

Aplastic Anaemia of Childhood: Marked Cytopenias

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ABSTRACT

Objective: Aplastic anemia of childhood: marked cytopenias

Design: Cross-sectional comparative study.

Place and duration of study: Haematology Department of Children's Hospital and Institute of Child Health Lahore during the period from April 2003 to December 2008.

Patients and methods: Two hundred and thirteen children fulfilling the criteria were included in the study and the results of patients were compared with the age matched controls. Student's 't' test was applied. The level of significance was significant, if the p-value was less than 0.05.

Results: Aplastic Anaemia was present at a frequency of 85.5%, Demographic characteristics showed that pallor is the most common symptom followed by fever and bruises. Epistaxis is also observed. Hematological abnormalities showed that the prominent hematological finding was anemia, leucopenia and thrombocytopenia. Levels of hemoglobin and values of leukocyte count, erythrocyte counts, reticulocyte count and platelet counts were decreased significantly when compared with controls.

Conclusion: The key issue in searching for the cause of cytopenia is to determine whether it is a self-limiting or a serious chronic disorder, such as a bone marrow failure syndrome that may progress to cancer. An accurate diagnosis of the type of bone marrow failure syndrome is important in order to counsel families on the natural history of the disease and provide effective treatment.

Key words: Aplastic anemia, childhood, pancytopenia

INTRODUCTION

Term "aplastic anemia" has been broadly applied to hypocellular BM irrespective of the respective histopathological features¹. The prevalence of infection in SAA patients was 86.0%². The disease appears more often in eastern Asian countries, where it affects about 15 out of every 1 million people. It can affect people of any age. At least one-fourth of children with aplastic anemia, have presented with thrombocytopenia in early infancy^{3,4}.

Aplastic anemia presents with malaise, pallor and associated symptoms such as palpitations. Patients with this type of anemia have reticulocytopenia, leucopenia and thrombocytopenia. Thrombocytopenia, leading to increased risk of hemorrhage, bruising and petechiae. Leukopenia, leading to increased risk of infection. Low reticulocyte counts usually show depression of all blood elements⁵.

Etiology is unknown, but one known cause is an autoimmune disorder in which white blood cells attack the bone marrow⁶. There may be chromosomal defects in aplastic anemia due to its precision/resolution and lack of reliance on cell division⁷. In 15% cases, drugs (chloramphenicol, carbamazepine, phenylbutazone etc) or infection

(viral hepatitis) can be identified that precipitates the BM failure/aplastic anaemia, although it is not clear why only some individuals are susceptible⁸. Aplastic anemia is also sometimes associated with exposure to toxins such as benzene. Exposure to ionizing radiation from radioactive materials or radiation-producing devices is also associated with the development of aplastic anemia⁹.

In aplastic anemia, the patient has pancytopenia resulting in decrease of all formed elements. The diagnosis can only be confirmed on bone marrow examination. Before this procedure is undertaken, a patient will generally have had other blood tests to find diagnostic clues, including a complete blood count, Bone marrow aspirate and biopsy: to rule out other causes of pancytopenia (i.e., neoplastic infiltration or significant myelofibrosis)¹⁰.

Criteria of severity of aplastic anemia include peripheral blood neutrophil count $<0.5 \times 10^9/L$, peripheral blood platelet count $<20 \times 10^9/L$ and Peripheral blood reticulocyte count $<20 \times 10^9/L$ ¹¹.

Inability to classify a disease can have a major impact on the family and the treating medical facility. First, some of the patients may receive unnecessary treatment. Second, a significant number of patients with aplastic anemia or bone marrow disorder undergo many diagnostic tests for months or even years, and still approximately one fifth cannot receive an accurate diagnosis. Study was carried out to find out the aplastic anemia based on hematological

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abnormalities like pancytopenia and typical symptoms.

PATIENTS AND METHODS

Two hundred and thirteen patients diagnosed on highest clinical suspicion, laboratory parameters with or without one or more somatic abnormalities at Haematology Department of Children’s Hospital and Institute of Child Health Lahore during the period from April 2003 to Dec 2008 were included. 100 age matched normal subjects with no history of any disease were considered as controls.

Inclusion and Exclusion Criteria: The inclusion criteria include patients diagnosed as aplastic anaemia, bone marrow failure and associated somatic abnormalities. The ages of the patients were from birth till 15 years. Children with cytopenias who also had hepatosplenomegaly were excluded from the study. Also children with Leukemia and an inherited syndrome not associated with antecedent marrow failure were excluded. Written consent was obtained from recruited patients or guardians. All patients and their parents were subjected to a detailed interview. Patient’s physical examination was undertaken along with a report on peripheral blood picture, Bone marrow aspirate and trephine. Any clinical or haematological clue to the disease progression was recorded. Findings were recorded with special reference to indicators of bone marrow failure.

