

Original Research Article

A study of aetiology and clinical profile of 50 patients presenting with pancytopenia

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ABSTRACT

Background: Pancytopenia is reduction of all the three cellular components which includes anemia, leukopenia and thrombocytopenia. Pancytopenia is striking feature of many serious and life threatening illness ranging from simple drug induced bone marrow hypoplasia, megaloblastic marrow to fatal bone marrow aplasia and leukemias. Pancytopenia has variety of etiologies but most common and reversible is Vitamin B12 deficiency, so early and accurate diagnosis may be lifesaving.

Methods: Study conducted prospectively in 50 patients of pancytopenia with age >12 years, who were admitted to department of medicine in Dr. M.K. Shah Medical College between 2018 to 2020. A complete clinical history and examination was carried out. They were evaluated for complete blood count with peripheral smear, liver function test, renal function test, vitamin B12 level, radiological imaging and bone marrow examination in selected patients.

Results: The etiological causes of pancytopenia were recorded as vitamin B12 deficiency (n 30;60%), Infections (n11;22%),Hypersplenism (n 4;8%), aplastic anemia (n 3; 6%), Drug induced (n 1; 2%) and SLE (n1; 2%). Presenting symptoms in these patients were lethargy, malaise, generalized weakness, dyspnoea on exertion and fever while signs were pallor, splenomegaly and hyperpigmentation. All patients of megaloblastic anemia had macrocytic picture in peripheral smear and all of them were improved after treatment with vitamin B12 supplement.

Conclusions: Pancytopenia is not an uncommon clinical entity and has various etiologies. Most common cause of pancytopenia was B12 deficiency and most common symptoms and signs were generalized weakness and pallor respectively. Most of the etiological causes could be diagnosed with laboratory analysis and radiological imaging without the need of a bone marrow examination.

Keywords: Megaloblastic anemia, Myelodysplastic syndrome, Pancytopenia, Vitamin B12 deficiency

INTRODUCTION

Cytopenia is a reduction in any of the three types of peripheral blood cell. A reduction in all the three of cellular components is termed pancytopenia and this involves anemia, leukopenia, and thrombocytopenia. Initially mild impairment in marrow function may go undetected and pancytopenia may become apparent only during times of stress or increased demand (e.g. bleeding

or infection). The presenting symptoms are usually attributable to anemia or thrombocytopenia.¹

Pancytopenia is a striking feature of many serious and life threatening illness ranging from simple drug induced bone marrow hypoplasia, megaloblastic marrow to fatal bone marrow aplasias and leukemias.² Etiological causes of pancytopenia often vary by geographical region, age, and gender. They include megaloblastic anemia, other

nutritional anemia, aplastic anemia (AA), splenomegaly, sepsis, leukemia, lymphoma, multiple myeloma, myelodysplastic syndromes (MDSs), alcoholic diseases, HIV and hepatitis viruses, autoimmune diseases, endocrine diseases and bone marrow infiltrating diseases (such as Gaucher's disease).³

Clinical features are those due to pancytopenia per se, and those due to underlying disorder with a different epidemiology, pathophysiology, clinical presentations, and clinical outcomes; identification of diseases is of primary importance, since this is the key to appropriate management.⁴

Deficiency of vitamin B12 is a well-known cause of megaloblastic anemia. It is a reversible cause of bone marrow failure and demyelinating nervous system disorder, so early detection and prompt treatment of vitamin B12 deficiency is essential. As a large proportion of pancytopenia is of reversible aetiology (especially B12 deficiency), early & accurate diagnosis may be lifesaving. Whereas the severity of pancytopenia and the underlying pathology determines the management and prognosis of the patients. So, present study is done to identify various aetiologies of pancytopenia and to study clinical profile of patients with pancytopenia.

Aims and objectives

- To study the various aetiological causes of pancytopenia.
- To study the clinical profile of patients having pancytopenia.
- To study the utility of peripheral smear examination to determine various aetiologies of pancytopenia.
- To study the outcome of pancytopenia patients after treatment according to aetiology.

METHODS

It is a cross-sectional observational study, conducted in Department of General Medicine, Dr M.K. Shah Medical College, Ahmedabad, for the duration of 2 year (January 2018 to January 2020). Number of patients included were 50.

