BONE MARROW EXAMINATION IN PATIENTS OF CYTOPENIA - A STUDY ON CLINICAL AND ETIOLOGICAL PROFILE

Pathology

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ABSTRACT

Introduction: Bone marrow examination is an important diagnostic tool and the cornerstone of hematology. Cytopenia is a descriptive term referring to a reduction in any of the three blood cell lineage erythrocytes, leukocytes and platelets. **Aims And Objectives:** This study aimed to determine the clinical and etiological profile in patients of cytopenias undergone bone marrow examination. **Material And Methods:** it was a prospective observational hospital based study conducted over a period of 18 months (July 2016 to January 2018) in the department of Pathology, Krishna Institute of Medical Science, Secunderabad. Complete history, physical examination, complete blood count, peripheral blood film and bone marrow aspiration was done in 400 patients who presented with cytopenias. **Results:** Out of 400 patients, 208 cases were male and 192 were females with Male: female ratio 1.08:1. Age ranging from 1 to 87 years with mean age of patient's was 43.5 years. Out of 400 patients of cytopenia 167 cases were neoplastic and 226 cases were non-neoplastic while 7 cases showed normal marrow findings. Findings in these cases included megaloblastic anemia, acute leukemia, immune thrombocytopenic purpura, and plasma cell myeloma as the commonest cause of pancytopenia, bicytopeia, thrombocytopenia and anemia respectively. **Conclusion:** Bone marrow evaluation is an important and effective tool in diagnosing and evaluating hematological disorders.

INTRODUCTION

Bone marrow examination is an important diagnostic tool and the cornerstone of hematology. The two most important techniques are aspiration biopsy and trephine biopsy[1]. Cytopenia is a descriptive term referring to a reduction in any of these three blood cell lineage erythrocytes, leukocytes and platelets, it is a not a disease entity but a set of findings that may result from a number of disease processes primarily or secondarily involving bone marrow.[2,3]

Bicytopenia is reduction in any of two cell lineage and pancytopenia is reduction in all the three. There is considerable overlap between the causes and diagnostic approach of bicytopenia and pancytopenia. The etiology of cytopenia varies widely ranging from transient marrow suppression to marrow infiltration by life threatening malignancy. Diagnosis and management of many haematologic diseases depend on the examination of bone marrow. This study was carried out to identify the underlying etiopathology in bone marrow in cases of cytopenia of any cell lineage includes bicytopenia and pancytopenia and to study the most frequent non neoplastic and neoplastic pathology in patients with cytopenias.

MATERIAL AND METHODS-

The present study was a prospective observational hospital based study conducted over a period of 18 months (July 2016 to January 2018) in the department of Pathology, Krishna Institute of Medical Science, Secunderabad. Patients of all age group with Hemoglobin level < 13 gm/dl for males and below 12gm/dl for females, Total leucocyte count below 4×10^9/L and platelet count below 100×10^9/L were included in the study. Inclusion criteria for pancytopenia were hemoglobin level <9gm/dl, Total leucocyte count <4x 10^9/L or ANC <1.5 x10^9/L and platelet count <140 x10^9/L. Patient who underwent/undergoing any radiation, chemotherapy or any G-CSF therapy, Pseudothrombopenia patient and pregnant women with physiological anemia were excluded from study.

A detailed history was taken in each case followed by clinical examination. CBC counts and peripheral blood film examination. The bone marrow aspiration obtained by using a salah needle from right/left posterior superior iliac spine under local anesthesia under strict aseptic precautions as per standard procedure[4,5]. The Bone marrow smears were air dried and stained with Leishman or Geimsa stain. The bone marrow smears were examined in details to see cellularity, haemopoiesis, M: E ratio, erythroid reaction, metastatic deposits, parasites, abnormal cells, fibrosis etc. Efforts were made to arrive at a diagnosis considering history, physical finding, CBC and PBF findings.