Table 1: Demographic characteristics

	Aplastic anemia (213)
Pallor	190 (++)
Bruises	155 (++)
Epistaxis	100 (++)
Fever	155 (++)
St stature café-au-lait patches	00
Micro- cephal	00
Mircro- ophthalmia	01 (++)
Pigmentation	00
Hypo plastic thumbs	00

Table 2: Hematological parameters in patients and controls

	Patients (213)	Controls (100)
Age (years)	8.70±3.26	9.12±2.5
Hb (gm/dl)	7.27±2.85**	12.38±0.42
WBC count	2.74±1.43**	7.8±6.11
RBC count	2.53±1.02**	4.39±0.08
Reticulocytes	0.47±0.34**	0.50±0.89
Platelet count	28.98±22.04**	235.20±13.08

*P<0.001= Highly significant difference

Fever: Presence of fever on and off and at the time of presentation, mostly settling down with an antibiotic course.

Pallor: Usually the first sign at presentation. Patient comes with recent packed red cell transfusion or is in a dire need to have one.

Bleeding diathesis: History suggesting bleeding gums, epistaxis, easy bruisability was recorded and clinical examination performed to look for any purpura.

Somatic abnormalities: Including skin spots, skeletal (absent thumbs, radial hypoplasia, scoliosis) genitourinary (underdeveloped gonads, horseshoe kidney), microcephaly, microphthalmia were recorded.

Statistical analysis: Statistical analysis was carried out by using SPSS 14.0. Mean and Standard deviation was determined. Student’t’ test was used to compare the value of patients with normal controls and find out the level of significance. P value of less than 0.05 is taken as significant.

RESULTS

In this study there were 262 cases of bone marrow failure including Aplastic Anaemia which presented at a frequency of 85.5%, Demographic characteristics were tabulated (Table 1). It was observed that pallor is the most common symptoms followed by fever and bruises. Epistaxis is also observed.

Hematological abnormalities were tabulated in Table 2. It was observed that at a mean age of 8.7 years after study entry, 213 patients developed severe aplastic anemia. Among patients with aplastic anaemia the prominent hematological finding was anaemia, leucopenia and thrombocytopenia. It was observed that the level of hemoglobin and values of leukocyte count, erythrocyte counts, reticulocyte count and platelet counts are decreased significantly (P<0.001) when compared with controls.

DISCUSSION

An important indication for bone marrow investigation is the presence of bone marrow failure, which manifests itself as pancytopenia. The causes of cytopenia are Fanconi anaemia, aplastic anaemia, myelodysplastic syndromes etc .Approximately 50% of patients develop aplastic anaemia, usually by the age of 5 years¹².

Demographic characteristics of present study showed that pallor is the most common symptom followed by fever and bruises. Epistaxis is also observed. It is reported by a group of workers¹³ that low numbers of red blood cells can cause a person to feel tired or weak, be short of breath and look pale. Low numbers of white blood cells can lead to frequent or severe infections. Low numbers of platelets can lead to easy bleeding or bruising and tiny red spots under the skin (petechiae), or bleeding

that is hard to stop. For a person with severe or very severe aplastic anaemia, infections or bleeding can be life-threatening. Our study is in accord with a study who also reported that pale face was the most common clinical manifestation, followed by bleeding and fever¹⁴.

Present study observed that the level of hemoglobin and values of leukocyte count, erythrocyte counts, reticulocyte count and platelet counts are decreased significantly ($P < 0.001$) when compared with controls. Study is in accord with studies who observed that aplastic anaemic patients had pallor, fever, epistaxis and bleeding from gums. Patient was found to have pancytopenia i.e., low hemoglobin level, leucopenia and thrombocytopenia^{15,16}.

Present study observed a significant decrease in reticulocyte count when compared with controls. According to a study, the number of reticulocytes is a good indicator of bone marrow activity, because it can be used to determine whether a production problem is contributing to anaemia, & can also be used to monitor progress of treatment for anaemia¹⁷.

Among patients with aplastic anaemia the prominent hematological finding was anaemia, leucopenia and thrombocytopenia. Our study is inline with a study which observed that patients have lower counts of all three blood cell types: red blood cells, white blood cells, and platelets, termed pancytopenia¹⁸. A study reported that Aplastic anaemia results from injury to the blood stem cells, immature cells in the bone marrow that give rise to all of other blood cells types. The injury causes a decrease in the number of every type of blood cell in the body-red cells, white cells, and platelets, a condition called pancytopenia¹⁹. Another study reported that Aplastic anaemia is an autoimmune disease characterized by destruction of hematopoietic tissue resulting in hyperfunction of effector T-lymphocytes¹⁰.

CONCLUSION

The key issue in searching for the cause of cytopenia is to determine whether it is a self-limiting or a serious chronic disorder, such as a bone marrow failure syndrome that may progress to cancer. An accurate diagnosis of the type of bone marrow failure syndrome is important in order to counsel families on the natural history of the disease and provide effective treatment.

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