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Original Research Article

A prospective study among cases of the pancytopenia on the basis of clinic-hematological analysis and bone marrow aspiration

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ABSTRACT

Background: Pancytopenia is consequence of many haematological condition with an extensive differential diagnosis. A prompt intervention is required to avoid complications. The severity and the underlying pathology determines the management and prognosis. Present study was conducted to assess the etiology, clinical profile and bone marrow morphology of pancytopenia.
Methods: A prospective study was carried out among 50 consecutive patients with pancytopenia. Blood samples of the patients were analyzed for complete blood count and peripheral smear along with presence and absence of immature cells and abnormal cells. In bone marrow examination, morphology of all cells lineage, cellularity, parasite and abnormal cells were scrutinized. Trephine biopsy was done if indicated. Special investigations were done to confirm the diagnosis.
Results: Among the 50 cases studied, age of the patients ranged from 1 to 70 years with a slight male predominance. Most common age group 11-20 years. Most of the patients presented with generalized weakness and fever. The commonest physical finding was pallor, followed by splenomegaly and hepatomegaly. The commonest marrow finding was hyper cellularity with megaloblastic erythropoiesis. The commonest cause for pancytopenia was megaloblastic anemia.
Conclusions: The present study concludes that hematological investigations along with other supportive tests are helpful to diagnose or to rule out the causes of pancytopenia. Megaloblastic anemia is commonest cause of pancytopenia in most Indian and subcontinent studies. Substantial number of patients had reversible etiology. Hence complete work up including clinical details with hematological examination along with bone marrow study will lead to early and proper diagnosis and management.

Keywords: Bone marrow, Hepatosplenomegaly, Megaloblastic anaemia, Pancytopenia, Pallor

INTRODUCTION

A multitude of disorders primarily or secondarily affecting the bone marrow manifests with various hematological derangements, which is reflected in the peripheral blood, commonly as pancytopenia.[1]

Pancytopenia is a clinical condition, which refers to simultaneous presence of anemia, leukopenia and thrombocytopenia. The causes of pancytopenia can be due to decrease in hematopoietic cell production in the marrow resulting from infections, toxins, malignant cell infiltration, chemotherapies and radiation.[2] Ineffective hematopoiesis with cell death in the marrow; formation of defective cells which are rapidly removed from circulation; sequestration and/or destruction of cells by the action of antibodies or trapping of normal cells in a hypertrophied and over-reactive reticuloendothelial

system.[3] Patients usually present with complaints related to anemia, leukopenia and thrombocytopenia, which if not diagnosed at an early stage, may be fatal.

Marrow cellularity and composition in cases of pancytopenia differ in relationship to underlying pathological condition. The marrow is generally hypocellular in cases of pancytopenia caused by a primary production defect. Cytopenia resulting from ineffective hematopoiesis, increased peripheral utilization or destruction of cells, and bone marrow invasive processes are usually associated with a normocellular or hypercellular marrow.[4]

The spectrum of disorders primarily or secondarily affecting the bone marrow may manifest with peripheral pancytopenia.[5] It is recommended that bone marrow aspiration and biopsy be done simultaneously in cases of pancytopenia. Aspiration smears are superior for morphological details while biopsy provides a more reliable index of cellularity and often reveals bone marrow infiltration, fibrosis and granulomas.[6]

The underlying pathology determines the management and prognosis of the patients. This study was carried out to analyse the presentation, to identify the causes and to find out the bone marrow morphology in cases of pancytopenia.

METHODS

To evaluate the cases of pancytopenia and to ascertain their causes, this prospective study was carried out in the department of pathology, over a period of 2 years, from September 2011 to September 2013. All the patients referred to hematology section for routine hematological investigations were screened for pancytopenia, and a total of 50 cases out of 59653 were selected based on the following three criteria-

- Hemoglobin (Hb) less than 9 gm/dl
- Total leukocyte count (TLC) less than 4000/mm3
- platelet count less than 150,000/mm3.

Complete medical history and clinical details were obtained for each patient. Detailed hematological investigations were done in the blood samples. Measurement of Hb, mean corpuscular volume (mcv), tlc, differential leukocyte count (dlc), and platelet count was done on sysmex kx-21 and cross-checked by peripheral blood smear examination for which Leishman stain was used.

