Severe Aplastic Anaemia - An Aetiological Correlation

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Khalid Hassan, Nadeem Ikram, Muhammad Jamil Akhtar, Tasneem Akhtar Bhatti (Departments of Haematology, Pathology; Rawalpindi Medical College, Rawalpindi.)
Muhammad Tahir (Department of Pathology, Federal Government Services Hospital, Islamabad.)
Mumtaz Hassan (Department of Paediatrics, Children's Hospital, Islamabad.)

Abstract

Over 4 years, 43 cases of severe aplastic anaemia (SAA) were seen. Etiologically 58.1% had idiopathIc, 39.5% secondary and 2.3% congenital aplastic. anaemia. Idiopathic $AA was more common in patients between 0-15 years of age, whereas secondary $AA was more frequent in 16-60 years age group. Males were more commonly affected with a maleiemale ratio of 3.3:1. Amongst 17 cases of secondary SAA, chioramphenicol was responsible for 4, septran for 3, insecticides for 2 and anti-scabitic drugs, anti-diabetic drugs and “kushta from hakeem in one patient each. Hepatitis associated SAA was suspected in 3 cases (JPMA 44:43, 1994).

Introduction

Aplastic anaemia occurs as a result of injury to pleuripotent stem cells of haemopoietic system and is therefore characterized by pancytopenia[1]. This condition is more common in orient than in western countries[2]. Annual incidence of aplastic anaemia in Bangkok (3.7 per million) is about 4 fold higher than in western countries[3]. A study from Armed Forces Institute of Pathology (AFIP), Rawalpindi, showed an average of 25 patients of aplastic anaemia diagnosed annually[4]. The prevalence rate of this disease in Pakistan, however, has not been established so far.

SAA occurs secondary to drugs as antibiotics, especially chloramphenicol[5], analgesics[6], antidiabetics[7], anti-convulsants[8] and anti-thyroid drugs[9]. Exposure to chemicals as benzene and benzene-related compounds including insecticides[1] are known to cause SM and ionizing radiation[1,10] is also an important etiological factor. Aplastic anaemia is also a noted complication of acute viral hepatitis of the B and non-A non-B type[11]. It usually occurs during the resolving phase of hepatitis or as long as six months after resolution. A study of aplastic anaemia in children in Taiwan showed that 23.9% of the patients had hepatitis[12]. Pols et al, however, have proposed that hepatitis C virus is not a frequent cause of non-A non-B hepatitis associated aplastic anaemia[13]. Idiopathic disease constitutes a large fraction of MA patients and is said to be much more common in patients below 50 years as compared to older patients[14]. The present study was designed to look into aetiological factors of SM seen at our hospital.

Patients and Methods

A total of 43 consecutive cases of SM diagnosed at pathology department of Rawalpindi Medical College from January, 1988 to December, 1992 were included in this study. For every patient, relevant clinical features were entered in a proforma including age, sex, pallor, fever, bleeding manifestations, jaundice, lymph-adenopathy, hepatomegaly and splenomegaly. A special note was taken of history of drug intake in recent past, with particular reference to antibiotics, analgesics, anti-diabetics and anti-convulsants. The adult patients were interrogated regarding their indulgence with chemicals, especially insecticides. Anti-coagulated blood samples were collected in vials containing EDTA for peripheral blood counts including reticulocyte count. Haemoglobin estimation was performed by cyanmet-

haemoglobin method and white cell and platelet counts by visual methods[15]. Differential leucocyte count was done byMay-GrunwaldGiemsa stain. For reticulocyte count, 1% brilliant cresyl blue was used. Bone marrow aspiration and trephine biopsies were performed at posterior superior iliac spine, using Saleh's and Islam's needles respectively. At least two well-made marrow smears and trephine imprints were stained by May-Grunwald-Giemsa stain. Trephine sections were stained by haematoxylin and eosin stains. The diagnosis of SM was based on Cammitta's criteria which are as follows:

A. Peripheral blood picture: Atleast two of the following should be evident.

1. Neutrophils less than $0.5x10^9/1$
2. Platelet countless than $20x10^9$ /1
3. Corrected reticulocyte count less than 1%

B. Bone marrow trephine biopsy:

1. Cellularity of the marrow less than 25% of normal
2. Cellularity between 25 and 50% with % remaining haemopoietic cells

After the diagnosis of SM was established we tried to correlate the disease with possible aetiologic agents which could be implicated with a strong suspicion from the history of the patient. Furthermore, the patients were grouped according to their ages as 0-15, 16-60 and 60 years, in an attempt to correlate various aetiologic agents in different age groups.

