A CLINICAL PROFILE OF APLASTIC ANEMIA

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INTRODUCTION:

Aplastic anemia is a disorder of hematopoiesis characterized by pancytopenia and hypocellularity of the bone marrow. It is a life-threatening disease, predisposing to bleeding tendencies and serious infections. Geographic variability is apparent within various study regions. In Western countries, it is a rare disease, the estimated incidence of aplastic anemia being 2-5 cases per million population per year.¹ Studies from our part of the world reveal a relatively higher incidence of aplastic anemia. Aplastic anemia appears to be as common as chronic myelogenous leukemia and more common than multiple myeloma and chronic lymphocytic leukemia in much of the Orient.² Most cases of aplastic anemia are acquired. However, for over half of the patients no cause can be determined (idiopathic aplastic anemia).

It has been observed that patients with aplastic anemia are admitted quite frequently in our medical wards. This prompted us to undertake this study, to analyze the profile of presentation at our centre and make an assessment of various etiological factors.

MATERIAL AND METHODS:

A hospital-based, retrospective study of all cases of aplastic anemia admitted in the medical wards from Ashwin 2054 to Ashwin 2056 was undertaken. All relevant data was recorded on a pro forma. For confirmation of diagnosis, the following conditions were obligatory (at least two of the following three criteria):

a) hemoglobin ≤ 100 gm / lt or hematocrit ≤ 30%

b) platelets, ≤ 50 x 10⁹ / lt, and
c) leukocytes ≤ 3.5 x 10⁹ / lt or granulocytes, ≤ 1.5 x 10⁹ / lt.

For bone marrow to confirm the diagnosis, there had to be an adequate bone marrow biopsy specimen showing the following:

a) a decrease in cellularity with the absence or depletion of all hematopoietic cells or normal cellularity due to focal erythroid hyperplasia with depletion of granulopoietic cells and megakaryocytes.
b) the absence of significant fibrosis or neoplastic infiltration.

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The patients were categorized into severe and non-severe, as per the criteria of the International Aplastic Anemia Study Group.

Management included cessation of further exposure to any suspected drug or toxic agent, maintenance of hemoglobin levels by blood transfusion and treatment of infection. Specific therapy of bone marrow transplantation was advised to patients less than 45 years; however, none of our patients could afford this form of therapy.

Cyclosporin A was administered in a dose of 5 mg/kg to ten patients. This was continued for at least 4-6 months. Patients were managed with supportive as well specific therapy. Nineteen patients received between 2-4 units of blood transfusion. Pulse methyl prednisolone was given to six patients in a dose of 20 mg/kg 1 to day 3, with gradual tapering off, over a period of 1 month and subsequent maintenance on 0.1 to 0.2 mg/kg/day. The response was assessed at 3 months and monthly thereafter. In case of response, the same dose was continued until the counts stabilized for 1 month. In patients who showed no response, alternative immunosuppressive agents were tried.

RESULTS:

Thirty one patients with aplastic anemia were admitted to the medical wards of BPKIHS over a two-year period. The age of the patients ranged from 15 to 65 years with a mean age at 40 years. Of these, twenty were in the age group 15-30 years. There were 20 males and 11 female patients. The mean age of males and females were similar.

<table>
<thead>
<tr>
<th>Age Distribution Table 1</th>
<th>Age group</th>
<th>Males</th>
<th>Females</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>15 - 30</td>
<td>13</td>
<td>9</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>31 - 45</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>46 - 60</td>
<td>3</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>&gt; 60</td>
<td>3</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>20</td>
<td>11</td>
<td>31</td>
</tr>
</tbody>
</table>

The most common clinical presentations included pallor, seen in nearly all the patients, bleeding-17 patients (54.8%), infection-12 patients (38.7%) and fatigue-11 patients (35.5%). There was a past history of jaundice in two patients. Ten patients (32.2%) gave a history of ingestion of medications (antibiotics and painkillers) in the past. None of the patients gave a history of exposure to radiation or antineoplastic drugs.

As per the International Aplastic anemia study group criteria, all the patients had moderate aplastic anemia. There was no patient with severe disease.

<table>
<thead>
<tr>
<th>Blood Picture Table 2</th>
<th>Haemoglobin</th>
<th>Absolute neutrophil count</th>
<th>Platelet count</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt; 4 g/dl</td>
<td>&lt; 500/mm3</td>
<td>&lt; 20,000/mm3</td>
</tr>
<tr>
<td></td>
<td>4 - 8 g/dl</td>
<td>500 - 1000/mm3</td>
<td>20,000 to 50,000/mm3</td>
</tr>
<tr>
<td></td>
<td>&gt; 8 g/dl</td>
<td>&gt; 1000/mm3</td>
<td>&gt; 1 lakh/mm3</td>
</tr>
</tbody>
</table>

DISCUSSION:

Thirty one patients of aplastic anemia over a two year period in this study implies that the incidence in Nepal is higher than that reported in a recently conducted European study. Seventy-one percent of our patients were in the age group of 15-30 years. This unusual peak in young people is almost four-fold higher than in comparable Western studies; this suggests an environmental etiology peculiar to Nepal. Similar results were obtained by Issaragrisil, et. al. who calculated the incidence rates for different age groups and found 7.2 cases/million population/year for the age group 15-24 years. A disproportionately large number of young males in our study compared to the nearly equal sex ratio in Western studies also points to an environmental etiology.

In our study there was no patient with severe aplastic anemia, hence it is unlikely that causative factors like exposure to benzene, radiation or antineoplastic drugs could be implicated in the etiology.
A significant number of our patients (32.2%) gave a history of ingestion of medications, like pain killers and antibiotics prior to the illness. However, it is difficult to prove the cause and effect of these drugs. Easy availability of over-the-counter medicines could be implicated in the etiology of aplastic anemia. The results of Issaragrisil, et. al. were quite contrary to our findings. Studies from Thailand implicated pesticide exposure as a common etiological agent for aplastic anemia. The Aplastic Anemia Study Group conducted a population-based case-control study and found an association with grain farming and agricultural pesticide exposure.

It would not be appropriate to implicate hepatitis virus as an etiological agent since only two patients gave a history of jaundice in the past. Brown et. al. concluded that "aplastic anemia does not appear to be caused by any known hepatitis virus". Immunosuppression is the only alternative form of therapy, since observations have revealed that some cases of aplastic anemia may be immunologically mediated. A randomized multicentre study, comparing the efficacy of antithymocyte globulin and prednisolone with that of cyclosporin as the first line of treatment, has demonstrated comparable response and survival rates followed by cross-over therapy for nonresponders. Cecil et. al. found low dose cyclosporin useful as a first line management of aplastic anemia. Response to immunosuppressive therapy is better if the patient is treated within 1 to 2 months after diagnosis. The chance of response is brighter in patients having a granulocyte count >200/mm³ and platelet counts >30,000/mm³.

To conclude, concrete steps are needed to decrease the morbidity and mortality from aplastic anemia. Strict regulation of the sale of medicines by the pharmacy could go a long way. Further, population-based case-control studies are needed to establish the role of pesticides in causing aplastic anemia.

REFERENCES: