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Original Article

Aetiology and Clinical Presentation of Pancytopenia in a Teaching Hospital

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Abstract:

Pancytopenia is a morphological description of the peripheral blood picture irrespective of its cause & it denotes simultaneous presence of anaemia, leucopenia and thrombocytopenia. The study was done to observe the demographic profile & the clinical presentations of pancytopenic patients and to find out the aetiology of pancytopenia. This cross sectional study was carried out in Medicine ward of Rajshahi Medical College Hospital from August 2005 to July 2006. A uniform protocol was followed in all cases, to have appropriate history, physical findings & laboratory investigations. The commonest cause of pancytopenia was aplastic anaemia (48%) which was followed by hypersplenism (22%) & acute leukemia (16%). The majority cases of aplastic anaemia were idiopathic (57.69%), only 42.31% cases were due to secondary causes. The majority (94%) of patients was in the age range of 14-60 years and up to 54% was in the age group of 20-40 years. The ratio of male to female in patients of pancytopenia was 1.5:1 and 3:1 in aplastic anaemia. In secondary causes of aplastic anaemia, insecticides and viral hepatitis was found to be causative agent in 45.45% cases of each followed by pregnancy in 9.10% of cases. The common presenting complains of aplastic anaemia were generalized weakness (100%), gum bleeding (76.92%), fever (76.92%) and pallor (96.15%).

Key words: Pancytopenia, Aplastic anaemia, Hypersplenism, Acute leukemia.

Introduction:

The term pancytopenia is a morphological description of the peripheral blood picture irrespective of its cause. It is the simultaneous presence of anaemia, leucopenia and thrombocytopenia. Pancytopenia therefore exists in the adult when the hemoglobin level is less than 13.5 gm/dl in males, or 11.5 gm/dl in females; the leukocyte count is less than $4x10^9$/L; and the platelet count is less than $150x10^9$/L[1].

All haematopoetic stem cells are derived from a pleuropotent stem cell that gives rise to precursors of erythroid, myeloid and megakaryoid forms. Injury to or suppression of this haematopoetic stem cell will result in pancytopenia[2].

The aetiology of pancytopenia is diverging. The morbidity and mortality of pancytopenia depends upon the variability of aetiology. It may be simple drug induced hypoplasia where recovery is excellent after drug withdrawn. On the other hand it may be fatal in primary aplastic anaemia, where death occurs in 60% of cases within six months. Drugs; specially, antirheumatic agents, phenylbutazone, anticonvulsants like hydantoins, carbamazepine, cytotoxic drugs (alkylating agents), antibiotics (chloramphenicol, sulphonamide), exposure to irradiation, insecticides, benzene, infections etc. All have been proved to have aetiological role in aplastic/hypoplastic anaemia. Congenital aplastic anaemia may also occur[3-5]. It is a serious disorder which frequently terminates in death within six months. Mortality rate vary in different

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series from somewhat less than 50% to as high as 80% in the first year after presentation. Allogenic bone marrow transplantation is highly successful in children and young adults, especially with HLA-matched siblings[6].

The treatment of choice for young adults (under age 40) who have HLA-matched siblings is allogenic bone marrow transplantation. For patients without suitable bone marrow donor high-dose immunosuppression with cyclophosphamide should be considered and has produced remissions in refractory cases. In non-aplastic group spontaneous recovery is common. Treatment is directed towards the primary cause when detected. Early diagnosis, removal of the causative agents and appropriate treatment may save many lives[7,8]. This study in designed to have an idea about aetiology & clinical presentation of pancytopenia in our country.

Materials & Methods:

This was a cross sectional study carried out in Medicine ward of Rajshahi Medical College Hospital during the period of one year from August 2005 to July 2006. A total of 50 patients of pancytopenia were collected as cases. Pancytopenia was diagnosed in the presence of anaemia (Hb level <13.5gm/dl or Hct Value <0.40 in men, Hb level <11.5gm/dl or Hct Value <0.35 in women), leucopenia (WBC $<4x10^9$/L) and thrombocytopenia (platelets $<150x10^9$/L). Patients under the age of 14 years and patients on cancer chemotherapy were excluded from the study. Data was collected by taking history and thorough clinical examination and all appropriate investigations were done. Data was analyzed by using SPSS (Statistical package for social sciences).

