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Original Research Article

An Institutional Study of Pancytopenia in Children

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Abstract

Background: The differential diagnosis of Pancytopenia varies according to the geographical distribution and still remains a diagnostic dilemma for the Pathologist and the Paediatrician both. The condition is reversible and easily treatable if identified early.

Aim: To study the clinical and haematological profile of children presenting with pancytopenia and to evaluate the causes in our setting.

Material and Methods: The present study was carried out in the Department of Pathology and Paediatrics of a tertiary care hospital in North India from January 2022 to June 2023. Total 61 cases of children with pancytopenia were subjected to bone marrow aspiration after routine haematological investigations (like Complete Blood Count) including peripheral blood smear examination (PBS).

Results: The present study comprised of 61 children in the age group of 2 years to 14 years. Megaloblastic anemia was the commonest cause of pancytopenia and responsible for 38 cases (62.3%). Acute lymphoblastic leukaemia accounted for about 07 cases (11.5%). Aplastic anemia was responsible for 06 cases (9.8%). Kala-azar, Malaria, Disseminated tuberculosis and Enteric fever accounted for about 6.6%. 4.9%, 3.3% and 1.6% cases respectively.

Conclusion: Bone marrow aspiration is crucial to arrive at a diagnosis of pancytopenia. Even in the absence of a final diagnosis, BMA can help the clinician in their approach to diagnosis and management of the patient.

Keywords: Bone marrow aspiration, Megaloblastic anemia, Pancytopenia.

Introduction

Pancytopenia is the simultaneous presence of anemia (hemoglobin [Hb] less than the normal for age), leukopenia (total leukocyte count [TLC]) < 4000/cubic mm and platelet count <1,50,000/ cubic mm. It is not a disease entity but a triad of findings that has many differential diagnosis. It is important to understand the vast causes of inherited and acquired pancytopenia to further guide the work-up and management of patients. An evaluation requires a careful review of past medical history, family history, and exposure history. A physical examination might reveal clues to an underlying genetic syndrome or other inherited causes of pancytopenia. A guided laboratory evaluation based on the history and physical exam findings can further narrow a patient's differential diagnosis. Most patients will require a bone marrow aspirate and biopsy as part of their evaluation though at times the bone marrow testing can be inconclusive.

Although a few authors have discussed pancytopenia as a separate entity, most of the discussion is centered on aplastic anemia, which is a relatively uncommon cause of pancytopenia in children [1,2]. The lack of an optimal investigative approach to pancytopenia (especially the role of bone-marrow examination) has also been previously highlighted [3].

The aim of the present study was to study the clinical and haematological profile of children presenting with pancytopenia and to evaluate the causes in our setting.

Material and Methods

The present study was carried out in the Department of Pathology and Paediatrics of Nalanda Medical College and Hospital, Patna retrospectively and prospectively during a period of one and a half year from January 2022 to June 2023 after approval from ethical committee.

In the present study, 61 cases of children from 2 years to 14 years with pancytopenia were studied. All the patients referred from the Department of Paediatrics to the Haematology section of Pathology Department underwent routine haematological investigations (like Complete

Blood Count) including peripheral blood smear examination (PBS). Children who received blood transfusion and were receiving cytotoxic chemotherapy were excluded from the study.Patients reported to have pancytopenia were subjected to bone marrow aspiration after taking informed consent along with full clinical history and physical examination. All PBS and bone marrow aspirates were stained with Leishman stain.

Results

The present study comprised of 61 children in the age group of 2 years to 14 years. The mean age of the children was 7.26 years. 30 cases were male and 31 cases female with a male to female ratio of 0.97:1, thus denoting a slight female prepon - derance.

The most frequent complaint was weakness and fatigue. Pallor was the most common physical finding followed by hepatosplenomegaly. The Hemoglobin concentration of the patients ranged from 2.1 to 8.5 gm/dl. The total leukocyte count of the patients ranged from 1200-3800/cubic mm. The platelet count of the patients ranged from 10,000-1,00,000/cubic mm. The most common bone marrow aspiration finding was a hypercellular marrow with megaloblastic reaction.

Table 1: Distribution of cases in our study

Diagnosis	No. of cases (%)
Megaloblastic anaemia	38 (62.3%)
Acute lymphoblastic leukaemia	07 (11.5%)
Aplastic anaemia	06 (9.8%)
Kala-azar	04 (6.6%)
Malaria	03 (4.9%)
Disseminated Tuberculosis	02 (3.3%)
Enteric fever	01 (1.6%)

Megaloblastic anemia was the commonest cause of pancytopenia and responsible for 38 cases (62.3%). Acute lymphoblastic leukaemia accounted for about 07 cases (11.5%). Aplastic anemia was responsible for 06 cases (9.8%) but no etiologic factors could be implicated in any of these children except two with probable heavy metal poisoning. The most common infection reported was kala-azar which was found in residents of endemic areas. 02 patients with disseminated tuberculosis were found to be over 8 years of age.

Table 2: Bone marrow examination

Bone marrow findings	Number of cases (%)
Hypercellular marrow with megaloblastic reaction	38 (62.3%)
Hypercellular marrow with predominance of lymphoblasts	05(8.2%)
Hypocellular marrow	06(9.8%)
Hypocellular marrow with predominance of lymphoblasts	02(3.3%)
Cellular marrow	10(16.4%)

Discussion

The results of this study show that pancytopenia can be the presenting feature of a wide variety of illnesses in the pediatric population of our country. In the present study Megaloblastic anaemia emerged as a recognisable cause of pancytopenia among 38 children (62.3%). Megaloblastic anemia was also the commonest cause of pancytopenia in studies by Bhatnagar *et al* and Ramesh C *et al* [8,9]. This was in contrast to the findings of Gupta *et al* which reported Aplastic anaemia (43%) to be the commonest cause in their study. Gupta *et al* reported only 6.7% cases of Megaloblastic anaemia [10].

