INCIDENTALLY DIAGNOSED BICYTOPENIA SHOWING A WIDE SPECTRUM OF PATHOLOGIES ON BONE MARROW MORPHOLOGY

Saadia Haroon Durrani[1], Muhammad Sayyar[2], Amreek Lal[3], Rashid Aslam[2]

ABSTRACT

Objective: Spectrum of bone marrow morphology in patients incidentally diagnosed as bicytopenia on routine hematological workup.

Study design: Descriptive study.

Place and duration of study: This study was carried out over a period of one year and six months (January 1st 2013-June, 30th 2014) at Pathology Department, Saidu Medical College, Saidu Sharif Swat.

Methods and Materials: Total of 100 cases of both sexes and all age groups presenting with bicytopenia on blood counts referred for bone marrow analysis were included in the study.

Results: Total of 100 cases with bicytopenia on blood counts underwent bone marrow aspiration. Age ranged from 1 year to 75 years with mean age 28.1±23.55 years. Male to female ratio was 1.5:1. Out of these bicytopenias the most common was anemia and thrombocytopenia (85% cases) followed by anemia and leukopenia (10% cases) and thrombocytopenia and leukopenia (5% cases). The most common bone marrow diagnosis was megaloblastic anemia (18% cases) followed by mixed nutritional deficiency anemia (17% cases), acute lymphoblastic anemia (14% cases), hemolytic anemia (10% cases), iron deficiency anemia (8% cases), hypoplasia (6% cases), visceral leishmaniasis (6% cases), acute myeloid leukemia, myelodysplastic syndrome (5% cases each), sepsis, multiple myeloma, malaria (3% cases each) and chronic myeloid leukemia (2% cases).

Conclusion: Bicytopenia is one of the common findings on blood counts, in the present study the most common cause on bone marrow analysis was found to be nutritional deficiency anemias in all age groups while acute lymphoblastic leukemia was the commonest cause in pediatric group. The present study will provide basis for further studies in category of bicytopenia especially in adult population because not much data is available in adult population.

Keywords: Peripheral cytopenia, bicytopenia, anemia, thrombocytopenia, leukopenia, megaloblastic anemia, mixed nutritional deficiency anemia

INTRODUCTION:

Cytopenia such as anemia i.e. reduction in Hemoglobin concentration (< 12g/dl in adult females and <13g/dl in adult men), thrombocytopenia i.e. reduction platelet count (< 150 x 10^9 /L) and leukopenia i.e. reduction in white blood cell count (< 4 x 10^9 /L)[1,2,3,4]. Bicytopenia is decrease in any two cell lineages of hematopoietic cells[5]. Pancytopenia is a condition in which all hematopoetic cell lineages are affected[3,4,6,7]. Bicytopenia is a common finding on blood counts and it can occur in a wide range of pathological events involving bone marrow directly or indirectly[8]. Bicytopenia is a very common clinical finding in variety of setups and the incidence and pathological spectrum which results in bicytopenia vary in different countries[9]. Bicytopenia can occur in a wide spectrum of diseases ranging from very benign viral infection or simple transient infective process suppressing some lineages of bone marrow precursors to more serious malignant conditions[3,10,11,12]. It can be combination of anemia and thrombocytopenia, anemia and leukopenia or thrombocytopenia and leukopenia[4,6,7,10,11,12]. Bicytopenia was found to be the most common type of cytopenias in study done by Naseem S et.al. (40%)[3] however pancytopenia accounted for 17.7%. In another done in Nepal reported incidence of pancytopenia to be 50% and bicytopenia 36% amongst 86% cases presenting with anemia while rest of the cases (14%) presented with thrombocytopenia alone[13]. It was also reported to be the commonest type of cytopenia in cases of malignant hematological disorders 34.88%[11]. In a study done on megaloblastic anemia it was found that 45% cases presented with bicytopenia on blood counts[13]. There is very little data available on evaluation of bicytopenia in adults however few studies in pediatric population are present reporting spectrum of

[1] Deparment of Pathalogy Rehman Medical College Peshawar - Pakistan.
[2] Department of Surgery HMC Peshawar - Pakistan.
[3] Department of Pathology SMC Swat - Pakistan.

