ORIGINAL RESEARCH PAPER

Medicine

STUDY OF ETIOLOGICAL PROFILE OF PANCYTOPENIA IN A TERTIARY CARE HOSPITAL IN NORTHERN INDIA

KEY WORDS: Anemia, hematological disorders, pancytopenia

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ABSTRACT

Background: Pancytopenia is defined as the simultaneous presence of anemia, leukopenia, and thrombocytopenia. The present study was undertaken to explore various causes and clinical manifestations of pancytopenia and to correlate them with severity of pancytopenia in adult patients in a tertiary care hospital of Jammu. The causes of pancytopenia are diverse. The spectrum of different etiologies leading to pancytopenia varies globally, as well as within different geographical regions of the same country like India.

Aims and objectives: To evaluate various causes of pancytopenia in patients admitted to a tertiary care hospital of Jammu.

Material and Methods: A total of 280 patients of pancytopenia over a period of 12 months were enrolled. Clinical history, relevant physical examination and primary haematological investigations followed by bone marrow aspiration and trephine biopsy were done in all patients.

Results: Among all the 280 cases with pancytopenia, the most common cause was megaloblastic anemia (169/280, 60.4%) followed by acute Leukemia (38/280, 13.6%) and multilple myeloma (25/280, 8.9%).Other uncommon causes include myelodysplastic syndrome (2.5%) and infections (like Tuberculosis 1.07 %). One sixty eight were males with one hundred twelve females in 280 studied patients with a mean age of 43.81 years.

Conclusion: Thus, a comprehensive clinical, and hematological study of patients with pancytopenia will usually help in identifying the underlying cause. The early detection of the underlying conditions would also help to enhance the prognosis of patients with pancytopenia.

INTRODUCTION

Peripheral pancytopenia is presence of anemia, leucopenia and thrombocytopenia simultaneously. Pancytopenia is not a disease per se, but a triad of findings because of decrease in levels of formed elements of blood (erythrocytes, leucocytes and thrombocytes) below a certain normal level [1]. By definition, hemoglobin less than 13.5g/dl in males or 11.5gm/dl in females, the leucocyte count less than 4x109/L and platelet count less than 150x109/L constitute pancytopenia.[2] Both hematopoietic and non-hematopoietic disorders can present as pancytopenia. The etiologies of pancytopenia range from simple drug induced bone marrow failure to fatal leukemias. Different mechanisms lead to development of pancytopenia like diminished production as in aplastic anemia, ineffective hematopoiesis in megaloblastic anemia, sequestration by overactive reticuloendothelial system as in hypersplenism, and bone marrow infiltration by cancer or abnormal cells as in glycogen storage diseases. [3]

Since underlying pathology and severity of pancytopenia define the management and prognosis of the patients, [4] and so it is imperative to find underlying cause of pancytopenia. Studies in this regard have shown variation as regarding spectrum of etiologies from different regions of India.[5] Similar studies from this region are lacking, so the present study was undertaken to evaluate various causes of pancytopenia, their distribution and various clinical features among study subjects.

MATERIALS AND METHODS

This was a prospective study carried out over a period of twelve months in the Department of Medicine, Govt. Medical College Jammu from January 2018 to December 2018. Patients admitted to department during this period and fulfilling the criteria of pancytopenia were included in the study. Inclusion criteria were simultaneous presence of blood haemoglobin level <13.5 g/dl in males, or 11.5 g/dl in females, leukocyte count <4 × 109/L, and the platelet count <150 × 109/L. Written consent was taken from all. Patients with diagnosed malignancy or on treatment of malignancy, radiation exposure in past were excluded.

In each individual patient detailed medical history including age, sex, smoking, alcohol intake, history of drug intake, toxic chemical or radiation exposure was asked. Particular attention was given to presence of easy fatigability, fever, bone pains, weight loss, anorexia, recurrent infections, easy bruising. A detailed physical examination was contemplated in every patient for pallor, jaundice, hepatosplenomegaly, lymphadenopathy, sternal tenderness and gum hypertrophy. In all patients complete blood counts and peripheral smear, liver function tests, kidney function tests, ultrasonography, X-ray chest were done. Additional investigations were done, if found necessary dictated by the patients clinical scenario which included erythrocyte sedimentation rate (ESR), urine and stool examination, liver serological investigations for enteric fever, malaria, blood culture, ELISA for HIV, hepatitis B and C viruses, coagulogram, skull and lumbar radiographs, urinary and serum electrophoresis. Vitamin B12 and folic acid levels were done. Blood count samples were collected in ethylene diamine tetra acetic acid (EDTA) vials and reported by semiautomatic cell counter (Sysmex KX-21). Peripheral blood smears were stained by Leishman's stain .

