CLINICO-HAEMATOLOGICAL STUDY OF PANCYTOPENIA IN A TERTIARY CARE CENTRE

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ABSTRACT

BACKGROUND

Pancytopenia is one of the pathological manifestation resulting from various underlying disease processes affecting the bone marrow. Hence, bone marrow examination is the diagnostic tool to detect the underlying aetiology of pancytopenia. Pancytopenia nowadays has become a relatively common haematological entity. The underlying cause is ranging from simple drug-induced bone marrow hypoplasia, megaloblastic anaemia to fatal bone marrow aplasias and leukaemias. Thus, identification of the correct cause will help in implementing appropriate therapy.

MATERIALS AND METHODS

This was a prospective study and 158 pancytopenic patients were evaluated clinically along with haematological parameters and bone marrow aspiration in Clinical Pathology, Department of Pathology, during the period of December 2016 to December 2017.

RESULTS

Among 158 cases, age of patients ranged from 3 to 88 years with a mean age of 45 years and male predominance. Most of the patients presented with fever and anaemia. The commonest physical finding was pallor followed by generalised weakness and splenomegaly. Dimorphic anaemia was the predominant blood picture. Among the 158 cases, 56 cases have undergone bone marrow aspiration in the department. The commonest bone marrow finding was erythroid hyperplasia with megaloblastic maturation (25%).

CONCLUSION

The present study shows the detailed primary haematological investigations along with bone marrow aspiration in pancytopenia patients, which is useful in understanding disease process. These are also helpful in planning further evaluation and management.

KEYWORDS

Megaloblastic Anaemia, Pancytopenia, Erythroid Hyperplasia.

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BACKGROUND

Pancytopenia is the commonest indication for bone marrow examination and there are numerous causes. New-onset pancytopenia in both children and adults can prove to be a diagnostic dilemma and causes include congenital and acquired bone marrow failure syndromes, peripheral destruction of haematopoietic cells, autoimmune disorders, infection, marrow space-occupying lesions and ineffective marrow production. Pancytopenia is simultaneous presence of anaemia, leukopenia and thrombocytopenia.[1,2]

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Leucopenia is a rare initial presentation, but can become a serious threat to life during the course of the disorder. Different studies done at different places revealed variable frequency of pancytopenia.[3,4,5] Identification of the disease is of prime importance, since this is the key to proper management.[3] Common clinical manifestations are generalised weakness, pallor, fever, fatigue, splenomegaly, lymphadenopathy, bleeding, weight loss, hepatomegaly and jaundice.[6]

Aims and Objectives- To study the clinical presentations in pancytopenia due to various causes and to evaluate various haematological parameters including bone marrow aspiration.

MATERIALS AND METHODS

A total number of 158 patients who were referred with various clinical presentations of pancytopenia were included in the study. The present study was done for a period of 1

year from December 2016 to December 2017 in the Department of Pathology in Andhra Medical College, King George Hospital, Visakhapatnam.

All the cases of pancytopenia with haemoglobin less than 10 gm/dL, total leucocyte count of less than 4000/mm3 and platelet count less than 1,50,000/mm3 were included in the study. In all the 158 cases, around 2 mL of EDTA (ethylenediaminetetraacetic acid) anticoagulated blood was collected and processed through Sysmex 6 part automated haematology analyser and 9 haematological parameters were obtained, which included haemoglobin, red blood cell count, total leucocyte count, differential leucocyte count, platelet count, Mean Corpuscular Volume (MCV), Mean Corpuscular Haemoglobin (MCH), Mean Corpuscular Haemoglobin Concentration (MCHC) and Packed Cell Volume (PCV). Erythrocyte Sedimentation Rate (ESR) was estimated in all cases by Westergren's method.

Peripheral smear was stained by Leishman stain for all the cases and examined in detail. Bone marrow aspiration was subsequently carried out under aseptic precaution after obtaining written consent from the patient or guardian. Final diagnosis was made by thorough light microscopic examination under oil immersion.

The details of clinical history and relevant investigation were obtained in every case and analysed. Bone Marrow Aspiration (BMA) was performed in 56 cases from posterior iliac crest of the patients. However, trephine biopsy was performed only in few cases.

Leishman stain was used routinely for bone marrow aspiration. Special stains PAS stain (periodic acid-Schiff) was done for AML and Gaucher's disease. MGG stain (May-Grunwald Giemsa), reticulin stain and Perls stain were used in this study. Perls stain was done in all cases for iron stores.

Trephine biopsy specimens were fixed in formalin fixative, kept for decalcification in 20% nitric acid solution and haematoxylin and eosin-stained sections were examined.