Results

The ages of the patients ranged between 2 to 88 years with majority (74.4%) falling between 2 and 20 years. There were 33 males and 10 females with 18 males and8 females belonging to below 15 years age group. The age and sex distribution is shown in Table I.

Table I. Age and Sex distribution.

Age (years)	Number of patients		Male:Female ratio	Total number of patients
	Male	Female		
<15	18	8	2.25:1	26
15-60	12	2	6.0:1	14
>60	3	-	3.0:1	3
All age groups	33	10	3.3:1	43

The correlation of SAA with various aetiological agents is shown in Table II.

Table II. Aetiological Agents.

Aetiological factor	Number of patients	Percentage
Congenital	01	2.3
Association with causative agents	17	39.5
Chloramphenicol	04	9.3
Septran	03	6.9
Insecticides	02	4.6
Kushtas from hakeem	01	2.3
Chlorpropamide	01	2.3
Anti-scabitic (α-Benzene derivative)	01	2.3
Hepatitis*	03	6.9
Multiple antibiotics*	02	4.6
Idiopathic	25	58.1

*Suspected and not established as aetiologic factors.

Majority of patients (25) belonged to the idiopathic group.

Table III. Aetiological factors and idiopathic:secondary (I:S) ratio in different age groups.

Age group years	Congenital	Chloram-phenicol	Septran	Antiscabitic	Kushta	Insecticide	Chlor-propamide	Multiple antibiotics	Hepatits	Idio-	I:S ratio*
0-15	1	3	1	0	0	0	0	2	2	17	2.12:1
16-60	0	1	2	1	1	2	1	0	1	5	1:1.8
>60	0	0	0	0	0	0	0	0	0	3	3:1
All age groups	1	4	3	1	1	2	1	2	3	25	1.47:1

*Congenital aplastic anaemia is not included in idiopathic group.

Table III displays the distribution of the idiopathic SAA and various aetiologi. cal factors for secondary SAA in different age groups.

Discussion

Severe aplastic anaemia (SAA) is an important haematological condition encountered in clinical prac¬tice. The determination of an exact cause for the pathology is usually an educated guess, supported by statistical correlation[1]. A search through the literature within Pakistan revealed only one published study[4] conducted on 124 patients. Secondary SAA was observed in 32.2% of these subjects. Causative agents could be established in 12.8% of this group (hepatitis and cgkiran¬phenicol in 3.2% each, anti- tuberculous drugs and septran in 2.4% each, anti-diabetic and diuretics in 0.8% each). 19.4% cases could be linked with drugs from hakims and homeopaths and antibiotics. The idiopathic to

secondary aplastic anaemia ratio was 2: 1.In the present study of 43 cases of SAA, the I:S ratio was 1.47:1 for all age groups. This ratio was 2.12:1 in patients below 15 years age, as compared to 1:1.8 in patients between 15 and 60 years. We observed that chloramphenicol and septran were collectively responsible for SAA in 16.28% of cases. Hepatitis related SAA was observed in 6.9% of patients. Other associated factors were insecticides and multiple antibiotics in 4.65% each and "lcushtas", anti¬scabitics and anti- diabetics in 2.3% each. In hepatitis associated SAA, a history of jaundice (clinically viral hepatitis) within the previous three months was ob¬served. Since the markers for hepatitis viruses could not be studied, the association of hepatitis with aplastic anaemia could be suspected and not established. It has been observed that hepatitis associated aplastic anaemia is relatively more common in areas where hepatitis is prevalent as compared to the western countries[12]. As hepatitis B and non-A non-B are prevalent in Pakistan, many of SAA patients may have an aetiological correlation with hepatitis. A study of viral antigens and antibodies would help to isolate the viral origin of many idiopathic cases of aplastic anaemia. Colony studies would further establish if aplastic anaemia was due to serum factor or stem cell factor. Young et al[2] have observed that aplastic anaemia was encountered more frequently in the adults in the western countries. In the east younger people are aifected more[2] and 62-70% of cases of aplastic anaemia in Korea, Thailand and China are below 30 years of age[4]. Our findings compare well with these studies as 60% of our SA SAA patients were below 15 years, 74% below 20 years and 81% below 30 years of age.

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