Bone marrow aspiration and trephine biopsy was done in posterior iliac spine in all patients after taking aseptic precautions and adequate anaesthesia using Salah and Jamshidi needles, respectively. All the patients in the study were investigated in a systematic manner, cause of pancytopenia was ascertained and the required data analysis done.

RESULTS

A total of 280 pancytopenia patients were studied. Males outnumbered females, with 168 males (60%) and 112 females (40%). Many cases were within the age group of 31 – 40 years, comprising a total of 68 patients (24.3%).The age of the patients ranged from 21 – 90 years with a mean age of 43.81 years. (Table 1)

The commonest presenting complaint was pallor (39.3%), generalised weakness (27.5%), and followed by fever (14.3%). Splenomegaly (3.6%) and Lymphadenopathy (2.8%) were the common physical examination findings. (Table 2)

The commonest etiologies of pancytopenia in the studied patients were megaloblastic anemia (60.4%) followed by acute leukemia (13.6%), multiple myeloma (8.9%), lymphomas (6.4%), aplastic anemia (6.4%), myelodysplastic syndrome (2.5%), infections(1.07%) and drug induced (0.71%). The results are shown in Table 3.

Megaloblastic anemia accounted for 169 cases whose age ranged from 16 – 80 years (mean age of 41.26 years). Males comprised 110 cases (65.1%) while 76 (44.9%) were females. Gender wise distribution of various etiologies of pancytopenia is shown in Table 4. Of the total 280 cases of pancytopenia, 38 were acute leukemia,

with a mean age of 46.11 years, with 32 patients of acute lymphoblastic leukemia (ALL) and 6 of acute myeloid leukemia (AML). We encountered 25 cases of multiple myeloma in the studied patients with a mean age of 64.71 years, with presenting complaint of fever in four patients and renal failure, bone pains and pathological fracture in rest of patients.

There were 18 cases of lymphomas, 10 non – Hodgkin's and 8 Hodgkin's with a mean age of 62.82 years. Eighteen patients of aplastic anemia and three of tuberculosis leading to pancytopenia were seen in this study. Lastly, two cases of drug induced pancytopenia were observed in the study, all the two patients were on antiepileptic drugs, one on phenytoin and other on carbamazepine.

TABLE 1- AGE AND GENDER WISE DISTRIBUTION OF CASES

AGE GROUP (YRS)	MALES (N)	FEMALES(N)	NUMBER OF CASES N (%)
21-30	25	15	40(14.3)
31-40	32	36	68(24.3)
41-50	29	29	58(20.7)
51-60	40	14	54(19.3)
61-70	25	12	37(13.2)
71-80	12	6	18(6.4)
ABOVE 80	5	0	5(1.8)
TOTAL	168	112	280(100)

TABLE 2- PRESENTING COMPLAINTS AND PHYSICAL FINDING IN PANCYTOPENIA PATIENTS

SYMPTOMS AND SIGNS	NUMBER OF CASES(N)	PERCENTAGE (%)
PALLOR	110	39.3
GENERALISED WEAKNESS	77	27.5
FEVER	40	14.3
BLEEDING MANIFESTATIONS	20	7.1
GIT SYMPTOMS	10	3.6
SPLENOMEGALY	10	3.6
LYMPHADENOPATHY	8	2.8
JAUNDICE	5	1.8
TOTAL	280	100

TABLE 3-DISTRIBTION OF VARIOUS ETIOLOGIES OF PANCYTOPENIA

ETIOLOGY	NUMBER OF CASES(n)	PERCENTAGE (%)
MEGALOBLASTIC ANAEMIA	169	60.4
ACUTE LEUKEMIA	38	13.6
MULTIPLE MYELOMA	25	8.9
LYMPHOMA	18	6.4
APLASTIC ANAEMIA	18	6.4
MYLEODYSPLASTIC SYNDROME	7	2.5
INFECTIONS (T.B)	3	1.07
DRUG INDUCED	2	0.71
TOTAL	280	100

TABLE 4-GENDER WISE DISTRIBUTION OF ETIOLOGIES OF PANCYTOPENIA

ETIOLOGY	MALES N (%)	FEMALES N (%)	TOTAL NUMBER OF CASES N (%)
MEGALOBLASTIC ANAEMIA	110(65.1)	76(44.9)	169
ACUTE LEUKEMIA	28(73.7)	1026.3)	38
MULTIPLE MYELOMA	21(84)	4(16)	25
LYMPHOMAS	11(61.1)	7(38.9)	18
APLASTIC ANAEMIA	12(66.7)	6(33.3)	18
MYELODYSPLASTIC SYNDROME	5(71.4)	2(28.6)	7
INFECTIONS(e.g T.B)	2(66.7)	1(33.3)	3
DRUG INDUCED	1(50)	1(50)	2
TOTAL	168	112	280