Peripheral smear examination was done systematically under low, high, and oil immersion for rbc morphology-i.e. Anisocytosis, poikilocytosis, chromia, polychromasia, nucleated red blood cells, and Presence of inclusions. Rouleaux formation, if present, was noted.

Anemias were then classified morphologically into four groups-normocytic normochromic, microcytic hypochromic, macrocytic, and dimorphic. Differential wbc count was done with a special note of defective granulation in neutrophils and hypo/hyper segmentation in neutrophils, and platelet count and morphology was analyzed.

Also, presence of any parasites was tested for. Informed consent was taken for bone marrow studies. Bone marrow aspiration was done from posterior superior iliac spine using Salah bone marrow aspiration needle. Simultaneously, from the same puncture site but from a different plane, bone marrow biopsy was done using Jamshidi-swaim needle, taking all aseptic precautions. Aspirate and biopsy was processed as routine and standard staining techniques used for staining slides. All cases were stained for iron and grading for iron stores was done. Special stain like Prussian blue stain, reticulin stain, myeloperoxidase, Sudan black and masson's trichrome stain were done whenever required.

RESULTS

A total of 50 out of 59653 patients who presented with pancytopenia were studied. They consisted of 26 males and 24 females with a male-to-female ratio of 1.08:1.

The age of patients ranged from 1 to 70 years. Out of 50 cases, pancytopenia was observed in 14 pediatric patients (1-18 years); they consisted of 09 males and 05 females. Most common age group presenting pancytopenia is 11 to 20 years comprising 13 (26%) cases. age and sex wise distribution of pancytopenia cases shown in Table 1. Table 1 shows that out of 50 cases most common age group presented with pancytopenia was 11 to 20 years (26 cases) and male to female ratio was 1.08:1 observed.

Table 1: Age and sex wise distribution of pancytopenia cases (no. 50).

Age group (years)	Male	Female	Total
0-10	4	1	5
11-20	7	6	13
21-30	4	3	7
31-40	1	8	9
41-50	5	2	7
51-60	2	2	4
61-70	3	2	5

Table 2 Shows that generalized weakness and fever were two most common complains presented in all cases (100%) followed by weight loss (58%); bleeding manifestation (20%) and dyspnea (20%). Although pallor was found in all 50 cases. On examination splenomegaly and hepatomegaly were found in nearly 50% of cases where as 18% of the cases were presented both.

Table 2: Clinical finding in pancytopenia cases (no. 50).

Sign and symptom	No of cases
Generalized weakness	50 (100%)
Dyspnoea	10 (20%)
Fever	50 (100%)
Bleeding manifestation	10 (20%)
Pallor	50 (100%)
Weight loss	29 (58%)
Splenomegaly	24 (48%)
Hepatomegaly	23 (46%)
Jaundice	4 (8%)
lymphadenopathy	2 (4%)
Hepatosplenomegaly	9 (18%)

Table 3 shows that the most common cause of pancytopenia was megaloblastic anaemia (58%) their age was ranging from 4 to 70 years followed by this; 8% of cases were of leukemia out of them; 3 patients of sub leukemic leukemia and 1 case of lymphoma was noted with their age was in between 4 to 30 years 4 cases of iron deficiency anaemia within 15 to 25 years of age group were noted.

Table 3: Causes attributed for pancytopenia (no. 50).

Megaloblastic anemia	29	58%
Ida	4	8%
Aplastic anemia	4	8%
Leukaemia	3	6%
Metastatic disease	1	2%
HIV	2	4%
Malaria	2	4%
Typhoid fever	1	2%
Storage disorder	1	2%
Visceral leishmaniasis	1	2%
Myelofibrosis	1	2%
Lymphoma	1	2%

Two cases of acute myeloblastic leukemia and one case of acute lymphoblastic leukemia found out of 3 cases of sub leukemic leukemia.

Aplastic anaemia was seen in 8% of the cases their age was ranging from 4 to 60 years. 4 cases of iron deficiency anaemia within 15 to 25 years of age group were noted.

