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CLINICO-HEMATOLOGICAL STUDY OF BONE MARROW EVALUATION IN A TERITARY CARE CENTRE.

Hematology

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ABSTRACT

Background: Bone marrow was first obtained from living patients for diagnostic purposes during the first decade of the 20th century but it was not until the introduction of sternal aspiration in the late 1920s which became an important diagnostic procedure.1 Bone marrow aspiration and biopsy are the obligatory tools, for the assessment of bone marrow cellularity, fibrosis, metastatic deposits and architectural patterns of histological diagnostic procedures. Bone marrow aspiration (BMA) examination is one of the most frequent and relatively safe invasive procedures. Though an invasive procedure, it can be easily performed even in the presence of thrombocytopenia with little or no risk of bleeding.2 **Methods:** A prospective study was conducted in the Upgraded Department of Pathology, Osmania government general hospital during July 2020 to June2022 that evaluated 368 patients referred for bone marrow evaluation. Detailed history, thorough clinical examination, complete hemogram, peripheral examination and reticulocyte count evaluation was performed in all the 368 patients. Bone marrow aspiration was performed in all 368 patients and in addition trephine biopsy was done in the same setting in patients where it is indicated. **Result:** The patients aged from 15 to 75 years, average age at presentation was 35.9yrs. The most common indication was pancytopenia (74%) followed by leukemia/lymphoma (18%), and ITP (3%). Majority (58%) of the patients had hyper cellular bone marrow followed by hypo cellular (34%) and norm cellular marrow (8%). **Conclusion:** Bone marrow examination helps to assess the spectrum of hematological disorder in both children & adult within a short span of time. The clinical findings and bone marrow examination provide precious information to help in planning investigations, such as immunophenotyping and cytogentic studies. In addition, an early recognition of the underlying conditions will certainly have an impact on the mortality and morbidity in vulnerable patients for better prognosis 3. Detailed primary hematological investigations coupled with bone marrow examination viewed in light of the history and physical findings are vital in establishing the diagnosis in pancytopenia patients. Bone marrow Aspiration and Trephine biopsy are complementary to each other in cases requiring both the procedures.

KEYWORDS

Pancytopenia, Megaloblastic anemia, Aplastic anemia, Bone marrow examination.

INTRODUCTION

The bone marrow is the largest and most widely distributed organ in the body. It is the principle site for blood cell formation. In the normal adult, its daily production and export of blood cells amounts to about 2.5 billion red cells, 2.5 billion platelets and 1.0 billion granulocytes per kilogram of body weight[1].

When peripheral blood smear is not informative, further bone marrow examination and higher investigations such as cytochemistry, immunophenotyping, cytogenetic analysis and molecular genetic studies can aid for arriving at a definitive diagnosis[4].

Bone-marrow aspiration is requested in various conditions including anemia, pancytopenia, and suspected cases of malignancies. Often, samples are inadequate on aspiration, and a biopsy needs to be performed simultaneously[5].

Anemia is very commonly encountered in developingcountries. Among the adult population in rural India, anemia is prevalent among 50% of the women, and 44.3%of the men.[6,7]

"Pancytopenia" is defined as the decrease in all the three formed elements in the blood that is erythrocytes, leucocytes and platelets which results in anemia, neutropenia and thrombocytopenia.[8]

Pancytopenia therefore exists in the adult when hemoglobin level is less than 13.5 g/dl in males or 11.5 g/dl in females; leucocyte count is less than 4 x 109/L and platelet count is less than 150 x 109/L.[9]

Pancytopenia is a serious hematological problem, the underlying cause of which is diagnosed by bone marrow aspiration and biopsy. Bone marrow examination is extremely helpful in the evaluation of pancytopenia.[10]

MATERIALS AND METHODS

The present study was conducted in the Upgraded Department of pathology, Osmania Medical College, Hyderabad on patients referred to hematology department for bone marrow study during the period of July 2019 to September 2021.