Address for correspondence:
Dr. Muhammad Sayyar
Department of Surgery, Hayatabad Medical Complex, Peshawar - Pakistan.
E-mail: dr_sayyar2000@yahoo.com

pathologies on bone marrow in bicytopenic patients[10]. This study was done with the aim of finding the spectrum of pathologies in incidentally diagnosed bicytopenic patients of all age groups, and further evaluates the association of the most common type of bicytopenia with cause and age of patients.

Method and Materials: This was descriptive study carried out over a period of one year and six months (1st January 2013 to 30th June 2014) at Pathology department, Saidu Medical College, Saidu Sharif, Swat. Permission from the hospital ethics committee was taken to conduct the study. Total of 100 patients of both genders with bicytopenia referred from Saidu Teaching Hospital for bone marrow cytology were prospectively included in this study after getting informed consent, while those not consenting to participate in study or not willing for bone marrow biopsy were excluded. Non-probability consecutive sampling technique was used. The patients were assessed by adequate history, thorough physical examination and investigations such as full blood counts, peripheral smear, differential leucocytes counts, red cell indices, bone marrow aspirate/biopsy. For blood counts and smear blood was taken in EDTA containing vacutainer and peripheral blood counts were obtained by running the specimen on automated hematology analyser (Sysmex KX-2IN). Following international protocols mentioned in Daice[8]. Peripheral smear were made fixed and stained with Geimsa stain following international protocols as mentioned in Daice[8]. while bone marrow aspirates were taken, slides prepared immediately were fixed after air drying. Fixed smears were stained with geimsa and special stains (Perl's. PAS and Sudan black B etc) were used where ever required following protocol mentioned in Dacie[8]. Multiple slides were prepared and fixed for each process. Then these slides were examined under multi-head microscope to diagnose each case. Data were recorded and documented in performa and frequency distribution of various variables was analyzed with SPSS version 16.

RESULTS:

Total of 100 cases with bicytopenia on blood counts underwent bone marrow aspiration. Age ranged from 1 year to 75 years, frequency distribution is shown in table 1. With mean age 28.1 and standard deviation of 23.55. Male to female ratio was 1.5:1, frequency distribution shown in table 2. Out of these bicytopenias the most common was anemia and thrombocytopenia (85% cases) followed by anemia and leukopenia (10% cases) and thrombocytopenia and leukopenia (5% cases). The most common bone marrow diagnosis was megaloblastic anemia (18% cases) followed by mixed nutritional deficiency anemia (17% cases), acute lymphoblastic anemia (14% cases), hemolytic anemia (10% cases), iron deficiency anemia (8% cases), hypoplasia (6% cases), visceral leishmaniasis (6% cases), acute myeloid leukemia, myelodysplastic syndrome (5% cases each), sepsis, multiple myeloma, malaria (3% cases each) and chronic myeloid leukemia (2% cases). Further segregation of each type is shown in table 3. The most common type of bicytopenia in adults (age range from 17.01-75 years) was found to anemia and thrombocytopenia (37 cases) amongst which there were 7 cases of megaloblastic anemia and mixed nutritional deficiency anemia, 5 cases of acute myeloid leukemias and myelodysplastic syndrome each, 3 cases of hemolytic anemia and multiple myeloma each, 2 cases of iron deficiency anemia and chronic myeloid leukemia each and 1 case of malaria, visceral leishmaniasis and hypoplasia each, followed by anemia and leukopenia (7 cases) amongst which there were 6 cases of megaloblastic leukemia and 1 case of hemolytic anemia. In children (age ranged from 1 year to 17 years) the most common type of bicytopenia was found to be anemia and thrombocytopenia (48 cases) amongst which there were14 cases of acute lymphoblastic leukemia, 10 cases of mixed nutritional deficiency anemia, 6 cases of iron deficiency anemia, 5 cases of megaloblastic anemia, 3 cases of hemolytic anemia, visceral leishmaniasis and sepsis each and 2 cases of hypoplasia and malaria each, followed by thrombocytopenia and leukopenia (5 cases) was found in 3 cases of hypoplasia and 2 cases of visceral leishmaniasis and finally anemia and leukopenia (3 cases) which were all of hemolytic anemia cases.