Age	Male	Percentage	Female	Percentage
1-10	4	2.5%	4	2.5%
11-20	17	10.75%	12	7.59%
21-30	21	13.29%	15	9.49%
31-40	12	7.5%	13	8.22%
41-50	18	11.4%	13	8.22%
51-60	12	7.5%	8	5.06%
61-70	2	1.26%	3	1.89%
71-80	1	0.63%	1	0.63%
81-90	2	1.26%	0	0
Total	**89 (56.32%)**		**69 (43.68%)**	

Table 1. Age and Gender Wise Distribution

Sl. No.	Clinical Features	Number of Cases	Percentage of Cases
1.	Generalised weakness	33	21%
2.	Dyspnoea	8	5%
3.	Fever	38	24%
4.	Bleeding manifestations	4	2.5%
5.	Pallor	46	29.02%
6.	Weight loss	11	7.4%
7.	Splenomegaly	5	3%
8.	Hepatomegaly	1	0.6%
9.	Jaundice	4	2.5%
10.	Lymphadenopathy	1	0.6%
11.	Hepatosplenomegaly	2	1.26%
12.	CKD	1	0.6%
13.	Diarrhoea	2	1.26%
14.	Pain abdomen	1	0.63%
15.	Ascites	1	0.63%
	Total	**158**	**100%**

Table 2. Clinical Features in Pancytopenia

Sl. No.	BMA Findings- Pancytopenia Patients	Number of Cases (56)	Percentage of Cases
1.	Erythroid hyperplasia	9	16.07%
2.	E.H. + normoblastic maturation	4	7.14%
3.	E.H. + micronormoblastic maturation	1	1.7%
4.	E.H. + megaloblastic maturation	14	25%
5.	Hypoplastic marrow	8	14.70%
6.	Megaloblastic marrow	9	16.07%
7.	Aplastic marrow	2	3.54%
8.	Myelodysplastic syndrome	4	7.14%
9.	Acute myeloid leukaemia	1	1.7%
10.	Gaucher's disease	1	1.7%
11.	Normal study	1	1.7%
12.	Dry tap	2	3.54%
	Total	**56 Cases**	**100%**

Table 3. Bone Marrow Aspiration Findings in Pancytopenia Patients

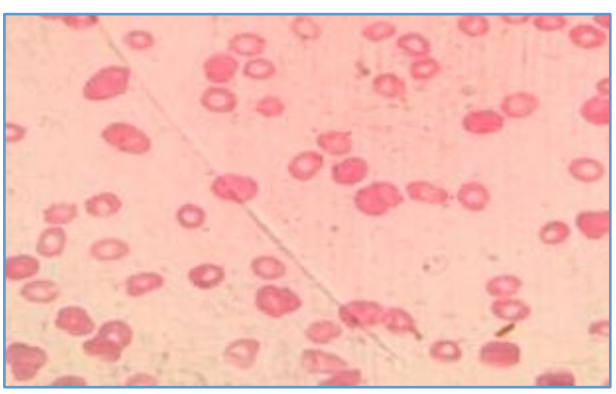

Figure 1. Photomicrograph of Pancytopenia with Dimorphic Anaemia; Smear shows Macroovalocytes (Leishman Stain 400x)

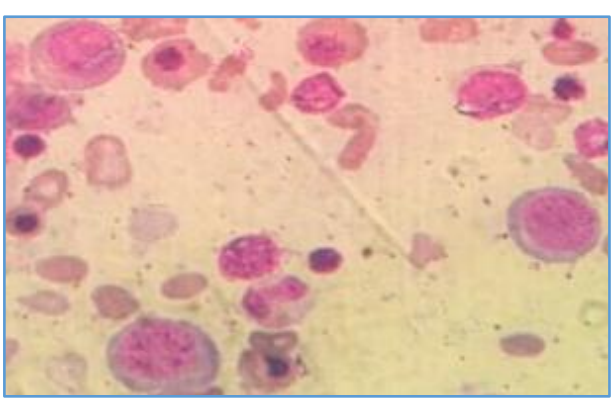

Figure 2. Photomicrograph of Megaloblastic Anaemia; Aspirate shows Megaloblasts with Sieve-Like Chromatin (Leishman Stain 1000x)

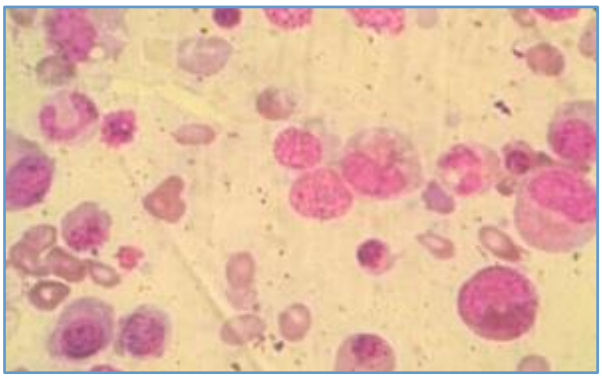

Figure 3. Photomicrograph of Megaloblastic Anaemia; Aspirate shows Micronormoblasts and Megaloblasts with Sieve-Like Chromatin (Leishman Stain 1000x)