Study Design: Prospective study.

Study Period: The present study was conducted during July 2019 to June 2021.

Method Of Collection Of Data

Source Of Data: Records of patients referred to hematology department of Upgraded Department of Pathology at Osmania Government General Hospital, Hyderabad.

Sample Size: 368 Patients

Sampling Procedure: Data collected from the records of Hematology section of Upgraded Department of Pathology, Osmania government general Hospital Hyderabad.

Selection Criteria

Inclusion Criteria

1. Patients with age more than or equal to 15 years.
2. Patients with indication for bone marrow study.

Exclusion Criteria

1. Patients with age less than 15 years.
2. Patients on cancer chemotherapy.

Procedure

The study was approved by the Ethical and Research Committee of Osmania government general Hospital, Hyderabad. During the study period, all patients presenting with and fulfilling the inclusion criterion were included in this study after obtaining informed written consent.

All patients underwent bone marrow examination. These patients were subjected to routine hematological investigations.

The peripheral smear was studied after staining with Leishman's stain. Satisfactory samples of bone marrow can usually be aspirated form the sternum, iliac crest or anterior or posterior iliac spines. bone marrow and stain them with Romanowsky dyes as peripheral blood films. A trephine biopsy and aspiration biopsy can be carried out through the

same skin incision but with the bone being entered at two different points. Fix the specimen in 10% formalin solution buffered to pH 7. Sections of marrow should be stained as a routine by haematoxylin and eosin.

RESULT

Patient's age ranged from 15 to 75 years. Maximum number of cases was in the age group of 15 to 24 years (38%) . Out of 368 patients, 213 patients (58%) were males and 155 patients (42%) were females. Accounting a ratio of male to female was 1.3:1.

The commonest presenting complaints were generalized weakness (73%) followed by pallor (52%), dyspnea (22%), fever (18%).

Among total 368 cases splenomegaly 136(37%), icterus 128(35%), hepatomegaly 69(19%) and lymphadenopathy 35 (9%) was seen on clinical examination.

Sixty percent (60%) of patients had hemoglobin value less than or equal to 6 gm%.

Majority 55% had total leucocyte between 2100 to 3000 cells/cmm followed by 45% had between 3100 to 4000 cells/cmm.

Patients (68%) whose platelet count was less than or equal to 50000 cells/cmm had more bleeding tendencies as compared to patients who had platelet count of more than 50000 cells/cmm.

Majority (64%) of the patients had dimorphic blood picture on peripheral smear followed by Microcytic hypochromic picture (20%).

Majority (58%) of the patients had hyper-cellular bone marrow followed normo-cellular marrow 24% and hypo-celluar marrow 16%.

On bone marrow evaluation the most common cause of pancytopenia was megaloblastic picture seen in 213cases (58%) followed by leukemia/lymphoma 66cases (18%), aplastic anemia 59cases (16%) ,myelofibrosis 11cases(3%),ITP 11cases(3%),multiple myeloma 4cases (1%) and storage diseases 4cases (1%) .

In majority of patients of megaloblastic anemia bone marrow is hyper cellular (93.5%). Majority of patients in megaloblastic anemia had iron stores 1+ (50%) when graded after perls stain.

66cases (18%) out of 368 patients of pancytopenia were due to malignancy of hematolymphopoietic system involving the marrow.

4 (1%) out of 368 cases with majority falling in age group of 45-54yr with peripheral blood picture showing Normocytic hypochromic (50%)/ Microcytic hypochromic (50%) had hypercellular (50%) to hypo cellular marrow (50%), had marrow plasmacytosis with marrow plasma cells more than 10%

The commonest indications for trephine biopsy were to investigate Hypo plastic marrow and dry tap in our institution

DISCUSSION

In the present study out of 368 bone marrow studies conducted most common indication was Pancytopenia secondary to Megaloblastic anemia (58%) followed by leukemia/lymphoma 48cases (18%), aplastic anemia (16%).

The commonest cause of pancytopenia, reported from various studies throughout the world has been aplastic anemia or Megaloblastic anemia .[11] In our present study the commonest cause of pancytopenia was megaloblastic anemia. This seems to reflect the higher prevalence of nutritional anemia in Indian subjects as well as in developing countries.

The principal hematologic manifestations are varying degrees of anemia, leucopenia and thrombocytopenia, anisopoikilocytosis, macro ovalocytes and hypersegmented neutrophils.

In the present study, In majority of patients (64%) red blood cell morphology was dimorphic with anisopoikilocytosis. In majority of patients the reticulocyte count falls in range of 0.1-2%.

Erythroid hyperplasia with megaloblastic maturation was seen in all the 58% of patients.

Gagandeep Kaur et al.[12] in their study studied 784 bone marrow aspirations performed during a 69 months period, 9cases(1.1%) patients showed metastatic/malignant bone marrow involvement . In present study 66 (18%) out of 368 cases were cases of malignant /metastatic deposits involving the bone marrow which indicates that this subset of cases vary according to the population covered and the referral done to that particular tertiary care center.

In patients with MM, pancytopenia may be due to: (1) heavy BM infiltration by plasma cells causing BM failure, (2) drugs causing myelosuppression such as cytotoxic chemotherapy and anti-microbials, (3) infections such as septicemia or leishmaniasis, (4) renal failure induced erythropoietin deficiency, (5) cytokine-mediated BM failure, (6) fasligand-mediated apoptosis, and (7) associated: Myelodysplastic Syndrome (MDS), aplastic anemia, vitamin B-12 deficiency and auto- immune disorders such as idiopathic thrombocytopenic purpura, Evan's syndrome, autoimmune hemolytic anemia and pernicious anemia.[13]

In our study multiple myeloma cases were 1% of total cases. The presence of pancytopenia may be misleading in such cases and hence may be a cause for delay in the diagnosis and treatment. A differential of myeloma must be thought of in elderly patients with pancytopenia as it can be easily diagnosed by bone marrow examination and quantitative serum protein electrophoresis.[14]

CONCLUSION

The present study reveals megaloblastic anemia is the commonest cause in Indian scenario where it presents as Pancytopenia and becomes commonest indication for bone marrow evaluation .The etiology is nutritional and wide spread use of certain traditional medicines unknown.

Bone marrow examination is an important diagnostic tool in hematology which is instrumental in confirming the underlying diagnosis, or excluding a primary marrow involvement and suggesting alternative investigations for diseases like hypersplenism, PNH etc.

Bone marrow aspiration is sufficient to make a diagnosis in cases of nutritional anemias and initial diagnosis of leukemia. However, aspiration is often unsuccessful and may yield a dry tap in patients with aplastic anemia or myelofibrosis or metastatic deposits in marrow. Bone marrow trephine biopsy is essential for diagnosis in such conditions or when the aspiration is inconclusive.

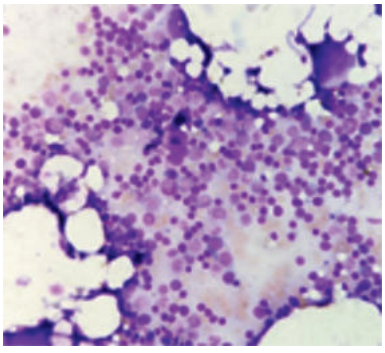

Fig-1 Bone Marrow Aspirate.

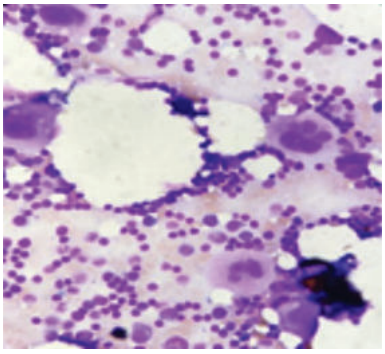

Fig 2- Increased Megakaryocytes

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