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Original Research Article

Analysis of Peripheral Smear and Bone Marrow Morphology in Evaluation of Bicytopenia: A Prospective Study

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Abstract

Introduction: Bicytopenia is an important clinico-hematological disorder. This study was conducted in Coimbatore Medical College Hospital to identify various causes of bicytopenia. It was done by analysing and correlating hematological indices, peripheral smear and bone marrow morphology of bicytopenia patients. *Materials and Methods* : It is a prospective study done for a period of one year. In this study, 50 cases of bicytopenia were included. *Results :* The most common cause of bicytopenia was Combined deficiency (42%) followed by Megaloblastic anemia (24%). The other causes include micronormoblastic erythroid hyperplasia, leukemia, myelodysplastic syndrome, immune thrombocytopenia, metastasis and plasmacytoma. Maximum number of cases seen in the age group of 21-40 years. *Conclusion:* In this study, causes of bicytopenia were evaluated as it is equally important as pancytopenia in the management of patients. The higher incidence of combined deficiency can be attributed to low socioeconomic status, poor hygiene, inadequate nutrition and lifestyle modification. So analysis of hematological indices, peripheral smear and bone marrow morphology becomes an important diagnostic tool for an early intervention of the patients with bicytopenia.

Keywords: Bicytopenia; Combined deficiency; Megaloblastic anemia.

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Introduction

Bicytopenia is an important clinico-hematological disorder. Cytopenias is defined as reduction in the cellular elements of blood- that is, red cells, white cells and platelets. Bicytopenia is reduction in any of the two cell lines and pancytopenia is reduction in all the three cell lines.[1] Many studies are done on pancytopenia but very few studies available on bicytopenia in the literatures. Bicytopenia is also an indicator for many malignant and non-malignant disorders. The etiology of bicytopenia varies widely from simple viral infection to a malignant process. The identification of causes is important in management of patients. A careful examination of peripheral blood film is often helpful in giving a lead to diagnosis and bone marrow examination usually establishes the diagnosis. In cytopenias, the cellularity of bone marrow varies with the

causes. The bone marrow may be normocellular, hypercellular or hypocellular.[2] The aim of the study was to evaluate the various causes and to correlate hematological indices and the peripheral blood findings with bone marrow aspirates in bicytopenia cases. This data would help in planning the diagnostic and therapeutic approach in patients with bicytopenia.

Materials and Methods

It is a prospective study conducted in Department of Pathology, Coimbatore Medical College Hospital, Coimbatore during the period from January 2017 to December 2017. The study included 50 cases of bicytopenia. For all 50 cases, complete blood count, peripheral smear and bone marrow examination were analysed for etiological diagnosis. Peripheral smear and bone marrow were stained with Leishman's stain. Special stains like Sudan Black B, Periodic Acid Schiff stain and Perl's stain were done when needed. The inclusion criteria were

1. Age-All ages
2. Gender-both male and female
3. Hemoglobin less than 10 g/dl
4. Total leucocyte count less than 4000/mm^3
5. Platelet count less than 1,00,000/mm^3.

The exclusion criteria were

1. Patients on chemotherapy and radiotherapy.
2. Patients received blood transfusion.

Results

During the study period, 50 cases of bicytopenia fulfilling the criteria were included. In this study, the minimum age of presentation was 2 years and maximum age was 75 years. Most of the cases come under the age group of 21–40 years (40%) followed by 41–60 years (30%). Males are affected slightly higher than females with male to female ratio of 1.2:1.

The most common form of bicytopenia was anemia and thrombocytopenia (90%) then anemia and leucopenia (10%). The mean laboratory values show hemoglobin 6.5 g/dl, total white cell count 5,714 cells/mm^3 and platelet count 80,735/mm^3. The mean value of mean corpuscular volume (MCV) was normal in bicytopenia (93.8 fl). The normal MCV value indicates dimorphic anemia was the most common type of anemia in cases of bicytopenia.

In peripheral smear, dimorphic anemia (64%) was the most common presentation followed by macrocytic anemia (24%). In this study, combination of macrocytes and microcytic hypochromic cells was the most common form of dimorphic anemia.

The most common etiology of bicytopenia is combined deficiency with megaloblastic and micronormoblastic maturation in 21 cases (42%). The second common is megaloblastic anemia in 12 cases (24%).

Discussion

The incidence of bicytopenia is increasing in frequency due to multifactorial causation. Bicytopenia is becoming a common hematological findings with variable clinical manifestations. It became a challenging one for the clinician to diagnose the correct etiology for the management of the patients.

