUSSION
In the present study 334 cases were included. Age of the cases ranged from 1 year to 85 years with mean of 43.59 years. Male:female ratio was 1.2:1. Khunger et al carried a study on 200 cases in which the age ranged from 2-70 years with male:female ratio of 1.2:1.

In a study by Tilak et al range of age was 5-70 with male female ratio of 1.14:1. Similar findings were seen in some other similar studies.

The incidence of megaloblastic anaemia varies from 0.8% to 32.26% of all pancytopenic patients. In the present study, megaloblastic anemia is the commonest cause of megaloblastic anaemia accounting for 30.8%. Megaloblastic anemia was characterized by erythroid hyperplasia with erythroblasts showing seive like chromatin (Figure 1). In a similar study done by Tilak et al megaloblastic anemia was the commonest cause of pancytopenia constituting 68%. Megaloblastic anemia was commonest cause of pancytopenia in a study conducted by Khodke et al accounting for 44%. In a study by Gayathri et al megaloblastic anemia was seen in 74.04%. Similar results were seen by some other studies of Khunger et al, Manzoor et al, Dahake et al and Rangaswamy et al. In the present study, dual deficiency anemia was seen in 20.7%. In a study conducted by Kulkarni et al, dimorphic anaemia was the
commonest cause of pancytopenia seen in 36.23% of cases.\textsuperscript{12}

Figure 1: Photomicrograph of Bone marrow aspiration smear of megaloblastic anemia showing erythroblasts with sieve like chromatin. (Leishman stain, 100X).

The incidence of acute leukemia varies between 1.61% - 14.5% in different Indian studies.\textsuperscript{13,14} In the present study, 11% of cases were of acute leukemia (Figure 2). In a study conducted by Mir et al, acute leukemia was the second commonest etiology present in 6.78% of total patients.\textsuperscript{15} Acute leukemia constituted 8.8% of total cases of pancytopenia in a study conducted by Pathak et al.\textsuperscript{16} Acute leukemia constituted third most common cause of pancytopenia in the study of Savage et al and similar finding was seen in study of Varma et al.\textsuperscript{17,18} In the study of Aziz et al, acute leukemia constituted almost 10% of cases of pancytopenia and was third most common cause of pancytopenia.\textsuperscript{19}

In a study by Kumar et al aplastic anaemia was the commonest cause of pancytopenia seen in (29%) of cases.\textsuperscript{20} Similarly in a study conducted by Dasgupta et al aplastic anemia constituted 33.5% of cases.\textsuperscript{13} However, in present study, Aplastic anemia was seen in 10.5% of cases. It was characterized by increased fat with diminished haematopoetic elements (Figure 3). Present study results are comparable to studies by Khodke et al, khungar et al and Manzoor et al where aplastic anemia constituted 14% of total cases.\textsuperscript{5,7,9}

Figure 2: Photomicrograph of Bone marrow aspiration smear of acute leukaemia showing blasts with increased N:C ratio, nuclei having fine chromatin with prominent nucleoli (Leishman stain, 100X).

Figure 3: Photomicrograph of Bone marrow aspiration smear of aplastic anemia showing mainly fat cells with decreased haematopoetic elements (Leishman stain, 100X).

In this study one case of Gaucher disease was diagnosed. Gaucher disease was seen in 0.7% of cases of patients with pancytopenia in the study of Ikram et al.\textsuperscript{22}

Figure 3: Photomicrograph of Bone marrow aspiration smear of multiple myeloma showing plasma cells with an eccentric nucleus, perinuclear hoff and basophilic cytoplasm (Leishman stain, 100X).

In present study 8.7% of cases showed normoblastic erythroid hyperplasia. This is very low as compared to study by Pathak et al where they found 20% of BMA showed erythroid hyperplasia.\textsuperscript{16} Khodke et al found Normoblastic erythroid hyperplasia with peripheral pancytopenia in 14% of cases.\textsuperscript{7}

Dasgupta et al, reported an incidence of 2.42% of myelodysplastic syndrome, while present study had 4.5% incidence of myelodysplatic syndrome.\textsuperscript{13} Mir et al in their study had mds with an incidence of 3.03%.\textsuperscript{15}
In present study, multiple myeloma was seen in 5% cases. More than 10% plasma cells were seen on BMA in these cases (Figure 4). This is comparable to studies by Mir et al and Khodke et al, with multiple myeloma constituting 5.3% and 4% of cases respectively.\(^5\) In present study Non-Hodgkin lymphoma infiltration was seen in 2.1% cases, this is comparable with Mir et al (3.78% of total patients).\(^5\) mostly non-Hodgkin’s lymphoma has incidence varying between 0.9% to 10% in different studies.\(^2\)

**CONCLUSION**

Bone marrow aspiration in patients of pancytopenia helps in the identification of the underlying cause in most of the cases. BMA is helpful for understanding the disease process; to rule out the causes of cytopenia; and in planning further investigations and management of cytopenia patients. Common causes of pancytopenia in our study are megaloblastic anemias, dual deficiency anemia, acute leukaemia and aplastic anemia.

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