Table I: Incidence of pancytopenia (n =50)

Cases	Number of patients (%)
Idiopathic aplastic anaemia	15 (30)
Secondary aplastic anaemia	11 (22)
Insecticides -5	
Viral hepatitis -5	
Pregnancy -1	
Hypersplenism	14 (28)
Kala-azar -11	
Hereditary haemolytic anaemia Thalassaemia-3	
Sub-leukaemic acute leukaemia	8 (16)
AML-5	
ALL -3	
Others	2 (4)
Megaloblastic anaemia -1	
SLE -1	
Total	**50 (100)**

Results:

Table I shows incidence of pancytopenia where 52% were due to aplastic anaemia of which 30% were idiopathic and 22% secondary. Hypersplenism due to Kala-azar, Hereditary haemolytic anaemia was 28% followed by Sub-leukaemic acute leukemia 16%.

Table-II shows age distribution where 54% of pancytopenic patients were between 20-40 years and 76.92% of patients of aplastic anaemia were between 20-40 years.

Table II: Age distribution: Pancytopenia and aplastic anaemia

Age in Years	Number of Pancytopenia Patients (%)	Number of Aplastic Anaemia Patients (%)
<20	11 (22)	2 (7.69)
20-40	27 (54)	20 (76.92)
41-60	9 (18)	2 (7.69)
>60	3 (6)	2 (7.69)
Total	**50 (100)**	**26 (100)**

Table III shows sex distribution where out of total 50 patients presenting with pancytopenia, 29 (58%) cases were male and 21 (42%) cases were female. In aplastic anaemia group, out of 26 patients of aplastic anaemia 19 (73.08%) were male and 7 (26.92) were female. Here pancytopenia and aplastic anaemia show male predominance.

Table III: Sex incidence: Pancytopenia and Aplastic anaemia

Sex Group	Number of Pancytopenia Patients (%)	Number of Aplastic Anaemia Patients (%)
Male	29 (58)	19 (73.08)
Female	21 (42)	7 (26.92)
Total	**50 (100)**	**26 (100)**

Most of patients had insidious onset. Table-IV shows presenting symptoms of pancytopenic patients.

Table-V shows out of 26 cases of aplastic anaemia, 100% presented with anaemia. Second common physical findings were gum bleeding (76.92%) and fever (76.92%). Other physical findings include purpuric spot (38.46%), retinal haemorrhage, mouth ulcer, ecchymosis etc. But no lymphadenopathy and splenomegaly were found in any cases.

Table IV: Aplastic anaemia: Presenting symptoms

Presenting symptoms	Number of Patients (%)
Generalized weakness	26 (100)
Palpitation	15(57.69)
Headache	15 (57.69)
Exertional dyspnoea	5 (19.23)
Pallor	25 (96.15)
Fever	20 (76.92)
Urinary complaints	5 (19.23)
Respiratory tract infection	6 (23.08)
Sore throat	8 (30.77)
Gum bleeding	20 (76.92)
Epistaxis	10 (38.46)
Haemoptysis	7 (26.92)
Heamatemesis	7 (26.92)
Melaena	6 (23.08)
Per rectal bleeding	5 (19.23)
Menorrhagia	6 (23.08)
Haematuria	1 (3.85)
Purpura	10 (38.46)
Blurring of vision	5 (19.23)

Table V: Aplastic anaemia: Physical findings

Physical findings	Number of Patients (%)
Anaemia	26 (100)
Gum bleeding	20 (76.92)
Fever	20 (76.92)
Purpuric spot	10 (38.46)
Retinal haemorrhage	5 (19.23)
Mouth ulcer	4 (15.38)
Echymosis	2 (7.69)
Lymphadenopathy	0 (0)
Splenomegaly	0 (0)

Discussion:

This study was done to find out the pattern of causative disorder and clinical presentation in 50 pancytopenic patients admitted into Rajshahi Medical College Hospital from August 2005 to July 2006.