RESULTS-

Four hundred patients with a hematological diagnosis of cytopenia were studied during the period of July 2016 to January 2018,in the department of pathology, KIMS, Secunderabad. Out of 400 patients, 208(52%) cases were male and 192(48%) cases were female with male female ratio of 1.08:1. Pancytopenia showed its highest incidence in age group of 51-60 years and its occurrence was less frequent in the age group of 81-90 years. Out of 130 patients of pancytopenia, males (53.8%) were slightly more than females (46.15%) with male to female ratio 1.16:1. Megaloblastic anemia was the commonest cause of pancytopenia constituting (20.7%) followed by Aplastic anemia (20%) (Table 1). Bicytopenia showed its highest incidence in age group of 41-50 years and its occurrence was less frequent in the age group of 81-90 years. Out of 110 patients of bicytopenia, males (59.9%) were more than females (40.9%) with male to female ratio 1.5:1. Acute leukemia was the commonest cause of bicytopenia constituting (39.09%) followed by autoimmune disorders (11.08%) (Table 2).

Thrombocytopenia showed its highest incidence in age group of 21-30 years and its occurrence was less frequent in the age group of 81-90 years. Out of 85 patients of thrombocytopenia, females (56.4%) were more than males (43.5%) with male to female ratio 1:1.3. Immune thrombocytopenic purpura was the commonest cause of thrombocytopenia constituting (56.47%) followed by Non-Immune thrombocytopenic purpura (24.7%) (Table 3).

Anemia showed its highest incidence in age group 61-70 years and its occurrence was less frequent in the age group of 0-10 years. Out of 75 patients of anemia, females (52%) were slightly more than males (48%) with male to female ratio 1:1.1. Plasma cell myeloma was the commonest cause of anemia constituting (26.6%) followed by chronic myeloid leukemia (18.6%) (Table 4). In 49 of 400 cases, no diagnosis

was made on bone marrow aspiration with sensitivity of 87.7% because the sample was hemodilute and no marrow particles were identified.
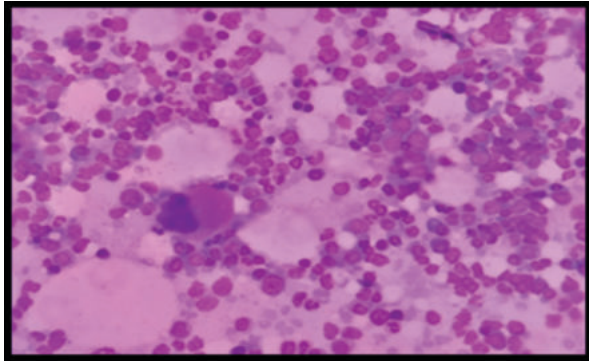

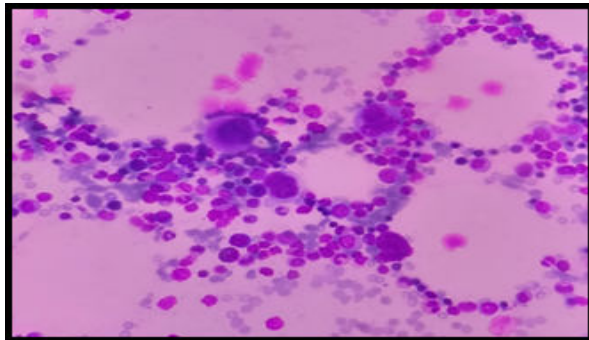Image 1:Aspirate from MA showing megaloblasts and giant metamyelocyte (Lesihman x40)

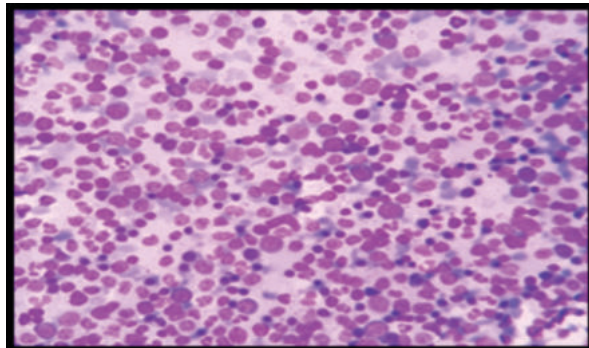Image 2:Aspirate from ITP showing Megakaryocytic Hyperplasia (Leishman x40)

Image 3: Aspirate smear of a case of AML showing Blast (Leishman, 40X)