One male patient 12 years old and one female patient of 23 years were diagnosed with malaria. Two cases of HIV infection having pancytopenia presented with low grade fever and weight loss one of them having multiple lymphadenopathy and sepsis. 16 years old patient with storage disorder presented pancytopenia along with fever, pallor and hepatosplenomegaly.

One case of visceral leishmaniasis 17 years male patient presented with pancytopenia, fever and hepatosplenomegaly. Individual cases of myelofibrosis, typhoid fever and metastatic adenocarcinoma were also presented with pancytopenia.

DISCUSSION

50 cases of pancytopenia were studied regarding age, gender wise distribution; presenting complains; peripheral smear examination; bone marrow aspiration with various causes of pancytopenia and the results were compared with numerous studies.

In current study; the age of the patients was ranging from 1 to 70 years; similar results were with the studies carried out by Tilak V et al, Kumar R et al, Khunger JM et al, Khodke et al, whereas a study carried out by age was ranged from 12-73 years gender wise distribution in current study m:f ratio 1.08:1 was found.[7-10] Similar results were found in the studies by tilak v et al, Khunger et al, Khodke et al, [7,910] where the Male:Female ratio was 1.2:1; 1.3:1 ; 1.14:1 respectively whereas a study carried out by Kumar R et al Male:Female was found 2.1:1 which was comparatively higher than current study.[8]

The most common presenting complaint in current study was generalized weakness and low-grade fever (100%), followed weight loss (58%). The most common physical finding was pallor (98%), followed by hepatomegaly (48%)and splenomegaly (46%). The presenting symptoms were usually attributed to anemia or thrombocytopenia. Leukopenia was an uncommon cause of the initial presentation of the patient but can become the most serious threat to life during the disorder.

Hemoglobin, total leucocyte count and platelet count were comparable with those in other studies. hyper segmented neutrophils were noted in 56.3% of cases compared to 84.9% in Tilak V et al, study and Khunger JM et al. Demonstrated no hyper segmented neutrophils in megaloblastic anemia. Also, relative lymphocytosis in aplastic anemia was noted in 50% of the cases in current study compared to 50% in Tilak V et al. Study and 85.71% in Khunger JM et al. study.[7,9]

In current study, we came across 14 pediatric pancytopenic cases; again, megaloblastic anemia was the common cause for pancytopenia, followed by aplastic anemia. Comparable results were reported by Bhatnagar et al.[11]

However, in a study by Gupta and Colleagues, 105 patients aged 1.5 to 18 years, with a mean age of 8.6 years, were included in the study.[12] Aplastic anemia was the most common cause of pancytopenia (43%), followed by acute leukaemia (25%). Infections were the third most common cause of pancytopenia, of which Kala-azar was the most common. megaloblastic anemia was seen in 6.7% of the patients by Khodke et al.[10] In another study,

64 children were identified with diagnosis of pancytopenia. The most common cases were infectious in origin (64%), followed by hematological (28%) and miscellaneous (8%) etiologies.[13]

Variations in the frequency of various diagnostic entities causing pancytopenia to have been attributed to difference in methodology and stringency of diagnostic criteria, geographic area, period of observation, genetic differences and varying exposure to myelotoxic agents, etc.[7]

The commonest cause of pancytopenia, reported in numerous studies throughout the world has been aplastic anemia.[7] This is in sharp contrast with the results of current study, where the commonest cause of pancytopenia was found to be megaloblastic anemia. Similar findings were observed in other studies conducted in india.[8-10] This seems to reflect the higher prevalence of nutritional anemia in Indian subjects.

Incidence of megaloblastic anemia was 74.04% in current study. Incidence of 72% was reported by Tilak V et al, by Khunger JM et al. and 68%.[7,9] All the above studies have been done in india, and they stress the importance of megaloblastic anemia being the major cause of pancytopenia. It is a rapidly correctable disorder and should be promptly notified.[9] although bone marrow aspiration studies are uncommon in suspected cases of megaloblastic anemia, if the diagnosis does not appear straightforward or if the patient requires urgent treatment and hematological assays are not available, bone marrow aspiration is indicated. As facilities for estimating folic acid and vitamin B12 levels are not routinely available in most centers in india, the exact deficiency is usually not identified.[8]

