A STUDY OF CLINICOHEMATOLOGICAL PROFILE OF PANCYTOPENIA IN RIMS RAIPUR CHHATTISGARH

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ABSTRACT The aim of our study was to study the incidence of the underlying etiology of pancytopenia presenting at our institution with a clinical and hematological correlation. A prospective study of 12 months' duration was carried out, which included patients of all age groups. Of the 60 patients presenting with pancytopenia, bone marrow aspiration and biopsy were done on 32 cases, after taking an informed consent. Patients who had received previous blood transfusion and were on chemo- and radiotherapy were excluded. A detailed clinical examination of all cases was carried out. The most common etiology of pancytopenia in our study was normoblastic erythroid hyperplasia (30%), followed by megaloblastic anemia (20%). This was followed by acute myeloid leukemia (13.3%) and closely by micronormoblastic erythroid maturation (10%) and miscellaneous etiologies. The varied causes of pancytopenia can be attributed to the geographic area, genetic differences, stringency of diagnostic criteria, and differences in the methodology used. There are varying trends in its clinical pattern, treatment modalities, and outcomes. The severity of pancytopenia and the underlying pathology determines the management and prognosis. Thus, identification of the correct cause will help in implementing the appropriate therapy.

Introduction

Pancytopenia is an important clinicohematological entity.It is a disorder primarily or secondarily affecting bone marrow, manifesting, with various hematological derangements, which is reflected in the peripheral blood as pancytopenia. It is a disorder in which all the three major formed elements of the blood (red blood cells,white blood cells, and platelets) are decreased in number. Pancytopenia exists in an adult when the hemoglobin level is less than 13.3 g/dl in males or 11.5 g/dl in females,the leukocyte count is less than 4×10^9/L, and the plateletcount is less than 150×10^9/L.Pancytopenia, most of the time, is insidious in onset.The presenting symptoms are usually attributable to anemia and thrombocytopenia, Leukopenia is an uncommon cause of initial presentation, but can become a serious threat to life during the course of the disorder. The essential investigations required to make a diagnosis of pancytopenia are routine hematology and bone marrow examination. Bone marrow biopsy plays a significant role in understanding the etiology of pancytopenia. Other tests required in selected cases are radiological, microbiological, and biochemical investigations. Pancytopenia is not a disease entity, but a triad of findings that may result from a number of disease processes — primarily or secondarily involving the bonemarrow. The incidence of various disorders causing pancytopenia varies due to geographical distribution and genetic disturbances. It is a striking feature of many serious and life-threatening illnesses, ranging from simple drug-induced bone marrow hypoplasia and megaloblastic anemia to fatal bone marrow aplasias and leukemia.There are varying trends in its clinical pattern, treatment modalities, and outcomes. The severity of pancytopenia and the underlying pathology determine the management and prognosis. Thus, identification of the correct cause will help in implementing the appropriate therapy.

Materials and Methods

The present study was undertaken for over a periodof one year in the Department of Medicine, in RIMS RAIPUR CG. During the study period a total number of 60 cases of pancytopenia were collected. Of these,32 cases underwent bone marrow evaluation, all of whom are included in the present study. Patients of all age groups and both genders were included. Case selection was based on the clinical features and supported by laboratory evidence of pancytopenia. Clinical details like age, clinical signs and symptoms, various hematological parameters, and indication for bone marrow aspiration were recorded in the proforma. Clinical details with regard to drug intake, weakness, fever, weight loss,organomegaly, lymphadenopathy, bone pain, and gum hypertrophy were also recorded. The peripheral smear was examined along with the reticulocyte count. For bone marrow examination, the procedure was explained to the patient in detail in his own language and informed consent was taken. A peripheral smear was made just prior to performing bone marrow aspiration and the smears were stained by the Leishman stain for all cases and examined in detail. Bone marrow aspiration was done in a conventional manner. Bone marrow trephine biopsies were performed in cases wherever possible.Institutional ethical clearance was obtained for the study Inclusion criteria were the presence of all three of thefollowing;1 Hemoglobin level less than 13.3 g/dl in males or 11.5 g/dl in females.2 Total leukocyte count less than 4×10^9/L.3 Platelet count less than 150×10^9/L.Exclusion criteria were:1 Patients who received blood and blood products.2 Patients on radiotherapy and chemotherapy. The data compiled were analyzed for various parameters like age incidence, presenting symptoms, salient clinical findings, peripheral blood findings, and bone marrow morphology, and a final diagnosis was formulated.

