Original Research Article

Clinico hematological profile of pancytopenia in pediatric patients: an institutional experience in North Himalayan region of India

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ABSTRACT

Background: Pancytopenia is a common clinical pattern with an extensive differential diagnosis, but literature search shows only limited studies of pancytopenia in Pediatrics patients in Uttarakhand state of India. The present study was therefore conducted to study the spectrum of pancytopenia with bone marrow and haematological profile in Pediatrics patients in this north Himalayan state of India.

Methods: Prospective observational study was conducted in the Department of Pediatrics in the teaching institute situated in Uttarakhand state of India over a period of 12 months. The study included all the patients of pancytopenia below 18 years of age who underwent bone marrow examination after written informed consent.

Results: The study included total 50 pediatric patients of pancytopenia with male to female ratio of 1.38:1. The mean age of patients was 10.58±4.94 with median age of 12 years. Mean hemoglobin was 5.31±2.09 g/dl, total leukocyte count was 2492.68±941.76/mm3, platelet count was 34724±26423/mm3, mean corpuscular volume was 90.95±16.65 fl, mean corpuscular hemoglobin was 30.11±6.07 pg, mean corpuscular hemoglobin concentration was 33.06±1.65% and reticulocyte count was 1.21±1.10%. Nutritional deficiency (28%) was the most common cause for pancytopenia followed by aplastic anaemia (24%). Megaloblastic anaemia was the commonest cause of nutritional deficiency anaemia (71.42%) with pancytopenia.

Conclusions: Pancytopenia is an important presentation in Pediatrics population with the most common cause being nutritional anaemia and aplastic anaemia. Megaloblastic anaemia is the commonest cause of nutritional anaemia with pancytopenia. The clinicians should be aware of spectrum of pancytopenia with clinical and haematological presentation in Pediatrics patients of this region so as to avoid unnecessary work ups and delay in treatment.

Keywords: Clinical, Haematological, Pancytopenia, Pediatrics

INTRODUCTION

Pancytopenia refers to a reduction below normal values of all the three peripheral blood lineages including leukocytes, platelets and erythrocytes.1 The spectrum of pancytopenia is different in children in comparison to adults and it also varies from developing world to developed countries.2 The mechanisms contributing to pancytopenia include decrease in hematopoietic cell production, marrow replacement by abnormal cells, suppression of marrow growth and differentiation, ineffective hematopoiesis with cell death, defective cell formation, antibody mediated sequestration or destruction of cells in a hypertrophied and overactive reticuloendothelial system.3 The presenting symptoms are often attributable either to the anaemia or thrombocytopenia, while leucopenia is often seen in the subsequent course of the disorder.3 Pancytopenia may
present with some benign or other serious conditions like bone marrow failure and acute malignancy cases specially associated with hepatosplenomegaly with varying differential diagnosis and usual clinical presentation of pancytopenia, we find limited studies in pediatric patients in Uttarakhand state of India.

The present study was therefore conducted to study the spectrum of pancytopenia with bone marrow and haematological profile in Pediatrics patients in this north Himalayan state of India.

**METHODS**

The study was conducted in the department of Pediatrics over a period of one year from October 2012 to October 2013. Subjects were recruited from patients presenting with a primary diagnosis of pancytopenia and after obtaining written informed consent. This is the observational type of the study. 50 consecutive patients presenting with pancytopenia in OPD/IPD were recruited for the study.

**Inclusion criteria**

- Age <18 years
- Pancytopenia measured by automated cell counter and confirmed via general blood picture, defined as
  - Anemia: hemoglobin <10 gm/dL.
  - Leukopenia: total white cell count <4 x 10^9/L.
  - Thrombocytopenia: platelet count <100x10^9/L.

**Exclusion criteria**

- Age ≥18 years
- Exposure to myelotoxic drugs
- Recent history of blood transfusion
- Patients not consenting for bone marrow examination

**Study tools**

Case recording form, routine blood counts, Abbott Cell-Dyn 3700, bone marrow examination, Jamshidi needle.

**Study protocol**

Patients presenting with the diagnosis of pancytopenia and signs and symptoms of fever, pallor, petechial rash, bleeding, bone pain, hepatomegaly, splenomegaly, lymphadenopathy were taken into the study.

**Baseline characteristics**

Details were recorded in subject proforma that included age, sex, address.

