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Clinical profile of cases with pancytopenia

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Abstract
Background: Pancytopenia is a manifestation of a wide variety of disorders which primarily or secondarily affect the bone marrow. It is a relatively common condition whose causative factors may vary with different geographical locations. Thus, to determine the causative agents and the clinical symptoms is essential for the management of this condition.
Methods: This study was conducted on 56 patients above the age of 18 years presenting with pancytopenia. All the patients were subjected to thorough clinical and physical examination. Blood samples were collected for complete blood analysis and biochemical tests and peripheral blood smear was taken. Urine and stool samples were also taken for occult blood analysis. Bone marrow aspiration and trephine biopsies were performed wherever necessary as per the clinical symptoms.
Results: Out of the 56 patients, 58.9% were males and 41.1% were females. The mean age of the patients was 34.9±4.3 years. The major presentation of the patients with pancytopenia was megaloblastic anemia, in 42.9 of the cases, followed by aplastic anemia in 23.2% of the cases. Among the common clinical symptoms, the most common one was pallor (73.2%) followed by weight loss (62.5%) and dyspnea (51.8%).
Conclusions: Megaloblastic anemia is the most common cause of pancytopenia followed by aplastic anemia, with pallor being the most common clinical symptom. Therefore, the clinical findings along with the hematological analysis along with bone marrow aspiration examination are very important for an early diagnosis of pancytopenia so that early intervention can be taken for the patient and enhance the survival rate.

Keywords: pancytopenia, megaloblastic anemia, aplastic anemia

Introduction

Peripheral pancytopenia is a manifestation of a wide variety of disorders which primarily or secondarily affect the bone marrow [1]. It is characterized by a decrease in all the three cellular elements of the peripheral blood, red blood corpuscles, white blood corpuscles and platelets [2]. This low concentrations which is usually caused by bone marrow failure, result in anemia, leucopenia and thrombocytopenia.[3] The common symptoms observe are pallor, dyspnea and bleeding with an increased tendency to get infections which can vary according to the geographical area and genetic mutations [3]. Pancytopenia mainly results from either failure of production of progenitors of hematopoiesis in bone marrow or malignant cell infiltration or antibody mediated bone marrow suppression, or ineffective hematopoiesis and dysplasia, or peripheral sequestration of blood cells in overactive reticuloendothelial system. The main causes of pancytopenia are aplastic anemia, hypersplenism, myelodysplastic syndrome, nutritional deficiencies leading to megaloblastic anemia, subleukemic (acute) leukemias, multiple myeloma, paroxysmal nocturnal hemoglobinuria and infections such as HIV, miliary tuberculosis, brucellosis, and leishmaniasis [4, 5]. Profound neutropenia and thrombocytopenia associated with sepsis and bleeding, more often reflect underlying marrow aplasia or leukemia, while glossitis, diarrhoea and paresthesias are associated with megaloblastic anemia. Out of the tests, a detailed history of the patients, thorough physical examinations and complete blood picture with reticulocyte count and peripheral blood smear are essential for the diagnosis of this disorder [3]. In the complete blood picture, pancytopenia is evident by the low values of Hb <10g/dl, WBC count of 4000 cu/mm and platelets <1 lakh/cu.mm. In the peripheral blood smear, blast cells having acute leukemias, hypergranulation and segmented neutrophils often indicate myelodysplastic syndrome. Hypersegmentation of neutrophils in pancytopenia or abnormalities of erythrocyte morphology with low serum Vitamin B12 and folate levels confirm megaloblastic anemia [3, 6].

Apart from peripheral blood smear, another test, which is very essential for the detection of pancytopenia, is bone marrow aspiration and trephine biopsy. These two procedures complement each other and are useful in the diagnosis of haematological and non haematological disorders [9-12].

A relatively easy and safe test, except for a mild discomfort to the patients, bone marrow aspiration plays a major role in determining the cause for pancytopenia, hematological malignancies, unexplained cytopenias and storage disorders [3, 5]. Trephine biopsy is mainly done when hypoplasia or aplasia of the bone marrow is suspected on aspiration [7].

As there is a difference of pancytopenia in different geographical areas, we had conducted this present study to identify the prevalence of pancytopenia and analyze the clinic-hematological features associated with it.