Results

A total number of 32 patients, who presented with pancytopenia were studied. The age of the patients ranged from six to seventy-five years (mean age,42.5 years) with a male to female ratio of 1.3:1. The most common age at presentation was between 30 and 55 years (70%).The maximum number of cases was seen in the third decade of life, with a slight male preponderance. The most common presentation was fever seen in 37% of the cases, followed by easy fatigability and weakness, seen in 20% each.Lymphadenopathy at presentation was seen in 10% of the cases. A secondary immunocompromised state was seen in 7% of the cases.The most common cause of pancytopenia in our study was normoblastic erythroid hyperplasia (30%), followed by megaloblastic anemia (20%), which was followed by Acute Myeloid Leukemia (13.3%), and closely by cases of micronormoblastic erythroid maturation (10%).Other causes were hypocellular marrow accounting for 6.6% of the cases, followed by other causes such as aplastic anemia, acute lymphoblastic lymphoma (ALL),multiple myeloma, non-Hodgkin lymphoma infiltration,histoplasmosis, and myelofi brosis, accounting for 1%each. The ratio of the malignant to non-malignantcondition was 1:4.

Discussion

Pancytopenia is a serious hematological problem, which makes the patient prone to anemic manifestations, infections, and a tendency to bleed. Underlying this condition are many diseases, which are diagnosed by a complete hemogram, bone marrow aspiration, and trephine biopsy. In the current study the age at presentation of the patients ranged from six to seventy five years (mean age, 42.5 years) with a female to male ratio of 1.3:1. The most common age at presentation was between 30 and 55 years (70%). The maximum number of cases was seen in the third decade of life, with a slight male preponderance. In a similar study, Gayathri et al. observed pancytopenia in the age group of two to eighty years with a mean age of 41 years and M:F ratio of 1.2:1. Jha et al., observed pancytopenia in the age group of one to seventy-nine years, with a mean age of 30 years and M:F ratio of 1.5:1. The most common presentation in our study was fever, which was seen in 37% of the cases. The next common complaint was easy fatigability and weakness, seen in 20% each. In a study by Khodke et al., fever (40%) was the most common symptom followed by weakness (30%) and bleeding manifestation (20%). In another study by Niazi and Raziq, weakness (68.2%) was the most common symptom, followed by fever (47.7%) and bleeding manifestations (33.7%). Ramaswamy et al., observed generalized weakness and easy fatigability (88%) as the most common presenting complaints. A number of studies have been done on pancytopenia in India, documenting the geographic and demographic trends in this diverse disease process. In a study at Chandigarh, the most common cause of pancytopenia, as revealed by bone marrow examination, was aplastic anemia (40.6%) followed by megaloblastic anemia (23.26%). Another study at New Delhi found megaloblastic anemia, aplastic anemia, leukemia, myelodysplatic syndrome, paroxysmal nocturnal hemoglobinuria, overwhelming viral infections, and drug induced pancytopenia. In contrast, a recent study from eastern India has reported aplastic anemia (92.72%) as the most common cause, followed by hypersplenism, due to chronic liver disease (11.71%) and leishmaniasis (9%).