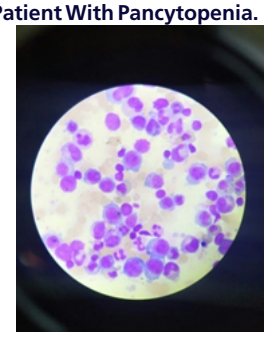
DISCUSSION

Pancytopenia is not a disease itself, but many serious and life threatening conditions can manifest with pancytopenia. It has different etiologies, with a variation in frequency of different diseases leading to pancytopenia in different population groups. Differences in methods, strict diagnostic criteria, period of observation, age groups under study and exposure to chemicals and myelosuppressive drugs are the reasons ascribed for this variation.

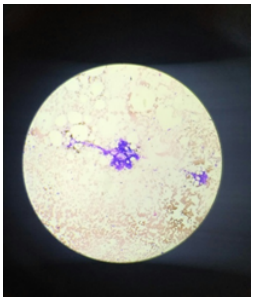
In the present study of 280 patients, definite male predominance was observed with males of 168 and females of 112 and a mean age of 43.81 years. In a similar study of 104 patients by Gayathri et al., the male to female ratio was 1.2:1 and mean age was 41 years [6]. Most common age group of presentation was 4th decade of life in our study, as shown in Table 1.

Megaloblastic anemia was commonest cause of pancytopenia in the present study, accounting for 169 patients (60.4% of total patients). Similar results were found in studies by Tilak V et al., and Gayathri BN et al., were megaloblastic anemia incidence was 68% and 74.04% respectively[6,7]. Khunger JM et al., found megaloblastic anemia in 72% of cases [8].

Picture 1 Shows Peripheral Blood Film With Hypersegmented Neutrophils Suggestive Of Megaloblastic Anaemia In A Patient With Pancytopenia.



Picture 2 Shows Bone Marrow Examination Of Pancytopenia Patient With Features Of Lost Cellularity With No Erythroid And Myeloid Series.



The incidence of acute leukemia varies between 1.61% - 14.5 % in different Indian studies.[8] Acute leukemia being the second commonest etiology in the present study, was present in 38 patients(13.6% of total patients). The results were comparable with Khunger JM et al., who found an incidence of 5% of acute leukemia in the studied patients[8]

We had twenty five cases (8.9% of total patients) of multiple myeloma. The study by Khodke K et al., reported an incidence of 4%. The results were still comparable[9] There were eighteen cases (6.4% of total patients) of lymphomas, mostly non-Hodgkin's lymphoma with incidence varying between 0.9% to 10% in different studies.[9]

Dasgupta et al., reported an incidence of 2.42% of myelodyspastic syndrome, while our study had 2.5 % incidence of myelodysplatic syndrome[10]. We had only eighteen patients (6.4% of total patients) of aplastic anemia, which has been reported as commonest etiology of pancytopenia in different

studies.[11,12,13] Reasons for low incidence of aplastic anemia could be selected admission, as our hospital does not admit pediatric patients which could have missed some patients of aplastic anemia especially with hereditary causes. Secondarily, incidence of aplastic anemia as etiology of pancytopenia varies between 7.7-52.7% and our findings were still comparable[14,15] . In our study we encountered three patients (1.07% of total cases) of tuberculosis, all of them presented with unexplained fever and weight loss. In developing countries like India, tuberculosis is a common disease. Pancytopenia is seen mostly with disseminated (miliary) tuberculosis, with degree of pancytopenia determined more by duration of tuberculosis than by its severity.[16,17] Despite advances in treatment of tuberculosis, mortality remains high if tuberculosis occurs with pancytopenia. We had two patients (0.71% of total cases) were drugs resulted in pancytopenia. All two cases were caused by antiepiletic drugs treatment, one patient was on phenytoin and other on carbamazepine[18,19]. All patients were taking treatment for epilepsy.

CONCLUSION

In the present study, the commonest etiology of pancytopenia was megaloblastic anemia followed by acute leukemia and multiple myeloma. In Indian scenario while evaluating etiology of pancytopenia, megaloblastic anemia should always be kept in mind and responds well to treatment. Thus, present study concludes that with detailed clinical history, physical examination and necessary hematological investigations including bone marrow in pancytopenia patients, helps in understanding disease process, to diagnose or to rule out the various etiologies and further laboratory testing and necessary treatment of these patients.

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