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Evaluation of Bone Marrow in Patients of Bicytopenia/Pancytopenia

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Abstract

Background: The present study has been undertaken to evaluate the various causes ofbicytopenia/ pancytopenia and to evaluate clinical signs and symptoms and hematological parameters along with bone marrow aspirate. Thus, it would help in planning the diagnostic and therapeutic approach in patients with pancytopenia.

Methods: A prospective randomized study was conducted in the Department of Pathology, Jhalawar Medical College & Hospitals from June 2019 to May 2020. The various causes of bicytopenia and pancytopenia were evaluated.

Results: Diagnosis of megaloblastic anemia was concordant in both peripheral blood film and bone marrow. In 12 cases of dimorphic anemia on peripheral blood film, 11 showed dimorphic anemia whereas one showed megaloblastic anemia. Out of 8 cases of microcytic hypochromic anemia, 6 were diagnosed concordant with BM and 2 as hypoplastic marrow. Haemolytic anemia, acute leukemia, chronic lymphoid leukemia and multiple myeloma were diagnosed concordant in both peripheral blood film and bone marrow. Out of 21 inconclusive cases on PBF, 2 were ITP, 3 werehypoplastic marrow, 4 were erythroid hyperplasia, 4 were normocellular marrow and 8 were consistent with hypersplenism on bone marrow examination.

Conclusion: Bone marrow examination can diagnose majority of cases of pancytopenia and bicytopenia along with comprehensive clinical and haematological study. It is also helpful in planning further investigations and management.

Keywords: Bone marrow, PBF, Pancytopenia and Bicytopenia

Introduction

The bone marrow is the largest & most widely distributed organ in the body. It is the principle site for blood cell production. In the normal adult, its daily production and export of blood cells amounts to about 2.5 billion red cells, 2.5 billion platelets and 1.0 billion granulocytes per kg bodyweight.[1]

Cytopenia is defined as reduction in any of the cellular elements of blood, i.e., red blood cells, white blood cells or platelets. When there is reduction in any of the two cell lines it is called bicytopenia. When there is decrease in all the three types of cell lines (red blood cells, white blood cells & platelets) below the normal reference range it is called pancytopenia.[2]

Peripheral smear study becomes so essential if cause of bicytopenia and pancytopenia was not apparent from clinical history and examination. If this fails to reveal the cause bone marrow aspiration or biopsy is needed.[3-4]

Bone marrow evaluation is an invaluable diagnostic procedure which may confirm the diagnosis of suspected cytopenia, from the clinical features and peripheral blood film examination or occasionally give a previously unsuspected diagnosis. [5]

The present study has been undertaken to evaluate the various causes of bicytopenia/ pancytopenia and to evaluate clinical signs and symptoms and hematological parameters along with bone marrow aspirate. Thus, it would help in planning the diagnostic and therapeutic approach in patients with pancytopenia.

Materials& Methods

A present prospective study "Evaluation of bone marrow in patient with bicytopenia/pancytopenia" was carried out during the period of 1 year from June 2019 to May 2020 of all patients with bicytopenia/pancytopenia coming to Jhalawar medical college [S. R.G. Hospital & S.H.K.B.M. Hospital]. Bone marrow aspiration study in patients with pancytopenia carried out in the department of Pathology, Jhalawar Medical College, Jhalawar.

Source of Data

Prospective data of patients who admitted in SRG Hospital & SHKBM Hospital with hematological diagnosis of bicytopenia/pancytopenia during the study period. General information regarding age, residence, literacy, dietary habits, occupational status, smoking habits and previous history of any chronic disease and treatment, family history asked by questionnaire methodology. General physical examination of all identified case of pancytopenia was done.

Inclusion Criteria

- Presence of two or three of following[84]
- ✓ Hb < 10 gm/dl
- ✓ TLC < 4000/mm³
- ✓ Platelets<1,00,000/mm³

Exclusion Criteria

- Subjects presenting with reduction in the solitary hematological cell lineage like anemia, leukopenia or thrombocytopenia
- Patients on myelotoxic chemotherapy
- Patients who were unco-operative or who did not give consent for the study.

Methodology

- After obtaining approval and clearance from the Ethical committee, only those patients meeting the inclusion and exclusion criteria were enrolled for the study.
- Informed consent obtained from each patient.
- After enrolment the following parameters considered and/or measured in all patient's: name, age, gender, religion, occupation, address, General physical examination.