Inclusion criteria

- Patient of either sex with age >12 years.
- Haemoglobin level for male patients <13.5 gm/dl and for female patients <11.5gm/dl.
- Leukocyte count <4000/cubic mm.
- Platelet count <1.5lakh/cubic mm.

Exclusion criteria

- Patients having <12years of age.
- Critically ill, intensive care unit patients.
- Patient not willing for further investigation.
- Diagnosed cases of malignancy and leukemia.

- Patients who were receiving chemotherapy or radiotherapy.

A complete history including presenting complaints, past history with specific to drug intake and radiation exposure have been taken. General examination was carried out and specific emphasis was given to pallor, icterus, petechiae, clubbing, skin changes and lymphadenopathy. All systems were examined in detail.

Following investigations were carried out in all the patients:

- Haemoglobin, Complete blood count with peripheral smear, blood indices and reticulocyte count.
- Renal function test, Liver function test, Electrocardiogram, Chest X ray, Ultrasound of abdomen, urine routine and microscopic examinations and stool routine and microscopic examinations (specific for occult blood).
- Specific investigations like serum vitamin B12 level, serum iron, serum TIBC, serum ferritin, culture and sensitivity of blood, urine and sputum, ANA, dS DNA, UGI scopy.
- Bone marrow examination was carried out as per requirement and condition of patient.

RESULTS

In present study megaloblastic anemia is the most common cause of pancytopenia found in 30(60%). The second most common cause is infection found in 11(22%), which includes *P vivax* malaria in 1(2%), *P falciparum* malaria in 2(4%), HIV/ disseminated koch's in 2 (4%), Acute hepatitis B in 2 (4%), Acute hepatitis C in 1(2%), Acute hepatitis E in 1 (2%), Dengue in 1(2%), Enteric fever in 1 (2%) cases. Other causes were Hypersplenism in 4 (8%), Aplastic anemia in 3(6%), Drug induced in 1 (2%) and SLE in 1 (2%) (Table 1).

The most common presenting symptom in present study was lethargy, malaise and generalized weakness in 31(72%) cases. 27(54%) cases presented with dyspnoea on exertion. Fever was present in 21(42%) cases, mainly in infections like Malaria, Tuberculosis, HIV, Hepatitis etc. Other symptoms were tingling and numbness in 17(34%), weight loss in 10(20%), chronic diarrhea in 8(16%) and anorexia in 8(16%). Gum bleeding was present in 3(6%) of cases which was more common in case with aplastic anemia due to severely decreased platelet count (Table 2).

In present study Pallor was present in all the 50(100%) cases, mainly due to decrease in hemoglobin level. Icterus in 16(32%) was mainly seen in patients with acute viral hepatitis, cirrhosis of liver and also in vitamin B12 deficiency due to ineffective erythropoiesis.

Table 1: Underlying aetiology wise distribution of cases.

Aetiology	No. of cases	Percentage [%]
Megaloblastic anaemia	30	60%
Infections	11	22%
<i>P vivax</i> malaria	1	
<i>P falciparum</i> malaria	2	
HIV / disseminated koch's	2	
Acute hepatitis B	2	
Acute hepatitis C	1	
Acute hepatitis E	1	
Dengue	1	
Enteric fever	1	
Hypersplenism	4	8%
Aplastic anemia	3	6%
Drug induced	1	2%
SLE	1	2%

Table 2: Symptoms wise distribution of cases.

Name of symptoms	No. of cases (n=50)	Percentage (%)
Lethargy, malaise and generalized weakness	36	72%
Dyspnoea on exertion	27	54%
Fever	21	42%
Tingling and numbness	17	34%
Weight loss	10	20%
Chronic diarrhoea	8	16%
Anorexia	8	16%
Abdominal distension	4	8%
Gum bleeding	3	6%
Hemetemesis	1	2%

Splenomegaly in 13(26%) cases, almost exclusively seen in Hypersplenism due to cirrhosis of liver and portal hypertension. Skin changes were seen in 10(20%) of cases. While clubbing, cirrhotic stigmata and Hepatomegaly were observed in 6 to 12% of cases. Petechiae in 4(8%) cases were due to low platelet count. Generalized wasting was seen in 4(8%) cases, mostly in cases of HIV associated disseminated koch's. Koilonychia in 4(8%) and tachypnea were observed in 3(6%) of cases.