Incidence of aplastic anemia varies from 10% to 52% among pancytopenic patients.[10] In studies done by Khunger JM *et al* and Khodke K et al, both observed an incidence of 14%.[9,10] A higher incidence, viz., 29.5%, was reported by Kumar R et al the incidence of hypoplastic anemia in current study was 8% only, thus prevalence of aplastic anemia varies.[8]

We encountered 6% incidence of sub leukemic leukaemia, compared to 5% reported by Khunger JM et al. Kumar r et al. Reported 12% incidence of aleukaemic leukaemia. Pancytopenia was the common feature in current study; this correlated with the corresponding finding in the studies by Kumar R et al, and Khunger JM et al.[8,9] The diagnosis of aml was based on bone marrow aspiration study. We reported 3 cases of aml-m2 and 1 case of all-l2. Khodke K et al, reported a case of aml-m2 out of 50 cases of pancytopenia. Kumar R et al, reported 5 cases of all, 13 cases of aml, 2 cases of hairy cell leukaemia out of 166 cases of pancytopenia, over a 6-year study period.[8]

We encountered one case of extramedullary lymphoma, bone marrow aspiration shows normocellular marrow with erythroid hyperplasia. Khunger JM et al, who have reported an incidence of 1%; Tilak V et al, who have reported an incidence of 2.5%; and Kumar R et al, who have reported an incidence of 6.02% of the total cases.[7-9] We encountered 2 cases of malaria in current study, constituting 4% of total cases-compared to Khunger JM et al, who have reported an incidence of 1%; Tilak V et al., who have reported an incidence of 3.9%; and Kumar R et al, who have reported an incidence of 3% of the total cases.[7-9]

Osama Ishtiaq et al, studied 100 patients having pancytopenia and encountered five cases of iron deficiency anemia (5%) as 4th common cause in his study which was comparable with current study where we also encountered 4 cases of iron deficiency anemia manifesting with pancytopenia.[14] Anita et al, also reported 13 cases which is second most common cause of pancytopenia in his study.[15] Iron deficiency anaemia is the second most common cause of nutritional deficiency in USA.[16] Iron deficiency anaemia can be associated with pancytopenia. Though iron deficiency is associated with a reactive thrombocytosis, increasing severity of iron deficiency leads to normalisation and occasionally even decrease platelet counts. The exact mechanism of this is unclear but may be related to the alteration in the activity of iron dependant enzymes in thrombopoiesis and leucopoiesis.[17,18]

In this study, 1 case of pancytopenia were diagnosed to have visceral leishmaniasis. The age is 17-years male: migrated from Bihar. Patient presented with fever and hepatosplenomegaly. Ld. bodies were seen in bone marrow aspirate. Single case of myelofibrosis, were obtained in the study. Which is comparable to study by Kumar R et al and Khunger JM et al, encountered two cases of myelofibrosis.[8,9] In myelofibrosis bone marrow aspirate had scanty cellularity, hence bone marrow biopsy done which had increased fibrosis.

Single case of typhoid fever and metastasis of adenocarcinoma were obtained in the study. In metastasis bone marrow aspirate had hypo cellular with all three lineages were suppressed. Like Kumar R et al, who also reported single case of typhoid fever and 2 cases of marrow metastasis.[8]

We have reported a single case of storage disorder, in a 16-years-old boy, who presented with hepatomegaly, splenomegaly and pancytopenia. Bm was normocellular with normoblastic erythropoiesis. Aspirated smears showed collection of large foamy histiocytes dispersed throughout the smear. Anita et al also reported one case of storage disease. Kumar R et al, Khunger JM et al, and Khodke et al. have not reported any case of storage disorder as a cause of pancytopenia in their studies.[8-10]

In present study 19 cases (38%) had hypercellular marrow, followed by normocellular (34%) and hypocellular marrow (28%)which was comparable with the studies done by Santra et al, who had 60/111 cases of cellular marrow and 50 cases of hypocellular marrow.[19]

Bone marrow aspiration was diagnostic value to the patients of pancytopenia.[19] Most common cause for hypercellular bone marrow was megaloblastic anemia in present study. Hypercellular marrow was noted in cases of myelodysplastic syndrome, multiple myeloma, non-Hodgkin lymphoma and sub leukemic leukaemia in the study done by Khunger et al. [9]

The causes of pancytopenia were treatable in 70% of the patients, who fully recovered from cytopenia. Death occurred in 20% of the cases, which was due to severe pancytopenia and overwhelming infections and complication.