These differences in the etiology of pancytopenia are due to differences in population characteristics such as, age pattern, nutritional status, socioeconomic parameters, and prevalence of infection in a geographic region. The most common cause of pancytopenia in our study was normoblastic erythroid hyperplasia, seen in nine cases (30%). This was the second most common etiology in a study by Kumar and Raghupathi. The relationship of normoblastic erythroid hyperplasia to anemia is uncertain. It is suggested that some of the cases with normoblastic erythroid hyperplasia represent a phase in the evolution of hypoplasia/aplasia. It has been suggested that some of these cases may just simply be cases of refractory anemia. However, it has been suggested that whatever the reason behind the possible cause for this bone marrow picture, the criteria for differentiation of these groups still remain unsatisfactory and these patients should be kept under regular hematological follow up. Normal bone marrow in pancytopenia patients can result due to sequestration and/or due to destruction of cells by the action of antibody-mediated cells or trapping of normal cells by a hypertrophied reticuloendothelial system. The second common cause of pancytopenia in our study was megaloblastic anemia (20%), similar to the study by Tariq et al. It was the first common etiology seen in various studies of Khunger et al., Chandra et al., and Gayathri et al. In other similar studies its frequency ranged from as low as 13.04% to as high as 68%. The variation of incidence of megaloblastic anemia depended on the status of the nutritional anemia in that particular region of the study. However, serum B12 and folate levels were not available in our study to ascertain the exact cause of megaloblastic anemia. People in India and other developing nations continue to suffer from vitamin deficiencies, which cause anemia and pancytopenia. These are easily preventable if diagnosed and treated early.

The next common cause of pancytopenia was Acute (Myeloid) Leukemia, accounting for 13.3% of the cases, with a male: female ratio of 1:1. This correlated with the studies by Savage et al., and

Varma and Dash. In a study by Aziz et al., acute leukemia constituted 10% of the cases of pancytopenia and was the third most common cause of pancytopenia. In a developed nation, the bulk of the disease causing pancytopenia was due to malignancy or marrow aplasia. A careful and individualized approach to the diagnosis and management of this condition was needed. The next most common cause for pancytopenia was micronormoblastic erythroid maturation with iron-deficiency anemia (on treatment) as a possible cause for pancytopenia. The possible etiology of pancytopenia in patients receiving iron therapy is a phenomenon known as 'stem cell steals'. This has been described as a phenomenon in which the sudden increased availability of iron will result in the iron-deficient erythroid precursors, leading to the stimulation of the pluripotent hematopoietic stem cells toward erythropoiesis, and this occurs at the expense of the other hematopoietic cell lines. When iron supply is inadequate, intense erythropoietin stimulation may cause thrombocytosis, but when iron supply is available, erythropoiesis predominates and megakaryopoiesis may be transiently decreased. Other causes were hypocellular marrow accounting for 6.6 % of the cases. This was followed by other causes such as aplastic anemia, ALL, multiple myeloma, non-Hodgkin lymphoma infiltration, histoplasmosis in an immunocompromised patient, and myelofibrosis, accounting for 1% each. We encountered one case of multiple myeloma, constituting 3.3% of the total cases, which is comparable to a study done by Khodke et al., who have reported an incidence of 4%, Tilak et al., who have reported an incidence of 1.3%; and Khunger et al., who have reported an incidence of 1% in their studies. The incidence of aplastic anemia varies from 10 to 52% among pancytopenic patients. The number of aplastic anemia cases encountered in the current study has been less (3.3%), in contrast to a few other studies. As a large proportion of this disease affects the patient in the second decade, it cannot be considered in the pediatric category. However, a maximum number of cases in our study have been in the third decade. This correlates with the findings that studies with younger subjects have reported aplastic anemia more commonly. Similarly other studies have included recipients of cytotoxic drugs and patients on chemotherapy, and therefore, have reported that marrow hypoplasia is being common. This group is specifically excluded in our study, as it is unclear in such cases whether the etiology of marrow suppression is due to primary disease or chemotherapy.

Conclusion

The various causes of pancytopenia can be attributed to the geographic area, genetic differences, stringency of diagnostic criteria, and differences in methodology used. There are varying trends in its clinical pattern, treatment modalities, and outcomes. The severity of pancytopenia and the underlying pathology determine the management and prognosis. Thus, identification of the correct cause will help in implementing the appropriate management protocol. Clinical assessment followed by a complete hemogram and bone marrow examination is a very essential step in planning further management and prognosis of pancytopenic patients.

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