Original Article

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Pathology Section

Aplastic Anemia in a Developing Country: The Present and the Need

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ABSTRACT

Introduction: Aplastic anemia (AA) a rare, yet a life threatening hematological disorder. Aplastic anemia if untreated results in very high mortality. Early diagnosis of Aplastic anemias is essential for appropriate management of the patient.

Aim: The aim of the study was to know the incidence of the disorder at our institution and categorize the patients into AA of varying severity aiding in their management protocol.

Materials and Methods: Study was conducted retrospectively between January 2011 to June 2012, and prospectively from july 2012 to December 2013 in the Department of Pathology at our institution. The peripheral blood, bone marrow aspiration and biopsy were slides assessed for various hematological parameters.

Results: Aplastic anemia has a male preponderance and bi modal age distribution. Anemia and thrombocytopenia were the commonest clinical manifestations.

Conclusion: A good knowledge on clinical and hematological parameters will certainly aid in early diagnosis of Aplastic anemia and sub-categorization for treatment. But in a developing country financial constraints and lack of awareness forms a major drawback in providing an apt patient management. Thus, management of aplastic anemia in a developing country is definitely a challenging task. It is the need of the hour that tertiary centers such as ours create awareness amongst the general population and develop hospital policies for a holistic approach in the management of aplastic anemia.

Keywords: Biopsy, Bone marrow aspiration, Severity

INTRODUCTION

Aplastic anemia (AA) is a rare hematological disorder in which there is failure of the stem cells to generate mature cells. The disorder is usually acquired and idiopathic or due to some underlying cause as drugs or pesticides [1,2]. A few of the cases are inherited.The exact incidence of AA is not known. According to a latin American study the incidence was 1.6 cases/1,000,000/year [3]. A prospective multi centric study reported incidence of 2.34 cases/ millon/year [4].

The patients with AA are at higher risk of infections and bleeding tendencies. An accurate diagnosis and timely management is essential to prevent morbidity and mortality of the patients. Bone marrow examination is gold standard for AA diagnosis. Very severe AA will require bone marrow transplantation. Proper guidance to patient regarding compliance to therapy and early referral to transplant centers is necessary.

We studied this rare disorder to assess the incidence of Aplastic anemia in our hospital and categorize the severity of the disorder in the patient for an apt management.

MATERIALS AND METHODS

The study was conducted retrospectively between January 2011 to June 2012, and prospectively from July 2012 to December 2013 in the Department of Pathology at Bangalore medical college and research institute, Bengaluru.

The inclusion criteria was patients with pancytopenia in the absence of hepatosplenomegaly. All patients with splenomegaly and pancytopenia were excluded from the study.

The clinical data of the patients were collected from the records. Complete blood examination of the patient which included hemoglobin (Hb) levels, total leukocyte count and platelet levels were done by automated cell counters. The bone marrow aspiration and biopsy slides reported as aplastic anemia were collected and assessed for various

hematological parameters in the retrospective part of the study.

In the prospective part of the study written consent was taken from the patientand bone marrow aspiration and biopsy were performed with all aseptic precautions on posterior superior iliac spine.

Out of 46 cases of pancytopenia, 15 cases of aplastic anemia were diagnosed as shown in [Table/Fig 1] based on the criteria laid down by the international agranulocytosis and aplastic anemia study group, 1987 which is defined as presence of at least 2 out of the following: (a) hemoglobin <10gm/dl, (b) platelet count < 50 x10^9/L, (c) neutrophil count < 1.5x10^9/L [5]. The cases of aplastic anemia thus diagnosed were sub classified as non severe, severe and very severe aplastic anemia.

The modified Camitta criteria are used to assess severity [5].

Severe AA; Marrow cellularity <25% (or 25-50% with < 30% residual haematopoietic cells), plus at least 2 of: a) neutrophils < 0.5 x 10^9/l; b) platelets < 20 x 10^9/l; c) reticulocyte count < 20 x 10^9/l reticulocyte count)

- Very Severe AA;

As for Severe AA but neutrophils < 0.2 x 10^9/L

- Non severe AA;

AA not fulfilling the criteria for severe or very severe AA.

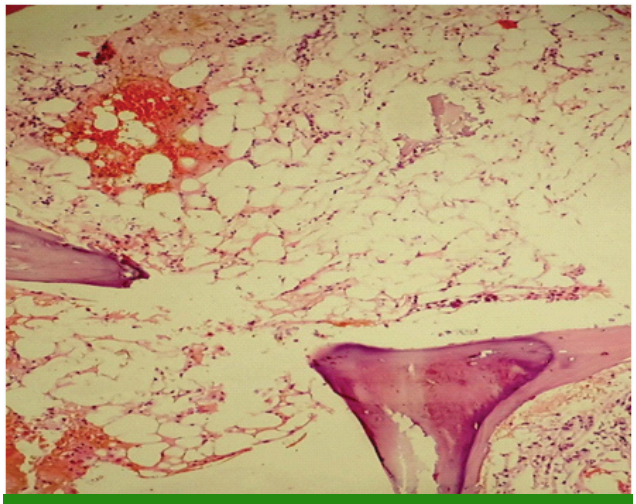
RESULTS

A total of 554 bone marrow aspirations were been done in our department during the study period. Among them in 85 cases, bone marrow study was done to evaluate pancytopenia. 46 pancytopenia patients who had no hepatosplenomegaly were included in our study. All 46 cases were investigated with both bone marrow aspiration and biopsy. Aplastic anemia was diagnosed in 15 cases. AA was 1.5 times common in males than in females. The gender and age group are as shown in [Table/ Fig-2].