Table 3: Signs wise distribution of cases.

Signs	No. of cases (n=50)	Percentage %
Pallor	50	100%
Icterus	16	32%
Splenomegaly	13	26%
Skin changes	10	20%
Hepatomegaly	6	12%
Generalized wasting	4	8%
Pedal oedema	4	8%
Petechiae	4	8%
Koilonychia	4	8%
Tachypnea	3	6%
Cirrhotic stigmata	3	6%
Tachycardia	3	6%
Lymphadenopathy	2	4%
Cyanosis	1	2%

Table 4: Peripheral blood smear finding of RBCs.

Peripheral Smear	Total no. of patients	Percentage (%)
Finding of RBCs		
Macrocytic	32	64%
Microcytic	12	24%
Normocytic	6	12%

Table 5: Final outcome of patients after treatment according to aetiology.

Causes	Cases	Discharged/Improved	Referred	Expired
Megaloblastic anaemia	30	30	0	0
Infections	11	7	0	4
<i>P vivax</i> malaria	1	1	0	0
<i>P falciparum</i> malaria	2	2	0	0
HIV / disseminated koch's	2	0	0	2
Acute hepatitis B	2	1	0	1
Acute hepatitis C	1	0	0	1
Acute hepatitis E	1	1	0	0
Dengue	1	1	0	0
Enteric fever	1	1	0	0
Hypersplenism	4	4	0	0
Aplastic anemia	3	0	3	0
Drug induced	1	1	0	0
SLE	1	1	0	0
Total	50	43	3	4

Tachycardia in 3(6%) and Lymphadenopathy were found in 2(4%) of cases. Cyanosis was found in 1(2%) of cases (Table 3).

In present study from 50 patients, 64% patients had macrocytic pictures in their peripheral smear, while 24% of patients had microcytic picture. Only 12% of patients had no change in peripheral smear and they contain normocytic pictures only (Table 4).

In this study 30(60%) patients had megaloblastic anemia as a cause of pancytopenia, all of them were improved and discharged after treatment, 4(8%) patients expired mainly due to infections like HIV/Disseminated Koch's and Hepatitis B and C. While 3(6%) patients of aplastic anemia were referred to higher centre (Table 5).

DISCUSSION

Many disease cause pancytopenia, and frequencies of those diseases vary by age, gender, and region. These causes tend not to be severe. For example, common cold viruses cause transient pancytopenia, but AA and MDS can have fatal consequences.⁵ Vitamin B12 deficiency and infective causes are common in underdeveloped and developing countries, while malignant causes predominate in developed country. For example, a study of Kemal et al. had reported that malaria and hypersplenism were most the common causes in Yemen followed by megaloblastic anemia.⁶

However, a study that evaluated the etiological causes in 195 cases with pancytopenia in South Africa revealed as causes of pancytopenia: bone marrow failure (67.7%), AA (11%), serious infections (9.7%), and hypersplenism (7.7%), respectively.⁷ In another study that had evaluated the etiology of pancytopenia with 77 patients' bone marrow biopsies in India, megaloblastic anemia was reported to be the most common cause (68%), whereas AA (7.7%), MDS and hemophagocytic syndrome, respectively, were rare causes.⁸ It emphasized that megaloblastic anemia should not be overlooked because it was a treatable cause of pancytopenia.⁹

Causes of pancytopenia commonly benign in the young adults, whereas chronic disease and malignant causes were observed at older ages. Hematological malignancies and chemotherapy-related pancytopenia were not evaluated in this study. It should be taken into consideration that immune hemolytic anemia and immune thrombocytopenia can develop in 10% of chronic lymphocytic leukemia (CLL) patients.¹⁰ Bone marrow biopsy shows hypocellular or hypercellular in patients with pancytopenia. The hypocellular bone marrow is seen in AA, Hypoplastic MDS, and paroxysmal nocturnal hemoglobinuria, whereas hypercellular view seen in megaloblastic anemia, MDS, hypersplenism caused by portal hypertension, malaria, and visceral leishmaniasis.¹¹