Age and sex

The age of presentation ranged from 2 years to 75 years. The maximum number of cases was seen in the age group of 21–40 years. Males are affected more than females with a male to female ratio of 1.2:1. Neelima bahal *et al*.[3] study also had maximum number of cases in second and third decades of life with male female ratio of 1.3:1. Aneeth singh *et al*.[4] had male female ratio of 1.6:1

Hemograms

In the present study, the hematological criteria were hemoglobin less than 10 gm/dl, total white blood cell count less than 4,000 cells/mm^3 and platelet count less than 1,00,000/mm^3. In cases of bicytopenia any two of the above criteria with other value being normal were included in the study. So the range of each parameter ranged from low to normal values. In 50 cases, the hemoglobin value ranged from 1.9 to 10 gm/dl, the total count ranged from 600 to 11,000 cells/mm^3 and the platelet count ranged from 3,000 to 2,82,000/mm^3.

The most common form of bicytopenia was anemia and thrombocytopenia (90%) then anemia and leucopenia (10%). The reason can be attributed to that the erythrocytes and megakaryocytes originate from a common progenitor cell CFU-EM (colony forming unit erythrocyte and megakaryocyte). Thus, any damage to this progenitor leads to bicytopenia with anaemia and thrombocytopenia. Neelima bahal *et al*.,[3] Aneeth singh *et al*.[4] and Mousa

SM[5] also had anemia and thrombocytopenia as common presentation seen in 57.97%, 62.1% and 70% of cases respectively.

Peripheral Smear Diagnosis

In 50 cases, the most common anemia in peripheral smear is dimorphic anemia in 32 cases (64%) followed by macrocytic anemia in 12 cases (24%). Microcytic hypochromic anemia seen in 8% of cases, Acute leukemia seen in 2% of cases and normocytic normochromic anemia seen in 2% of cases. Bone marrow aspiration study yielded the final etiological diagnosis.

Causes of bicytopenia

The most common etiology of bicytopenia is combined deficiency with megaloblastic and micronormoblastic maturation in 21 cases (42%). The second common is megaloblastic anemia in 12 cases (24%) followed by myelodysplastic syndrome (8%), immune thrombocytopenia (8%), leukemia (6%), micronormoblastic erythroid hyperplasia (6%), metastasis (4%) and plasmacytoma (2%). Comparison of various etiology of bicytopenia in different studies were shown in Table 1.

Table 1: Comparison of Various Etiology of Bicytopenia in Different Studies

Studies	Bicytopenia	
	First Cause	Second Cause
Neelima Bahal *et al*.[3] India 2016	Megaloblastic anemia (28.98%)	Leukemia (23.18%)
Aneeth singh *et al*.[4] India 2018	Megaloblastic anemia	Acute myeloid leukemia
Mousa SM[5] Egypt 2014	Clonal hematopoietic disorders (34%)	Immune thrombocytopenia (24%)
Kirti S Dagdia *et al*.[6] India 2016	Megaloblastic anemia (29.3%)	Aplastic anemia (18.6%)
Akhtar Munir *et al*.[7] Pakistan 2014	Malignant hematological disorders (33.1%)	Megaloblastic anemia (18.2%)
Present study	Combined deficiency (42%)	Megaloblastic anemia (24%)

Combined deficiency

In the present study, 42% cases of bicytopenia were diagnosed as combined deficiency with megaloblastic and micronormoblastic maturation. Kirti S Dagdia *et al*.[6] showed combined deficiency as third most common etiology of bicytopenia in 12% cases. The mean corpuscular volume (MCV) value is normal. The peripheral smear showed dimorphic anemia composed of macrocytes, macroovalocytes and microcytic hypochromic cells. The predominant of which cell type varies with type of deficiency, in case of increased deficiency of iron than vitamin B12 and folic acid, the microcytic hypochromic cells are predominant than macrocytes and vice versa in case of increased vitamin B12 and folic acid deficiency. It is because of high prevalence of nutritional deficiency in India, combined deficiency is increasing.

In our hospital, most of the patients were from low socioeconomic status, so they presents with deficiency of iron, vitamin B12 and folic acid. The dimorphic anemia patient's bone marrow showed a cellular marrow with erythroid hyperplasia having megaloblastic and micronormoblastic maturation as shown in (Fig. 1).