CONCLUSION

Pancytopenia is not an uncommon hematological problem encountered in clinical practice and should be suspected on clinical grounds when a patient presents with unexplained anemia, prolonged fever and tendency to bleed. Bone marrow aspiration is an important diagnostic tool in hematology which helps to evaluate various cases of pancytopenia. Bone marrow aspiration is sufficient to make a diagnosis in cases of nutritional anaemia and initial diagnosis of leukemia.

The present study concludes that detailed primary hematological investigations along with bone marrow aspiration in cytopenic patients are helpful for understanding the disease process; to diagnose, or to rule out the causes of, cytopenia; and in planning further investigations and management of cytopenic patients. Severe pancytopenia has significant relation with the clinical outcome and can be used as a prognostic indicator.

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REFERENCES

1. Kumar DB, Raghupathi AR. Clinicohematologic analysis of pancytopenia: Study in a tertiary care centre. Basic Applied Pathol. 2012;5(1):19-21.
2. Kar M, Ghosh A. Pancytopenia. J Indian Acad Clin Med. 2002;3:29-34.
3. Khodke K, Marwah S, Buxi G, Yadav RB, Chaturvedi NK. Bone marrow examination in cases of pancytopenia. J Indian Academy Clin Med. 2001;2:1-2.
4. Niazi M, Raziq F. The incidence of underlying pathology in pancytopenia. J Postgrad Med Inst. 2004;18:76-9.
5. Williams WJ, Bentkr E, Erskv AJ. Hematology. third edition. Singapore, McGraw hill book company; 1986:161-184.
6. Jha A, Sayami G, Adhikari RC, Panta AD, Jha R. Bone marrow examination in cases of pancytopenia. J Nepal Med Assoc. 2008;47(169):12-7.
7. Tilak V, Jain R. Pancytopenia-a clinico-hematologic analysis of 77 cases. Indian J Pathol Microbiol. 1992;42:399-404.
8. Kumar R, Kalra SP, Kumar H, Anand AC, Madan M. Pancytopenia-a six-years study. J Assoc Physicians India. 2001;49:1079-81.
9. Khunger JM, Arculselvi S, Sharma U, Ranga S, Talib VH. Pancytopenia-a clinico-hematological study of 200 cases. Indian J Pathol Microbiol. 2002;45:375-9.
10. Knodke K, Marwah S, Buxi G, Vadav RB, Chaturvedi NK. Bone marrow examination in cases of pancytopenia. J Academy Clin Med. 2001;2:55-9.
11. Bhatnagar SK, Chandra J, Narayan S, Sharma S, Singh V, Dutta AK. Pancytopenia in children: etiological profile. J Trop Pediatr. 2005;51:236-9.
12. Gupta V, Tripathi S, Tilak V, Bhatia BD. A study of clinico-hematological profiles of pancytopenia in children. Tropical Doct. 2008;38:241-3.
13. Pine M, Walter AW. Pancytopenia in hospitalized children. A five-years review. J Pediatr Hematol Oncol. 2010;32:192-4.
14. Ishtiaq O, Baqai Hz, Anwer F, Hussai N. Patterns of pancytopenia patients in a general medical ward and a proposed diagnostic approach. Connective Tissue. 2007;4(5):5.
15. Anita P, Vijay D. Clinico-hematological analysis of pancytopenia: a bone marrow study. National J Laboratory Med. 2013;2(4):12-7.
16. Lopas h, Rabiner SF. Thrombocytopenia associated with iron deficiency anemia. Clin Pediatr. 1966;5:609-16.
17. Ganti AK, Shonka NA, Haire WD. Pancytopenia due to iron deficiency worsened by iron infusion: a case report. 2007;1:175-7.
18. Jhamb R, Kumar A. Iron deficiency anemia presenting as pancytopenia in an adolescent girl. Int J Adolesc Med Health. 2011;23(10):73-4.
19. Santra G, Das BK. A cross sectional study of the clinical profile and aetiological spectrum of pancytopenia in a tertiary care center. Singapore Med J. 2010;51(10):806-12.

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