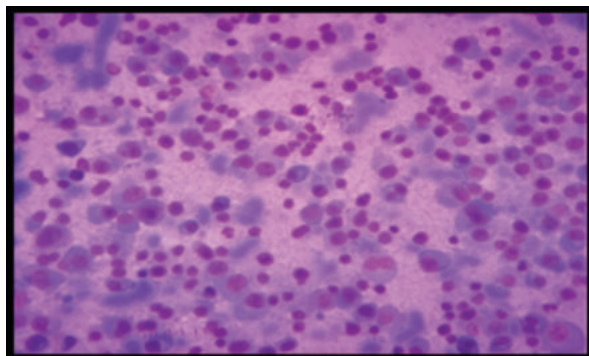Image 4: Aspirate smear showing plasma cells in a case of myeloma, shows a binucleated plasma cell (Leishman, x40)

Table 1: Etiology of Pancytopenia

Causes	Number of cases	Percentage (%)
NEOPLASTIC	43	33%
Acute leukemia	18	13.8%
MDS	10	7.69%
Myelofibrosis	5	3.84%
Lymphoma	3	2.3%
PCM	7	5.38%
NON -NEOPLASTIC	87	67%
Aplastic Anemia	26	20%
Autoimmune	12	9.2%
Ineffective haematopoiesis	7	5.38%
Megaloblastic Anemia	27	20.7%
Sepsis	3	2.3%
Normocellular	2	1.53%
TOTAL	130	100%

Table 2: Etiology Of Bicytopenia

Causes	Number of cases	Percentage (%)
NEOPLASTIC	71	64.5%
Acute leukemia	43	39.09%
MDS	6	5.45%
Metastasis	3	2.72%
Myelofibrosis	8	7.27%
PCM	11	10%
NON-NEOPLASTIC	39	35.5%
Autoimmune	13	11.08%
Hypersplenism	4	3.63%
Hypoplastic marrow	4	3.63%
IEM	7	6.36%
Nutritional anemia	8	7.27%
Normocellular	2	1.81%
Sepsis	1	0.9%
TOTAL	110	100%

Table 3: Etiology Of Thrombocytopenia

Causes	Number of cases	Percentage (%)
NEOPLASTIC	6	7.05%
Acute leukemia	2	2.35%
CLL	3	3.52%
Lymphoma	1	1.17%
NON-NEOPLASTIC	79	92.95%
ITP	48	56.47%
NI-TCP	21	24.7%
Ineffective megakaryopoiesis	6	7.05%
Hypersplenism	2	2.35%
Sepsis	2	2.35%
Total	85	100%

Table 4: Etiology Of Anemia

Causes	Number of cases	Percentage (%)
NEOPLASTIC	48	64.0%
Acute leukemia	4	5.3%
CML	14	18.6%
Lymphoma	4	5.3%
MDS	3	4.0%
Myelofibrosis	3	4.0%
PCM	20	26.6%
NON-NEOPLASTIC	27	36.0%
ACD	3	4.0%
Autoimmune	6	8.0%
Hypersplenism	2	2.6%
IDA	9	12.0%
Megaloblastic anemia	4	5.3%
Normocellular	3	4.0%
TOTAL	75	100%

DISCUSSION

Bone marrow examination remains a cornerstone in the diagnosis of various hematological disorders. In the present study, bone marrow aspiration findings of four hundred patients who presented with various hematological disorders were studied and compared with other studies published in literature.

Megaloblastic anemia was the commonest cause of pancytopenia (20.7%) in this study followed by aplastic anemia (20%). This was comparable with many other studies. In the study by Nadeem et al

(2018)[6] on 66 patients megaloblastic anemia was the commonest cause (34.84%) followed by aplastic anemia (7.57%), which is comparable with our study.

Acute leukemia was the commonest cause of bicytopenia (39.09%) in this study followed by autoimmune disorder (11.08%). Commonest form of bicytopenia was anemia and thrombocytopenia seen in 94 cases (85.45%), followed by anemia and leukemia in 10 cases (9.09%). This was comparable with the study done by Shano naseem et al (2011)[7] in 396 children of bicytopenia which revealed acute leukemia as the commonest cause (66.9%) followed by ITP (5.2%). Commonest form of bicytopenia was anemia and thrombocytopenia seen in 77.5% cases, followed by anemia and leucopenia in 17.3% cases.