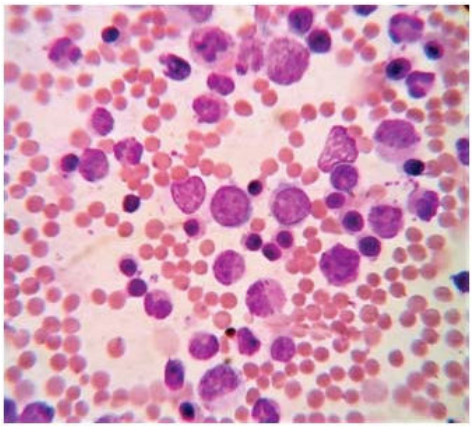

Fig. 1: Micronormoblasts and megaloblasts in bone marrow aspirate (Leishman stain-Oil Immersion)

Megaloblastic anemia

In the present study, 24% cases of bicytopenia was diagnosed as megaloblastic anemia. Neelima bahal *et al*.[3] had 28.98%, Kirti S Dagdia[6] had 29.3% cases and Akhtar munir *et al*.[7] had 18.2% cases of megaloblastic anemia. The peripheral smear showed macrocytes and macroovalocytes in all cases with hypersegmented neutrophils in most of the cases as shown in (Fig. 2). The bone marrow aspiration showed cellular marrow with erythroid hyperplasia and predominance of erythroid precursors showing sieve like chromatin. Giant band forms, metamyelocytes and hypersegmented neutrophils are seen in all cases of megaloblastic anemia as shown in (Fig. 3). Few of the cases show dysplastic features in erythroid precursors like nuclear budding and binucleation which constitutes less than 5%. It is important because if it is more than 10%, then myelodysplastic syndrome must be ruled out.

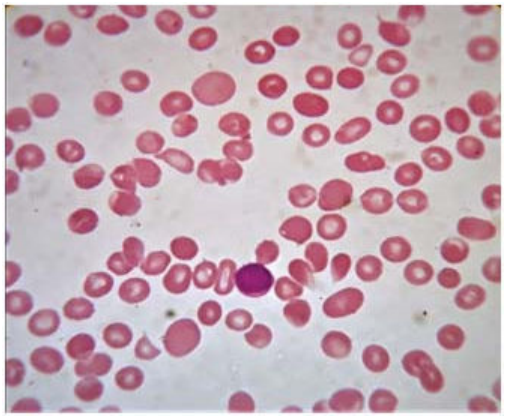

Fig. 2: Macrocytes and macroovalocytes in peripheral smear (Leishman stain-Oil Immersion)

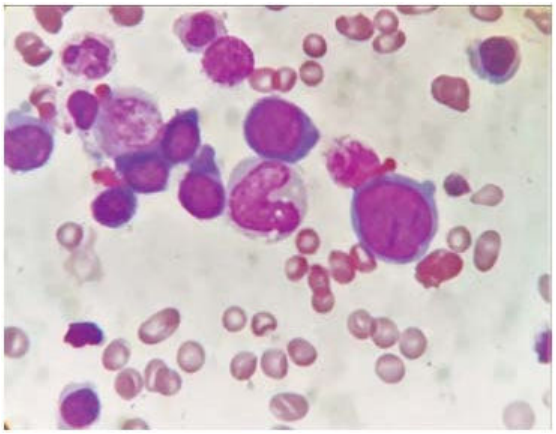

Fig. 3: Megaloblasts and giant band forms in bone marrow aspirate (Leishman stain-Oil Immersion)

Micronormoblastic erythroid hyperplasia

In the present study, 6% cases of bicytopenia was diagnosed as micronormoblastic erythroid hyperplasia. The study done by Akhtar Munir *et al*.[7] had 9.5% cases of iron deficiency anemia. In case of iron deficiency, microcytic hypochromic anemia is a common finding. Leucopenia may be present. But as a reactive process, increased erythropoietin stimulates megakaryopoiesis so that platelet count may be normal or increased. In this study, iron deficiency anemia presented with microcytic hypochromic anemia and leucopenia with normal platelet count.

Myelodysplastic syndrome

In this study, 8% cases of bicytopenia was diagnosed as Myelodysplastic syndrome (MDS). Mousa SM[5] had 6.5% cases and Kirti S Dagdia *et al*.[6] had 8% cases of MDS. Myelodysplastic syndrome classified into many subtypes according to cytopenias and dysplastic lineages. As per 2016 revised WHO classification, out of 4 cases of bicytopenia, 3 cases

diagnosed as MDS with multilineage dysplasia and 1 case as MDS with single lineage dysplasia. The MDS presented with dimorphic anemia in all 4 cases. Bone marrow aspiration study showed more than 10% dysplastic features in erythroid, myeloid and megakaryocytic lineages as shown in (Fig. 4). Ring sideroblasts are not seen in Perl's stain.