Out of the 38 cases, 24 cases(63.2%) showed pure Megaloblastic anaemia of varying severity, whereas 14 cases(36.8%) showed a combination of Iron deficiency and Megaloblastic anaemia in varying proportions. Sen R *et al* too reported 75 cases of pure Megaloblastic anaemia and 36 cases of combination of iron deficiency and Megaloblastic anaemia [5]. This reflects the high prevalence of nutritional anaemias in Indian subjects. Although megaloblastic anemia was found to be the commonest cause of pancytopenia among children, a diagnosis of megaloblastic anemia should not be based on the presence of macrocytes on the peripheral smear alone, as this finding is also found in those with aplastic anemia and also acute leukemia.

Severe thrombocytopenia was reported in 10 % cases in our study as compared to 30% cases by Bhatnagar *et al* [8]. Majority of the cases had platelet counts between 50,000-1,00,000/cubic mm. The total leukocyte counts of the patients ranged from 1200-3800/cubic mm. The haemoglobin concentration of the patients in the study ranged

from 2.1 to 8.5 gm/dl. Of the 61 cases, 23 cases had haemoglobin levels between 3-5 gm/dl, suggesting severe degree of anaemia at the time of presentation as pancytopenia.

Acute lymphoblastic leukaemia was the next most common cause of pancytopenia in this study accounting for about 11.5% cases followed by Aplastic anaemia with 9.8% cases. Similar findings were reported by Bhatnagar *et al* [8]. In our study ,the peripheral blood examination of the patients diagnosed as acute lymphoblastic leukaemia on BMA showed aleukemic or sub leukemic blood picture with occasional blasts.

Various infectious conditions due to microorganisms also induce pancytopenia in children. In the present study Kala-azar (6.6%) was the most common infectious cause of pancytopenia in children. All the patients with kala-azar in this study came from endemic areas, had history of prolonged fever with a massive splenomegaly, and the diagnosis was clinically suspected prior to bone marrow examination. This low frequency could again have been due to the referral nature of the patients. This is in contrast to the study by Bhatnagar *et al* who reported 30% cases of Enteric fever among the children. Isolated cytopenias, bicytopenias and pancytopenia in enteric fever are well-documented in literature[14]. 3.3% cases of disseminated tuberculosis presented as pancytopenia in our study. Pancytopenia was found in 19% of the patients with disseminated or miliary tuberculosis in a study by Singh *et al* [15]. The various postulated mechanisms for pancytopenia include splenic sequestration, immune-mediated bone marrow depression and malnutrition. As tuberculosis is quite common in our country, it may be coincidentally present in quite a few patients of pancytopenia. Presence of pancytopenia and disseminated tuberculosis in a pediatric patient does not therefore imply causation, and BMA or biopsy should demonstrate granuloma to definitively ascribe pancytopenia to be because of the tubercular infection.

There are a wide variety of causes of pancytopenia, the uncommon ones of which were not found in our study. Inherited pancytopenias account for approximately 30% of cases of paediatric marrow failure [16]. Interestingly few of the inherited bone marrow failure syndromes such as Fanconi anaemia, Dyskeratosis Congenita, and Schwachman-Diamond anaemia may be initially diagnosed in adulthood. Fanconi anaemia is the most common of these disorders. Unclassified inherited bone marrow failure syndromes are heterogeneous disorders that may be either atypical presentations of identifiable diseases or new syndromes. The criteria for the diagnosis of the same has been laid down in the Canadian Inheried Marrow Failure Registry.

Drugs, chemicals, toxins, infectious agents, radiation and immune disorders can result in pancytopenia by direct destruction of hematopoietic progenitors, disruption of the marrow microenvironment, or immune-mediated suppression of marrow elements [16]. A careful history of exposure to known risk factors should be obtained for every child presenting with pancytopenia. Even in the absence of the classic associated physical findings, the possibility of a genetic predisposition to bone marrow failure should always be considered. The majority of cases of acquired marrow failure in childhood are “idiopathic”, in that no causative agent is identified. Many are probably immune-mediated through activated T-lymphocytes and cytokine destruction of marrow progenitor cells. The overall incidence of acquired aplastic anaemia is relatively low with an approximate incidence in both children and adults in the United States and Europe of 2-6/ million population/ yr. The incidence is higher in Asia, with as many as 14 cases/ million population/ yr in Japan [16]. Patients with bone marrow failure should also be evaluated for inherited forms of marrow failure, paroxysmal nocturnal haemoglobinuria and collagen vascular diseases. Pancytopenia without peripheral blasts may be caused by bone marrow replacement by leukaemic blasts or neuroblastoma cells.

Conclusion

Pancytopenia in children still remains a diagnostic challenge for both the Pathologist as well as the Pediatrician. In our study Megaloblastic anaemia emerged as a recognisable cause of pancytopenia . Bone marrow aspiration is crucial to arrive at a diagnosis. Even in the absence of a final diagnosis, BMA can help the clinician in their approach to diagnosis and management of the patient. However our study had limitations since it had a small sample size and required bone marrow biopsy facilities.

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