Relevant medical history were taken involving present illness, past illness, personal and family history. Complete clinical examination was done.

Routine blood examination were sent to measure various blood indices viz. hemoglobin, red blood cell count, total leukocyte count, differential leukocyte count, platelet count, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), packed cell volume (PCV), Mean Platelet Volume (MPV).

Confirmation was done by peripheral smear stained by Leishman stain for all the cases. Bone marrow aspiration was subsequently carried out under aseptic precaution after obtaining written consent from the patient or guardian.

**Data management and statistical analysis**

Interpretation and statistical analysis of obtained results was done using SPSS version 22.

**RESULTS**

The study included total 50 pediatrics patients of pancytopenia with male to female ratio of 1.38:1. The mean age of patients was 10.58±4.94 with median age of 12 years. Maximum numbers of cases were seen in 11-18 years group (56%). Majority of children (64%) were completely immunized for age and no un-immunized child was seen in the study. Maximum number of cases belonged to upper lower class (44%) and 64% were vegetarian in their dietary habits. Common presenting symptom of patients was fever (86%) followed by generalized weakness, abdominal pain, vomiting and bleeding manifestations. Table 1 shows the clinical presentation of the cases. It shows that pallor was present in all the cases while hepatop-splenomegaly was observed in 40% of cases. Equal no (24%) of subjects had skin bleeds and lymphadenopathy.

**Table 1: Clinical presentation of the cases.**

| Clinical presentation                  | Number of cases (% of total cases) |
|---------------------------------------|-----------------------------------|
| Pallor                                | 50 (100%)                         |
| Tachycardia                           | 34 (68%)                          |
| Tachypnea                             | 11 (22%)                          |
| Skin Bleeds (Petechiae, Purpura, Echymosis) | 12 (24%)                        |
| Lymphadenopathy                       | 12 (24%)                          |
| Hyper Pigmented Knuckles              | 6 (12%)                           |
| Bony Tenderness                       | 3 (6%)                            |
| Hepatomegaly                          | 11 (22%)                          |
| Splenomegaly                          | 1 (2%)                            |
| Hepatosplenomegaly                    | 20 (40%)                          |

According to WHO grading the anemia was severe in 86% while moderate in 14% cases. Mean haemoglobin was 5.3±2.09 g/dl, total leukocyte count was 2492.68±491.76/mm³, platelet count was 3472±26423/mm³, mean corpuscular volume was 90.95±16.65 fl, mean corpuscular haemoglobin was...
DISCUSSION

More no of male children in the present study is in harmony with other studies from Indian sub-continent.4-6 The reason for this may be the deep rooted mind set of this society toward concern and care of male children. In this study median age of presentation of 12 years was higher in comparison to other studies where pancytopenia children presented at median age of 6-8 years.7,8 The main presenting features of children with pancytopenia were progressive pallor (100%) and fever (86%). Memon et al, also reported pallor (87%) and fever (65%) as the main presentations of pancytopenia.9 The most common cause of pancytopenia in this study was nutritional anemia (28%) followed by aplastic anemia (24%). This is in contrast to previous study which reported megaloblastic anemia and leukemias as a cause of pancytopenia in only 13% of children.9 Pine et al, observed that infectious etiolo (64%) (including bacterial sepsis, non-EBV viral infections and sepsis syndrome) and aplastic anemia (11%) were two important causes of pancytopenia.8 Lack of vitamin B12 or folic acid in cases of megaloblastic anemia may accelerate the early death of hematopoietic stem cells; leading to ineffective erythropoesis, leukopenia, thrombocytopenia and may incriminate pancytopenia.10 There were two cases (4%) of combined nutritional deficiency anemia in this series. Memon et al, reported 8.06% cases of mixed nutritional deficiency anemia in their study which was more than the present study.9

In this study, out of 11 subjects with infections, kala-azar accounted for 7(63.63%) patients. Kala-azar in itself is not a common cause of pancytopenia but isolated cytopenias in form of anemia, leucopenia, thrombocytopenia or bicytopeny, are encountered frequently.11 Although visceral leishmaniasis (VL) is endemic in various parts of India but is rarely reported from the hilly areas of India.12 A good number of cases in the pediatric age group highlights the fact that Garhwal region should be considered as an endemic region of VL. The hematological changes were reversed after the