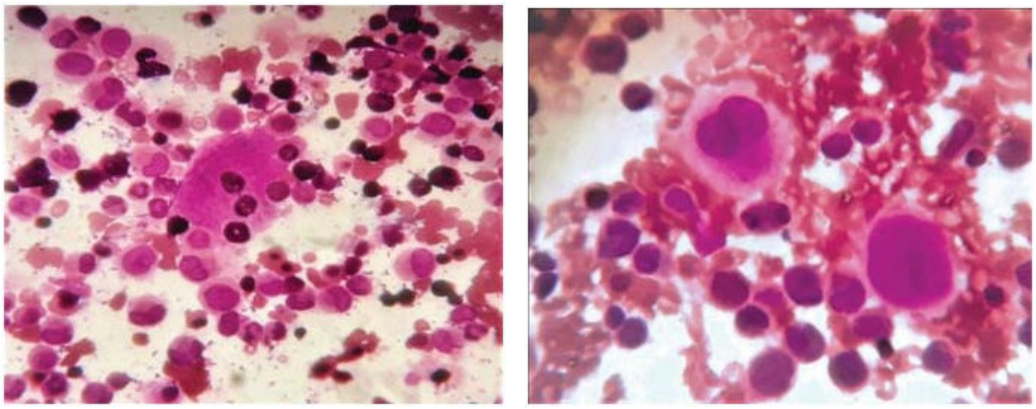

Fig. 4: Dysplastic megakaryocytes in bone marrow aspirate (Leishman stain-Oil Immersion)

Immune thrombocytopenia

In the present study, 8% cases of bicytopenia were diagnosed as immune thrombocytopenia. Aneeth singh *et al*.[4] had 5.5% cases, Mousa SM[5] had 24% cases and Akhtar Munir *et al*.[7] had 10.1% cases of immune thrombocytopenia as second most common etiology of bicytopenia among non-malignant disorders. Immune thrombocytopenia usually presents as thrombocytopenia, but our cases presented with anemia and thrombocytopenia. It is because of chronic bleeding in the patients leads to anemia. The peripheral smear findings are dimorphic anemia with normocytic normochromic cells and microcytic hypochromic cells and thrombocytopenia with giant platelets. The bone marrow aspiration showed increased megakaryocytes with many hypolobated and hypogranular forms.

Acute leukemia

In this study, 3 cases (6%) of bicytopenia was diagnosed as Acute leukemia. Aneeth singh *et al*.[4] had 7.25% of cases, Mousa SM[5] had 10% and Kirti S Dagdia *et al*.[6] had 17.3% cases of leukemia. In bicytopenia cases, one case presented with more than 20% blasts in peripheral smear and confirmed with bone marrow aspiration study. Other two cases showed no blasts in peripheral smear. These two cases were diagnosed only after bone marrow examination which showed 30–40% blasts. Cytochemical stains were done for morphological diagnosis. Out of 3 cases, 1 case was diagnosed as Acute lymphoblastic leukemia morphologically subtyped as ALL-L2 and 2 cases was diagnosed as Acute myeloid leukemia morphologically typed as acute promyelocytic leukemia (APML).

Metastasis

In the present study, two cases (4%) of bicytopenia were diagnosed as metastatic deposits. Kirti S Dagdia *et al*.[6] had 1.3% cases of metastasis to bone marrow. The peripheral smear showed normocytic normochromic anemia. Bone marrow aspiration showed atypical epithelial cells.

Plasmacytoma

In this study, only 1 case (2%) of bicytopenia diagnosed as plasmacytoma. Kirti S Dagdia *et al*.[6] also had 1 case (1.3%) of plasmacytoma. The peripheral smear showed dimorphic anemia with rouleaux formation. The bone marrow aspiration showed more than 10% plasma cells and its immature forms.

Conclusion

Many studies were done on pancytopenia but for bicytopenia very limited number of studies available. In this study, causes for bicytopenia were evaluated as it is equally important as pancytopenia in the management of patients. The causes of cytopenias differ between countries according to health problems which is prevalent there. In other countries hematological malignancies are the most common cause of bicytopenia. The higher incidence

of combined deficiency in our country can be attributed to low socioeconomic status, inadequate nutrition, poor hygiene and lifestyle modification. So analysis of hematological indices, peripheral smear and bone marrow study are very important for an early intervention to enhance the survival rate for the patients presenting with cytopenias.

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