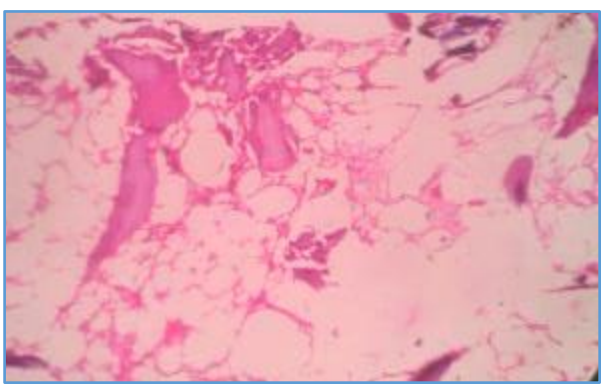

Figure 4. Photomicrograph of Aplastic Anaemia- Bone Marrow Biopsy Shows Mainly Fat with Marked Reduction in Haematopoietic Cells (Leishman Stain 100x)

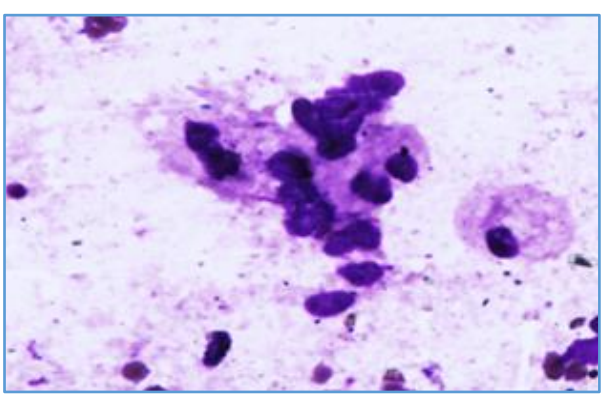

Figure 5. Photomicrograph of Gaucher's Cell in Bone Marrow Aspiration (Leishman Stain 100x)

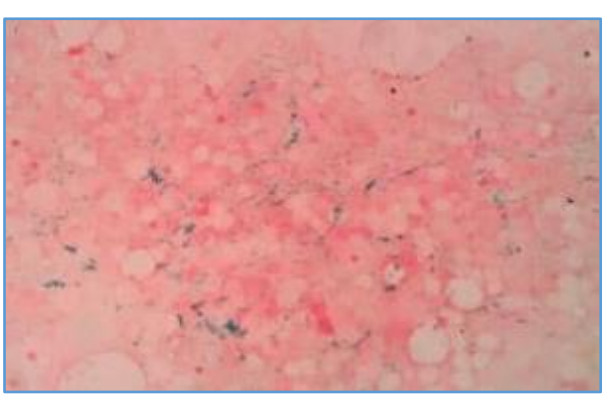

Figure 6. Photomicrograph of Bone Marrow Aspirate Smear showing Perls Stain Positive (400x)

RESULTS

The present study was prospective study of pancytopenia cases diagnosed during period of December 2016 to December 2017 in Clinical Pathology Department at King George Hospital, Visakhapatnam. The aetiology of pancytopenia was assessed in correlation with various clinicohaematological parameters and bone marrow aspiration cytology.

In the present study of 158 patients, bone marrow aspiration was performed on 56 cases. Among them, 89 (56.32%) study subjects were males and 69 (43.68%) were females with male:female ratio of 1.2:1 (Table 1). In present study, the age range of study subjects are from 3-88 years and the mean age is 45.5 years. Patients presented with various clinical complaints like pallor, fever, generalised weakness, dyspnoea, organomegaly, weight loss, etc (Table 2). Pallor and generalised weakness was noted in most of the cases. Splenomegaly and hepatomegaly were seen in cases of megaloblastic anaemia and acute myeloid leukaemia. Two cases of pancytopenia with chronic kidney disease were reported.

In present study, peripheral smear showed dimorphic anaemia in most of the cases (Figure 1). Bone marrow aspiration was done in 56 cases. The most common finding of pancytopenia was erythroid hyperplasia with megaloblastic maturation (Figure 2), which was seen in 14 (25%) cases, followed by megaloblastic anaemia seen in 9 (16.07%) cases and hypoplastic marrow seen in 8 (14.70%) cases (Table 3). Bone marrow biopsy was performed in few cases where aplastic marrow was reported in H and E sections.