In this study, the most common cause was megaloblastic anemia found in 30(60%) patients mainly due to vitamin B12 deficiency. Nuclear maturation abnormality in cells leads to macrocytic picture in peripheral smear which correlates with MCV level and gives hint for diagnosis.^{12,13} Elevated blood lactic dehydrogenase and indirect bilirubin can also occur in B12 deficiency and recovery of pancytopenia occurs in 1-2 weeks after vitamin B12 substitution.¹⁴

The second most common cause of pancytopenia in study was Infections 11(22%), which includes *P. vivax* malaria in 1(2%), *P. falciparum* malaria in 2(4%), HIV/Disseminated Koch's in 2(4%), Acute hepatitis B in 2(4%), Acute hepatitis C in 1(2%), Acute hepatitis E in 1(2%), Dengue in 1(2%), Enteric fever in 1(2%) cases. So apart from Vitamin B12 deficiency, malaria, and hematological are important etiological causes of pancytopenia.¹⁵⁻¹⁷

Other causes were Hypersplenism in 4(8%), Aplastic anemia in 3(6%), Drug induced in 1(2%) and SLE in 1(2%). In patients with pancytopenia due to hypersplenism, males were more affected than females as cirrhosis was more common in males mainly due to alcohol consumption which leads to hypersplenism.¹⁸

Symptoms were mainly due to anemia and thrombocytopenia. The most common presenting symptoms in present study were lethargy, malaise, and generalised weakness found in 36(72%), due to decreased oxygen carrying capacity of blood to various organs. Second most common presenting symptom in present study was dyspnoea on exertion found in 27(54%), due to same reason as mentioned above. Fever was present in 21(42%) patients which was more common in cases with Infections like malaria, hepatitis, HIV etc. The most common sign on examination in present study was pallor found in all 50(100%) cases. It is mainly due to decreased Hb level. Other signs were Icterus in 16(32%), Splenomegaly in 13(26%) and Skin changes like hyperpigmentation in 10(20%) cases.

Peripheral smear can be very useful for determining certain aetiologies of pancytopenia like in B12 deficiency, smear shows macrocytic picture with hyper segmented neutrophils and in malaria, smear shows morphologies of parasite. In this study 32(64%) patients had macrocytic RBCs in their peripheral smear, most of them having megaloblastic anemia while 12(24%) patients had either isolated microcytic or mix microcytic plus macrocytic or normocytic RBCs. Only 6(12%) patients had no change in peripheral smear and they contain normocytic RBCs. Maximum 30(60%) patients had megaloblastic anemia as a cause of pancytopenia, all of them were improved and discharged after treatment with injectable vitamin B12 supplementation which suggests that B12 deficiency is easily reversible and treatable cause of pancytopenia. 4(8%) patients expired mainly due to infections like HIV/Disseminated Koch's

in which patients had multisystem involvement an. While 3(6%) patients of aplastic anemia referred to higher centre for further management. So, if patients of pancytopenia are detected early and properly managed then mortality can be decreased.

CONCLUSION

Pancytopenia is not an uncommon clinical entity and has various etiologies. Most common cause of pancytopenia is megaloblastic anemia which is mainly seen in females between 2nd and 3rd decade of life and is mainly due to nutritional deficiency. Infectious diseases like malaria, acute viral hepatitis and HIV/Disseminated Koch's etc. are important and treatable causes of pancytopenia. Other important causes are aplastic anemia, hypersplenism, drug induced and SLE. Most common presenting complaints of patients with pancytopenia is generalised weakness followed by dyspnoea on exertion, while most common finding on clinical examination is pallor followed by icterus. From presence of macrocytic RBCs, macroovalocyte and hyper segmented neutrophil on peripheral blood smear finding, we can suspect Vitamin B12 deficiency as a cause of pancytopenia. In patients with pancytopenia due to Vitamin B12 deficiency, after supplementation of Vitamin B12, there is not only improvement in laboratory parameters of pancytopenia, but also there is improvement in clinical outlook of the patients. Except in megaloblastic anemia and in *P vivax/P falciparum* malaria no specific feature of particular condition is found on peripheral smear to point out a specific diagnosis.

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