Table 3: Comparison of hematological indices in various aetiologies of pancytopenia.

| Indices                | Megaloblastic anemia | Aplastic anemia | Acute Leukemia | Infection  |
|------------------------|----------------------|----------------|----------------|------------|
| Hemoglobin (g/dl)      | 4.44±1.63            | 4.55±2.01      | 6.61±2.21      | 5.73±1.68  |
| TLC (/mm³)             | 2561±974.53          | 2525±836.27    | 30010±23280    | 16791.66±9917.88 |
| MCV (fl)               | 112.95±12.08         | 91.55±8.87     | 85.49±5.65     | 77.98±13.13 |
| MCH (pg)               | 37.59±4.79           | 30.87±3.11     | 28.49±1.73     | 25.37±4.90 |
| MCHC (%)               | 33.52±1.71           | 33.68±1.03     | 33.47±1.45     | 32.45±1.33  |
| Platelet Count (/mm³)  | 45920±24380.17       | 16791.66±9917.88 | 35900±23105.45 | 30010±23283.53 |
| Retic (%)              | 1.7±1.45             | 0.49±0.29      | 1.21±0.89      | 1.02±0.85  |

It was found that this study revealed more cases of megaloblastic anemia (24%) followed by aplastic anemia (28%) in children. The results of this study are in harmony with various other studies.14-16 The most common cause of megaloblastic anemia in this study was nutritional deficiency (28%) followed by aplastic (60%). The diagnostic approach of megaloblastic anemia in children is based on the presence of macrocytic anemia, microcytic anemia or normocytic anemia with megaloblastic bone marrow changes.15-17 The megaloblastic anemia was associated with low vitamin B12 and folate levels in children. This is in harmony with a study which revealed that 83% of children had low vitamin B12 levels and 50% had low folate levels in megaloblastic anemia.13 The children with megaloblastic anemia in this study were found positive for EBV infection in 4 cases (16.6%) which is in harmony with another study.15

In this study, aplastic anemia was seen in 7(28%) cases with 1(4.16%) of cases revealed positive for EBV infection. The aplastic anemia in children was associated with low reticulocytes count (1.7±1.45%) and low hemoglobin levels (4.44±1.63 g/dl). This is in harmony with a study which revealed that aplastic anemia was associated with low reticulocytes count (4.55±2.01%) and low hemoglobin levels (4.44±1.63 g/dl).13

The children were found positive for EBV infection in 11(44.44%) cases which is in harmony with another study.15 The children with aplastic anemia in this study were associated with low reticulocytes count (4.55±2.01%) and low hemoglobin levels (4.44±1.63 g/dl). This is in harmony with a study which revealed that aplastic anemia was associated with low reticulocytes count (4.55±2.01%) and low hemoglobin levels (4.44±1.63 g/dl).13
in institution of appropriate therapy with parenteral sodium stibogluconate in 6 patients and amphotericin B in 1 patient which was contrary to recent reports of refractoriness of sodium stibogluconate in treating VL thereby reinforcing the fact that VL of Garhwal region is sodium stibogluconate sensitive.13 One patient in this study had disseminated Koch’s coexisting with Staphylococcal septicemia. Pancytopenia can be a rare presentation of disseminated TB and occasionally it can be appreciated in pulmonary tuberculosis as well.14 However, pancytopenia as the presenting feature of disseminated tuberculosis is extremely rare both in children and adults.15,16 In this study 10 patients of pancytopenia had the eventual diagnosis of acute leukemia comprising 20% of all cases. This is reported less than the studies which previously observed 23% and 26.6% cases of acute leukemia in their series of pancytopenia patients.4,5

Important limitation of this study were small sample size which may not be representative of the population. In addition, as the study was carried out in the tertiary care centre so the exact prediction of pancytopenia in this region may have not been predicted.

CONCLUSION

Pancytopenia is an important presentation in pediatric population with the most common cause being nutritional anemia and aplastic anemia. The commonest cause of nutritional deficiency anemia with pancytopenia is megaloblastic anemia. Leishmaniasis which is considered to be non-endemic in this north Himalayan region constituted an important cause of pancytopenia in children of this region. The clinicians should be aware of spectrum of pancytopenia with clinical and hematological presentation in pediatric patients of this region so as to avoid unnecessary work ups and delay in treatment.

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