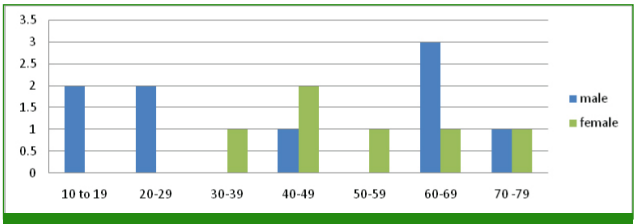
Clinical presentations of the patients showed easy fatigability in 8 cases, bleeding manifestations in 4 cases, fever in 2 cases and fever with bleeding manifestations in 1 case.

The various hematological parameters of these cases were analyzed which included hemoglobin levels, absolute neutrophil count, platelet levels, reticulocyte count and bone marrow aspiration with biopsy. The cases were then categorized into non severe, severe and severe types.

The hemoglobin level was < 5 gm/dl in 6 and between 5-10 gm/dl in 09 cases. The platelet levels < 20,000 in 7 cases, between 20,000- 50,000 in 6 cases and between 50,000 – 1,00,000 in 2 cases. The absolute neutrophil count was between 0.5- 1.5 x10^9/L in 9 cases and between 0.2- 0.5 x10^9/L in 5 cases and <0.2 x10^9/L in one case. The bone marrow aspiration of the patient showed dry tap in 6 cases. All the cases were hypocellular with cellularity of 25-50% in 7 cases. The marrow cellularity was <25% in 10 cases. Based on the various hematological parameters, aplastic anemia was subcategorized as shown in [Table/ Fig-3].



[Table/Fig-1]: Bone marrow biopsy showing marrow cellularity of <25% in a 17 years male.



[Table/Fig-2]: Shows age and gender distribution of aplastic anemia cases.

	Non severe AA	Severe AA	Very severe AA
No of cases	09 (60%)	05 (33%)	01(6.6%)

[Table/Fig-3]: Shows severity distribution of aplastic anemia.

DISCUSSION

Aplastic anemia is a rare but a life threatening hematological disorder. This disorder is clinically significant as awareness of the disease and through investigation with bone marrow examination is essential for diagnosis and its treatment. A well planned management protocol will have to be individualized for every patient along with monitoring for their progress and outcome [6]. The incidence of AA is 2-3 per million per year in Europe, but higher in East Asia [2]. The exact incidence of aplastic anemia in India is not known. Studies have shown that aplastic anemia is common in asian countries [7]. Hospital based studies show that 20 -40% of the pancytopenias are diagnosed as aplastic anemia [7]. In our study aplastic anemia accounted for 10.7% of pancytopenia cases. Male preponderance is seen in many

studies, similar to our study [8]. Montane et al., showed that there is a biphasic distribution, with peaks at 10-25 years and over 60 years similar to our study [4]. Anemia and bleeding tendencies were the commonest clinical presentation in our study similar to other studies.

Severe and very severe Aplastic anemia were more common than non-severe aplastic anemia in many studies [8,9]. But our study showed more of non-severe aplastic anemia, probably because the comparison data were from the referral centers. The assessment of degree of disease severity is important in treatment decisions. Bone marrow transplantation is considered best treatment option if matched sibling donor is available if not then immune suppressive therapy is considered next best option [10].

In our study follow-up of the patients through medical records was available only in 5 cases of which 2 were of severe and 3 of non-severe Aplastic anemia. All 5 cases had received only blood transfusions. According to the protocol of management as described by Marsh et al., the patients with severe and very severeAplastic anemia should be treated with anti thymocyte globulin with cyclosporine and bone marrow transplantation [5].

LIMITATIONS

The major limitation of the study was majority of our cases were lost on follow-up. All though a very well defined international treatment protocol is been set implementation of the same is difficult in many centers of India including ours although it's a tertiary center. Expensive medications and treatment option makes it certainly difficult to get patient compliance.

CONCLUSION

Aplastic anemia is a rare hematological disorder with a male preponderance and bi modal age distribution. Anemia and thrombocytopenia are the commonest clinical manifestations. A good knowledge of clinical and hematological parameters will certainly aid in early diagnosis of Aplastic anemia and sub-categorization of the disorder for better treatment. But in a developing country financial constraints and lack of awareness forms a major drawback in providing an apt patient management. Thus, management of aplastic anemia in a developing country is definitely a challenging task. It is the need of the hour that tertiary centers such as ours create awareness amongst the general population and more studies for affordable alternative treatment options should be established.

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