Table 1: frequency distribution of various age groups

Age Groups	Frequency	Percent (%)
<= 10.00	28	28.0
10.01 - 30.00	36	36.0
30.01 - 50.00	14	14.0
50.01 - 70.00	18	18.0
70.01+	04	04.0
Total	100	100.0

Table 2: frequency distribution of gender

Gender	Frequency	Percent (%)
Male	60	60.0
Female	40	40.0
Total	100	100.0

DISCUSSION:

The commonest form of bicytopenia in the present study was anemia and thrombocytopenia, followed by anemia and leukemia, and thrombocytopenia and leukemia. Similar to our study, commonest form of

Table 3: frequency distribution of bicytopenia on bone marrow findings

Bone marrow diagnosis	Frequency (n)	Type of bicytopenia	Age distribution of each type of according to bone marrow findings	
			Adults >16 yrs	Children 1-16 yrs
megaloblastic anemia	18	12 (A+T)	7	5
		6 (A+L)	6	0
mixed nut. def. anemia	17	17 (A+T)	7	10
ALL	14	14 (A+T)	0	14
hemolytic anemia	10	6 (A+T)	3	3
		4 (A+L)	1	3
iron def. anemia	8	8 (A+T)	2	6
hypoplasia	6	3 (A+T)	1	2
		3 (T+L)	0	3
visceral leishmaniasis	6	4 (A+T)	1	3
		2 (T+L)	0	2
AML	5	5 (A+T)	5	0
myelodysplastic syndrome	5	5 (A+T)	5	0
Sepsis	3	3 (A+T)	0	3
Multiple myeloma	3	3 (A+T)	3	0
Malaria	3	3 (A+T)	1	2
CML	2	2 (A+T)	2	0
TOTAL	100			

(ALL= acute lymphoblastic leukemia, AML= acute myeloid leukemia, CML= chronic myeloid leukemia, A+T= anemia and thrombocytopenia, A+L= anemia and leukopenia and T+L= thrombocytopenia and leukopenia)

bicytopenia in Indian study was anemia and thrombocytopenia seen in 77.5% cases, followed by anemia and leukopenia in 17.3% and thrombocytopenia and leukopenia in 5.5% cases[4]. The most common cause of bicytopenia in this study was megaloblastic anemia, mixed nutritional deficiency anemia and acute lymphoblastic leukemia. However according to age wise distribution the most common cause of anemia and thrombocytopenia in adults was megaloblastic anemia and mixed nutritional deficiency anemia. In children the most common cause of anemia and thrombocytopenia was acute lymphoblastic leukemia followed by mixed nutritional deficiency anemia. Anemia and leukopenia was found only in cases of megaloblastic anemia and hemolytic anemia while thrombocytopenia was found in cases of hypoplasia and visceral leishmaniasis. A study done over two year period in India showed acute leukemias to be the most common cause of bicytopenia (66.9%) out of which acute lymphoblastic leukemia was most common, followed by idiopathic thrombocytopenia purpura (5.2%), megaloblastic anemia (3.7%), marrow hypoplasia (2.9%) and visceral leishmaniasis (2% cases)[4]. A study done in Egyptian pediatric population showed also showed difference and the most common cause of bicytopenia was clonal hematopoietic disorders (34%), followed by ITP (24%) and hyperspenism (18%)[3]. Lymphoid neoplasms (10%) were the most common type of clonal disorders causing bicytopenia followed by acute myeloid leukemia (6%) and acute lymphoblastic leukemia, MDS and multiple myeloma (were 4% each). The differences were due to the study population (pediatric), ethnicity and environmental factors and also geographic region. In two studies done in Pakistan also reported megaloblastic anemia to be the most common cause of bicytopenia[14,15]. The most common hematological malignancy causing bicytopenia in present study was acute lymphoblastic leukemia (17%) followed by acute myeloid leukemia and myelo-

dysplastic leukemia (5% each), multiple myeloma (3%) and chronic myeloid leukemia (2%). In a study done by Jha in Nepal reported most frequent cause of bicytopenia in malignant hematological disorders was acute lymphoblastic leukemia (27 cases), myelodysplastic syndrome (2 cases) and multiple myeloma (1 case)[5]. The differences were due to study population, ethnic group and also that in this study only hematological malignancies were studied.

CONCLUSION:

Bicytopenia is one of the common findings on blood counts, in the present study the most common cause on bone marrow analysis was found to be nutritional deficiency anemias in all age groups while acute lymphoblastic leukemia was the commonest cause in pediatric group. The present study will provide basis for further studies in category of bicytopenia especially in adult population because not much data is available in adult population.

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