Investigations Required For study

Two ml of blood mixed with k2 EDTA anticoagulantwas collected for complete hemogram & processed within 2 hours of collection with Sysmex XN-1000, a fully automated 5 Part CBC analyzer. Following investigations were done –

- ➢ Hemoglobi

- RBC coun
- WBC count (total & differential)
- Platelet count
- Red cell indices (MCV, MCH, MCHC)
- Peripheral Blood Smear
- Special stains- PAS Stain, Myeloperoxidase, Pearls stain etc.
- Bone Marrow aspiration
- Bone Marrow Biopsy (whenever possible).

Data Analysis

Data was recorded as per Performa. The data analysis was computer based; SPSS-22 was used for analysis. For categoric variables chi-square test was used. For continuous variables independent samples's *t*-test was used. *p*-value <0.05 was considered as significant.

Results

Maximum number of patients (24.29%) were of age group 11-20years, followed by (19.63%) in age group 21-30years, and minimum 3.74% were of age group >80years. 57.94% were males and 42.06% were females. Males are involved more than females with a male to female ratio of 1.4:1.

Table 1: Distribution of Study Subjects According To Vital Hematological Parameters

Vital Hematological Parameters		Bicytopenia (N=29)		Pancytopenia(N=78)	
		Frequency	Percentage	Frequency	Percentage
Hb	1-4	6	20.68	15	19.23
	4.1-7.0	11	37.93	45	57.69
	7.1-10.0	11	37.93	18	23.07
	>10	1	3.45	0	0
TLC	<1000	0	0	1	1.28
	1001-2500	5	17.24	38	48.72
	2501-4000	5	17.24	37	47.44
	>4000	19	65.52	2	2.56
Platelet Count	<50000	9	31.03	32	41.02
	51000-75000	7	24.14	24	30.77
	76000-100000	7	24.14	22	28.21
	>100000	6	20.69	0	0

Haemoglobin levels in both the groups were observed in the range of 4.1-7.0 and 7.0-10.0. TLC levels were of range of 1001-4000 in pancytopenia. But in bicytopenia, maximum number of patients had high TLC count of range of >4000. In both the groups, maximum number of patients had platelet count <50,000.

Table 2: Distribution of Study Subjects According To Peripheral Blood Picture

Peripheral Blood Picture	Cases	
	Frequency	Percentage
Normocytic normochromic	34	31.78
Microcytic hypochromic	10	9.35
Macrocytic	50	46.73
Dimorphic	12	11.21
Hemolyticanemia	1	0.93
Total	107	100

Maximum number of patients (46.73%) had macrocytic peripheral blood picture, 31.78% had normocytic normochromic, 11.21% dimorphic, 9.35% microcytic hypochromic and minimum 0.93% were having haemolytic anemia.

Table 3: Distribution of Study Subjects According To Cellularity of Bone Marrow

Cellularity of Bone Marrow	Bicytopenia		Pancytopenia	
	Frequency	Percentage	Frequency	Percentage
Hypercellular	9	31.03	20	25.64
Hypocellular	2	6.89	8	10.25
Normocellular	18	62.07	50	64.1
Total	29	100	78	100

Maximum number of study subjects have normocellular marrow and minimum had hypocellular type.

Table 4: Comparison of Diagnosis on PBF & BM

PBF	NO.	BMA	NO.
Megaloblastic Anemia	50	Megaloblastic Anemia	50
Dimorphic Anemia	12	Dimorphic Anemia	11
		MEGALOBLASTIC ANEMIA	1
Microcytic Hypochromic Anemia	8	Micronormoblastic Anemia	6
		Hypoplastic Marrow	2
Hemolytic Anemia	1	Normoblastic Hyperplasia	1
Acute Leukemia	12	Acute Leukemia [Aml+All]	12
Chronic Lymphoid Leukemia	1	Chronic Lymphoid Leukemia	1
Multiple Myeloma	2	Multiple Myeloma	2
Inconclusive	21	ITP	2
		Hypoplastic Marrow	3
		Erythroid Hyperplasia	4
		Normocellular Marrow	4
		Hypersplenism	8
Total	107		107

Diagnosis of megaloblastic anemia was concordant in both peripheral blood film and bone marrow. In 12 cases of dimorphic anemia on peripheral blood film, 11 showed dimorphic anemia whereas one showed megaloblastic anemia. Out of 8 cases of microcytic hypochromic anemia, 6 were diagnosed concordant with BM and 2 as hypoplastic marrow. Haemolytic anemia, acute leukemia, chronic lymphoid leukemia and multiple myeloma were diagnosed concordant in both peripheral blood film and bone marrow. Out of 21 inconclusive cases on PBF, 2 were ITP, 3 were hypoplastic marrow, 4 were erythroid hyperplasia, 4 were normocellular marrow and 8 were consistent with hypersplenism on bone marrow examination.