Immune thrombocytopenic purpura was the commonest cause of thrombocytopenia (56.47%) in this study followed by non-immune thrombocytopenia purpura (24.7%). In the study done by Sengupta et al (2012)[8] immune thrombocytopenic purpura (20%) was the commonest cause of thrombocytopenia followed by acute leukemia (14.1%). Other studies showed 6.21%, 14.5%, 6.8% and 5% cases of ITP respectively in their studies (kibria et al 2010, Ahmed et al 2011, Pudasaini et al 2002, Knodke et al 2001).[9,10,11,12]

We also evaluated the etiological profile of patients with anemia. Plasma cell myeloma (26.6%) was the commonest cause of anemia followed by chronic myeloid leukemia (18.6%). Patient age ranges from 1-71 years with highest incidence in age group of 61-70 years (22.6%). There was female preponderance and male to female ratio of 1:1.1. To the best of our knowledge no study has evaluated bone marrow examination in cases of anemia alone.

CONCLUSION

Bone marrow evaluation is an important and effective tool in diagnosing and evaluating hematological disorders. Complete evaluation of bone marrow samples requires a detailed patient history, CBC, peripheral blood examination, BMA smears and biopsy sections. This study analysed the etiological profile of 400 patients of cytopenias requiring bone marrow examination. Findings in these cases included megaloblastic anemia, acute leukemia, immune thrombocytopenic purpura, and plasma cell myeloma as the commonest cause of pancytopenia, bicytopeia, thrombocytopenia and anemia respectively.

Limitation

In the present study ancillary techniques were not available in all cases. Isolated leucopenia was not identified in our study and hence it could not be reviewed.

REFERENCES

1. Bain BJ, Clark DM, Wilkins BS. Bone marrow pathology. 4th ed. Sussex: Wiley-Blackwell; 2010:14-16.
2. Cytopenias-Anemia, leucopenia, neutropenia, thrombocytopenia. www. oncologychannel.com /-46K-6/24/2007.
3. Guinan EC,shimamura A.Acquired and inherited aplastic anemia syndromes in:Greer JP,Forester J,Lukens JN, Rodgers GM,Paraskevas F,Glader B edts,Wintrobe's Clinical Hematology ,11th edn,Philadelphia : Lipincott Williams and Wilkins 2004:p.1397-1419.
4. Firkin F,Chesterman C ,Penington D,Rush B. De Gruchy's Clinical haematology in Medical practice.6th Adapted ed; Daryaganj , New delhi. Wiley India Pvt.Ltd.2013.
5. Briggs C,Bain BJ. Basic hematological techniques. In: Lewis SM, Bain BJ, Bates I, Laffan MA, editors.Dacie and Lewis practical hematology.11th ed. New Delhi: Elsevier; 2012; 37-38.
6. Nadeem Ahmad, Nihida Akhter, Tufail Ahmad. Pancytopenia – A study on clinical and etiological profile at a tertiary care institute. 2018; 6(1):33-36.
7. Shano Naseem, Neelam Varma, Reena Das, Jasmina Ahluwalia, Man Updesh Singh Sachdeva, Ram Kumar Marwaha. Pediatric patients with bicytopenia/pancytopenia: Review of etiologies and clinic-hematological profile at a tertiary center.2011. Indian Journal of Pathology and Microbiology; 54(1):55-80.
8. Dr. Moumita Sengupta, Dr. Kaushik Saha, Dr.Chetna J. Mistry. Bone Marrow Aspiration Study in Thrombocytopenia. IJSR. Dec 2012; 1(7):136-9
9. Kibria, S. G., Islam, M. D. U., Chowdhury, A. S. M. J. et al. (2010). Prevalence of Hematological Disorder: A Bone Marrow Study of 177 Cases In a Private Hospital at Faridpur. Faridpur Med. Coll. J, 5, 11-13.
10. Ahmad, S. Q., Khan, O. U., Zafar, N. (2011). Utility of Bone Marrow Examination in a Secondary Care Hospital. JRMC, 15, 40-41.
11. Pudasaini, S., Prasad, K. B. R., Rauniyar, S. K., Shrestha, R., Gautam, K., Pathak, R., Koirala, S., Manandhar, U., Shrestha, B.(2002).Interpretation of bone marrow aspiration in hematological disorder.Journal of Pathology of Nepal, 2, 309-312.
12. Knodke, K., Marwah, S., Buxi, G., Yadav, R. B.,Chaturvedi, N. K. (2001). Bone marrow examination in cases of pancytopenia.J Academy Clin Med, 2, 55–59.