DISCUSSION

In the present study, male:female ratio was 1.2:1. Similar results were found with the studies carried out by Tilak V et al,[7] Kumar R et al,[8] Khunger JM et al,[9] Khodke et al[10] with male-to-female ratios of 1.2:1; 2.1:1; 1.3:1 and 1.14:1 respectively with Kumar R et al study comparatively being higher than present study.

Pancytopenia mostly manifests as a serious and life-threatening conditions. It has different aetiologies with a variation in frequency of different diseases leading to pancytopenia in different population groups.[11] The different causes of pancytopenia depend on various factors such as geographical variations, nutrition, prevalence of certain infections and exposure to different toxic chemicals or pesticides in a particular population under study.[12]

In present study, the most common presentation was pallor, generalised weakness and dyspnoea, which was correlated with Gayathri et al study.[13]

Haematological parameters of different pancytopenia showed different values. Haemoglobin level was as low as 1.7 gm/dL in case of dimorphic anaemia, TLC as low as 500/cu mm in megaloblastic anaemia and platelets as low as 3000/cu mm in hypoplastic marrow.

In present study, among 20 paediatric pancytopenic cases, peripheral smear showed 9 (45%) cases of dimorphic anaemia with relative lymphocytosis and 8 (40%) cases of

microcytic hypochromic anaemia were reported. In most of these cases, bone marrow showed erythroid hyperplasia with megaloblastic maturation (Figure 3) and the common cause for pancytopenia followed by aplastic anaemia (Figure 4). Comparable results were reported by Bhatnagar et al.[14]

One case of complicated malaria with pancytopenia was reported. Gaucher's disease was encountered in this study in 11-year-old female child where the peripheral smear showed dimorphic anaemia and bone marrow revealed focal accumulation of large ovoid histiocytic cell with abundant finely fibrillary pale blue cytoplasm with wrinkled paper appearance with small round nuclei (Figure 5).

Hypersegmented neutrophils were noted in 66.8% of cases compared to 84.9% in Tilak V et al study[7] and Khunger JM et al.[9] Also, relative lymphocytosis in dimorphic anaemia was noted in 45% of the cases in present study compared to 50% in Tilak V et al study and 85.71% in Khunger JM et al study.[7,9]

Peripheral smear showed dimorphic anaemia in 70 (44%) cases, microcytic hypochromic anaemia in 44 (28%) cases, normocytic hypochromic anaemia in 25 (16%) cases and macrocytic anaemia in 11 (7%) cases. Leucopenia and thrombocytopaenia were seen in all cases.

In 56 cases of bone marrow aspiration, 32 cases were males and 24 cases were females with a male-to-female ratio of 1.3:1. The mean age was 50 years with a range from 12 to 88 years. There was a predominant male preponderance among all the groups especially above the age of 40 years. Peripheral smear showed normocytic normochromic to microcytic hypochromic RBC picture. Macrocytes were seen in six cases of hypoplastic marrow. Erythroid hyperplasia was seen in 9 (16.07%) cases, dry tap was observed in 2 (3.54%) cases. Bone marrow study showed hypocellularity in some cases with suppression of all erythroid, myeloid and megakaryocytic cell lineages with a relative lymphocytosis. Two cases of pancytopenia showed aplastic anaemia in trephine biopsy.

According to recent studies by Chandra et al[15] 2011, Parajuli et al[16] and Khan et al[17] erythroid hyperplasia is the predominant diagnosis, which were comparable to our study.

Erythroid hyperplasia with megaloblastic marrow was observed in 14 cases. There were 8 males and 6 females with male-to-female ratio of 1.3:1. The age ranged from 14 to 60 years with mean age of 37 years. Macrocytes, macroovalocytes and hypersegmented polymorphs were seen in the peripheral smear study. Bone marrow aspiration showed megaloblastic erythroid hyperplasia. Megaloblasts had the characteristic feature of nucleus showing sieve-like nuclear chromatin, nuclear cytoplasmic asynchrony in maturation with some of the cells showing cytoplasmic blebs.

Four interesting cases of myelodysplastic syndromes were encountered complaining of anaemia, fever and generalised weakness since 3 months. They were on medication but did not show any response and suspected refractory anaemia by the clinicians. In bone marrow aspiration, maturation defect with abnormal cells in myeloid series showing promyelocytes, myelocytes of large size with hypogranularity was seen. Perls stain was done in the bone marrow aspiration smears (Figure 6).

CONCLUSION

Pancytopenia is one of the common haematological disorder that we come across in routine practice. Pancytopenia was observed in middle age group with male preponderance. Most of patients with pancytopenia had megaloblastic anaemia followed by aplastic anaemia. Bone marrow aspiration and biopsy evaluation are necessary to detect the causes of new-onset pancytopenia and plan for future investigations. Aspiration smears are superior for morphological details, while biopsy provides a most reliable index of cellularity and reveals various underlying causes of pancytopenia.

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