Methods

This study was conducted on 56 patients above the age of 18 years presenting with pancytopenia (Hb <10g/dl, WBC count of 4000 cu/mm and platelets <1 lakh/cu.mm) at admission from December 2016 to April 2018 at Gulbarga institute of medical sciences by the Department of General Medicine. Patients less than 18 years of age and those who are receiving or have received platelet transfusion prior to the admission have been excluded from the study. Those patients of chemotherapy for neoplasms have also been excluded from the study.

After clearing the study with the institutional ethical committee, the nature of study was properly explained to the patients and their relatives and an informed consent was obtained from all the patients. All the patients were subjected to thorough clinical and physical examination. General demographic details such as age, sex, height, weight etc were noted. Palpitations, fever, fatigue, shortness of breath and other symptoms of pancytopenia were also carefully noted. Examinations for the conditions of internal organs such as X-rays of chest, ultrasound of the abdomen were performed on all the patients. Blood samples were collected in EDTA tubes for complete blood analysis and in plain tubes for biochemical tests and peripheral blood smear was taken. Urine and stool samples were also taken for occult blood analysis. The complete blood analysis was performed on automated hematology analyzer and the platelet count thus obtained was further confirmed by manual methods and peripheral smear examination. Bone marrow aspiration and trephine biopsies were performed wherever necessary as per the clinical symptoms. Bone marrow aspiration and the staining were carried out by standard techniques and were stained by Giemsa staining. Paraffin block were made for the trephine biopsies and the sections form them were made into thin smears and stained by hematoxylin and eosin stains. When required, the aspirated samples were stained by Sudan black, periodic acid Schiff (PAS) stains. The biopsies were stained when required by Reticulin stain.

Chi square test and unpaired t test were the statistical tests used and a p value of <0.05 was taken as the significant value.

Results

Out of the 56 patients, 33 (58.9%) were males and 23 (41.1%) were females (Figure 1). The mean age of the patients was 34.9±4.3 years.

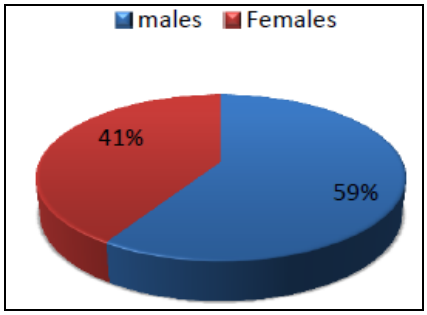

Fig 1: gender wise distribution of patients with pancytopenia

The major presentation of the patients with pancytopenia was megaloblastic anemia, which comprised of 24 (42.9%) of the cases. This was followed by aplastic anemia in 13 (23.2%) cases (Table 1). Megaloblastic anemia was also more common in males than in females although this difference was not significant. Similar was the case with aplastic anemia where both males and females showed a prevalence of less than 25%.

Table 1: causes of pancytopenia in males and female

Causes	Total	Male N=33 (%)	Females N=23 (%)
Megaloblastic anemia	24 (42.9)	14 (42.4)	10 (43.5)
Aplastic anemia	13 (23.2)	8 (24.2)	5 (21.7)
Malaria	4 (7.1)	3 (9.1)	1 (4.3)
Rheumatoid arthritis	4 (7.1)	2 (6.1)	2 (8.7)
Cancer	2 (3.6)	0	2 (8.7)
Liver disease	1 (1.8)	1 (3)	0
Disseminated intravascular coagulation	3 (5.4)	2 (6.1)	1 (4.3)
Septicemia	2 (3.6)	1 (3)	1 (4.3)
Dengue	1 (1.8)	0	1 (4.3)
Multiple myeloma	1 (1.8)	1 (3)	0
Tuberculosis	1 (1.8)	1 (3)	0

Among the common clinical symptoms, the most common one was pallor (73.2%) followed by weight loss (62.5%) and dyspnea (51.8%). Weakness, hepatomegaly and pain in leg were also seen in considerable number of cases (Figure 2).