In present study of pancytopenia, the incidence of aplastic anaemia is highest (52%) which was followed by hypersplenism (28%), and sub-leukaemic acute leukaemia (16%). This is roughly consistent with the study of BSMMU[9,10], where aplastic anaemia is found in 80% followed by leukaemia 10.48%. On a worldwide basis, both in developed and developing countries most of the aplastic anaemia is idiopathic. In the present study out of 50 cases of pancytopenia, 52% were aplastic anaemia and among these 57.69% were idiopathic and 42.31% were secondary. This finding is consistent with the study of Scott JL et al, on aplastic anaemia, where 56.59% were primary & 43.41% were secondary[11,12]. In the study of Shafiqur Rahman Patwary, 31.70% aplastic anaemia was secondary[9,13].

The variation of the incidence of secondary aplastic anaemia was probably due to difference in the number of patients included in the studies, variation in geographical distribution and on technique adapted for the study.

Prakash Shashi et al[14] in their study of 305 cases of leukaemia at Pondicherry in India found that 13% cases of AML and 7.1% cases of ALL were subleukaemic at onset. In this study 10% were AML and 6% were due to ALL which is also similar to above mentioned study.

The age distribution in the present study was from 14 to 65 years. The majority of patients (94%) of aplastic anaemia were within the age range of 14 to 60 years. Of these the maximum incidence of aplastic anaemia is up to 54% in age group 20 to 40 years. This is generally consistent with age incidence and distribution in studies carried out by Scott et al[11] & Hows J et al showing 76.9% cases under the age of 40 years and median age of onset as 28 years. Other studies carried out by Bomford et al[15] and Wetkind et al showed similar picture. In a study in India[16] median age of onset of aplastic anaemia is 23 years. Study of Dr. Shafiqur Rahman and Patwary[9,13] shows 84.60% were within the age between 13 to 40 years. The majority (82.92%) of patients of aplastic anaemia were with in the age of 14 to 40 years which is more nearer to (72%) in the present study.

In the leukaemic group of pancytopenia, the age incidence was between 14-65 years. In ALL group most of the patients were within the age between 14-18 years. In AML group most of the patients were within the age of 20-65 years. Kushwaha et al[17] in their study found that 80% of all patients were within age of 20 years, 68% of AML within the age of 10 to 30 years. In this study 5 patients of AML and 3 patients of ALL present with pancytopenia. The variation of age incidence and number of patient is probably due to the very small number of patients and different criteria for selection of patients in the present study.

Out of 50 patients, 29 (58%) were male and 21 (42%) were female. This study is roughly consistent with the study of IPGMR (BSMMU). In the study of IPGMR the incidence of male and female were 63% and 37% respectively. In the study of Dr. Shafiqur Rahman Patwary[9,13] 76% were male and 24% were female. In the Aplastic anaemia group 66.66% were male and 33.33% were female. This figure is consistent with the study of Kuchupilli et al[18] carried out in India where 75.60% were male and 24.40% were female.

In the aplastic group the onset of symptoms were insidious in most cases. Anaemia (100%), generalized weakness (100%), gum bleeding (76.92), fever (76.92)

and pallor (96.15) were common manifestations. On examination, all patients were anaemic. In the study of Scott JL et al in 1959 purpura (71.80%), anaemia (100%) unaccompanied by hemorrhagic phenomenon and episodes of systemic infection were the presenting features. The markedly higher incidence of generalized weakness and anaemia in present study could be related to the fact that most of the cases in the present study presented later in the course of their disease.

Conclusion:

Pancytopenia as a clinical syndrome is not uncommon in practice. This is a small scale study pointed out the aetiological factors and clinical presentation of pancytopenia. A wide variety of disorders can cause pancytopenia and aplastic anaemia is the most common aetiological factor of pancytopenia. Most of the pancytopenic patients present with pallor, weakness, bleeding manifestation and fever. The natural history of aplastic anaemia is rapid deterioration and death; patients with severe aplastic anaemia have a rapidly fatal illness if left untreated. Early aetiological diagnosis of pancytopenia and appropriate measures may save many lives.

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