Table No. 5: Sensitivity, Specificity, Ppv, Npv& Accuracy of PBF

Calculations:

SENSITIVITY=A/(A+C) × 100 = 83%

SPECIFICITY= D/(D+B) × 100 =57.14%

POSITIVE PREDICTIVE VALUE (PPV)= A/(A+B) × 100 = 96.51%

NEGATIVE PREDICTIVE VALUE (NPV)= D/(D+C) × 100 = 19%

ACCURACY = A+D/(A+B+C+D)= 81.30%

	Disease	Non-Disease	Total
Positive	TP-83 (A)	FP-3 (B)	Test Positive
Negative	FN-17 (C)	TN-4 (D)	Test Negative
Total	100	7	107

Sensitivity	Specificity	PPV	NPV	Accuracy
83%	57.14%	96.51	19%	81.30

Disease was revealed in 100 cases with 83 true positive and 17 false negative diagnosis. 7 cases were non disease cases with 4 case true negative and 3 false positive. A total of 83 cases were observed with true positive diagnosis and 3 shows false positive diagnosis. 4 cases show true negative and 17 show false negative. Sensitivity of PBF examination observed to be 83%, specificity 57.14%, PPV 96.51%, NPV 19% and Accuracy 81.30%.

Discussion

A comprehensive clinical, haematological & bone marrow study of patients usually helps in identification of the underlying cause. Aspiration of the marrow is necessary to the study of hematopoietic disorders, if performed correctly. It is simple, safe and can be repeated. In case of trephine biopsy the greater value is that it can provide information about the structure of relatively large pieces of bone marrow. At the same time morphological features of individual cells may be identified by making imprint from the material obtained.[6]

The complete hematological workup with good clinical correlation is of greater importance to evaluate the cause of pancytopenia as its treatment is dictated by the nature of underlying disease. Aspiration of the bone marrow is an indispensable adjunct to the study of haematopoietic disorders, if performed correctly, it is simple, safe and can be repeated.[7]

Bone marrow examination involving the study of bone marrow aspirates, imprint smears and trephine biopsy is an effective way of diagnosing and evaluating hematologic and metastatic neoplasm as well as non hematological disorders responsible for cytopenia. These three procedures are complementary to each

other and superiority of one method over the other depends on the specific disease process.[8]

In our study, Sensitivity, specificity, PPV, NPV and Accuracyof PBF examination wascalculated. A total of 107 cases were observed. Disease was revealed in 100 cases with 83 true positive and 17 false negative. 7 cases reveled non disease with 4 cases true negative and 3 false positive. A total of 83 cases were observed to be true positive and 3 false positive. 4 cases were true negative and 17 were false negative. Sensitivity of PBF examination was observed to be 83%, specificity 57.14%, with 96.51% of PPV, 19% NPV and 81.30% Accuracy.

Although in most cases, a definitive diagnosis could be made based solely on bone marrow aspirate & biopsy interpretation, a significant fraction of cases in both children and adults demonstrated nonspecific marrow finding that required clinical follow-up and/or repeat biopsy for definitive diagnosis.

Bone marrow examination can diagnose majority of cases of pancytopenia and bicytopenia along with comprehensive clinical and haematological study. It is also helpful in planning further investigations and management.Thepresent study concludes that bone marrow microscopic examination is helpful in understanding of the underlying disease process and in diagnosing the various causes of pancytopenia and bicytopenia in majority of cases, along with comprehensive clinical and haematological investigations findings. It is also helpful in planning further investigations and management of pancytopeniaand bicytopenia cases.

Conclusion

Bone marrow examination can diagnose majority of cases of pancytopenia and bicytopenia along with comprehensive clinical and haematological study. It is also helpful in planning further investigations and management.

As the present study is the first study in the region of Jhalawar Medical College, Rajasthan, it will be extremely helpful to the clinicians in understanding of the underlying disease process and in diagnosing the various causes of pancytopenia and bicytopenia in majority of cases with the help of bone marrow microscopic examination, along with comprehensive clinical and haematological investigations findings. It is also helpful in planning further investigations and management of pancytopenia and bicytopenia cases.

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