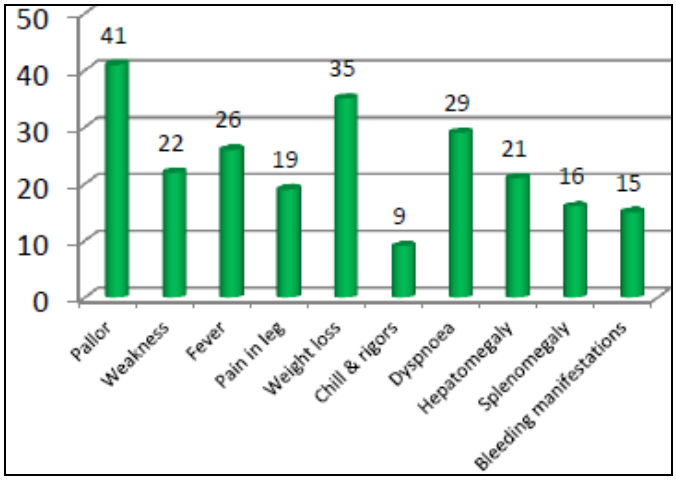

Fig 2: Clinical symptoms in cases with pancytopenia.

Discussion

Pancytopenia is one of the common conditions observed in our day to day practice. It is not a disease but a triad of findings which result from a number of disease processes primarily or secondarily involving the bone marrow. [8]

There are very limited studies on the frequency of the etiology of pancytopenia especially in the Indian subcontinent [13]. This variation in the frequency of the causes of pancytopenia has

been attributed to the differences in methodology and stringency of diagnostic criteria, period of observation, varying exposure to myelotoxic agents apart from the geographical area and genetic mutations [14, 15].

The prevalence of pancytopenia was more in males (59%) than in females (41%) in our study. In a similar study, Das *et al* observed an incidence of 58% in males and 42% in females [9], 62.9% males and 37.09% females with pancytopenia was found in yet another study by Dasgupta *et al*. [18] Prasad *et al* also in his study found a slight preponderance of males over females [17] and Reddy *et al* found 54.8% to be males and 45.3% to be females [16]. In contrast, a female preponderance of 54.28% was seen in a study by Agarwal *et al* [20]. as was seen in another study by Kumar *et al* [21].

The incidence of megaloblastic anemia is said to vary from 0.8% to 32.26%. But in our study, this incidence was higher with 42.9%. Yadav *et al* found an incidence of megaloblastic anemia to be 35.84%3, while Reddy *et al* of 38.1%.16 A very high incidence of 68% of megaloblastic anemia was reported by Tilak *et al* in their study [15], while only 1.43 % was observed by Agarwal *et al*. [20]

The second most common cause of pancytopenia in our study was aplastic anemia, which accounted for 23.2% of the cases. Similar results were observed by Reddy *et al* who reported 26.2% incidence. The incidence of aplastic anemia worldwide is said to vary between10%-52.7%. In the study by Agarwal *et al*, aplastic anemia was the second most common cause of pancytopenia accounting for 14.28%, after malaria, which was the most common cause accounting for 30%. In our study, malaria accounted only for 7.1% of the cases. Aplastic anemia was the most common cause of pancytopenia in several other studies [18, 21, 22]. Acute leukemia was found to be the major cause especially in children by Naseem *et al* in his study [23].

Pallor was observed as the most common symptom in our study with more 73.2%, followed by weight loss in 62.5% of the cases. Dyspnea was observed in 51.8% of the patients. This was corroborated by Yadav *et al*, who reported 60% of the patients to be presenting with pallor, followed by 41.5% with fever. In a study by Agarwal *et al*, the most common presenting symptom was fever with 64.28 % followed by pain in legs in 34.28% [20]. Similar results were found by Khodke *et al*, who also found fever to be the most common symptom [24].

Conclusion

Pancytopenia is not an uncommon hematological condition and is observed often in the clinical practice. In our study, megaloblastic anemia was the major contributor to cause this condition followed by aplastic anemia. Other causes such as tuberculosis, dengue, septicemia etc were also present but rare. In terms of clinical presentations, the most common was pallor, followed by loss of weight, dyspnoea, fever. Other contributors were hepatomegaly, splenomegaly and weakness. Therefore, the clinical findings along with the hematological analysis along with bone marrow aspiration examination are very important for an early diagnosis of pancytopenia so that early intervention can be taken for the patient and enhance the survival rate.

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