



A Study of Bone Marrow Aspiration Smears and Trephine Biopsy in Pancytopenia Cases

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ABSTRACT

Background: Pancytopenia is the simultaneous presence of anemia, leucopenia and thrombocytopenia. Peripheral pancytopenia may be a manifestation of a wide variety of disorders which primarily or secondarily affects the bone marrow. Bone marrow failure syndromes and malignancies are serious and life threatening causes, but certain non-malignant conditions such as infection, and nutritional anemia are equally important. The severity of pancytopenia and the underlying pathology determine the implementation of correct management and prognosis.

Methods: A prospective study was conducted in the Upgraded Department of Pathology, Osmania government general hospital during July 2011 to September 2013 that evaluated 110 patients fulfilling the criteria of pancytopenia. Detailed history, thorough clinical examination, complete hemogram, peripheral examination and reticulocyte count evaluation was performed in all the 110 patients. Bone marrow aspiration was performed in all 110 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 30.9 yrs. The most common cause of pancytopenia was Megaloblastic anemia (53%) followed by Nutritional anemia (16%), aplastic anemia (9%) and Leukemia's (7.4%). Majority (79%) of the patients had hyper cellular bone marrow followed by hypocellular (13%) and norm cellular marrow (8%).

Conclusion: A 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.

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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 weight¹.

“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.²

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 $4 \times 10^9/L$ and platelet count is less than $150 \times 10^9/L$.³

The spectrum of disorders primarily or secondarily affecting the bone marrow may manifest with peripheral pancytopenia. Patients usually present with complaints pertaining to anemia, thrombocytopenia and rarely leucopenia which in later stages is responsible for downhill course. Various factors encompassing geographical distribution and genetic disturbances may cause variation in the incidence of disorders causing pancytopenia^{4,5,6}. Underlying pathology determines the management and prognosis of the patients⁷.

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.⁸

Materials and Methods

The present study was conducted in the Upgraded Department of pathology, Osmania Medical College, Hyderabad on patients with pancytopenia during the period of July 2011 to September 2013.

Study Design: Prospective study.

Study Period: The present study was conducted during July 2011 to September 2013.

Source of Data: Patients diagnosed as pancytopenia after hemogram in the Upgraded Department of Pathology at Osmania Government General Hospital, Hyderabad.

Sample Size: 110 Patients with pancytopenia.

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

Inclusion Criteria

1. Patients with age more than or equal to 15 years.
2. Patients with pancytopenia.

Hemoglobin: Less than 13.5 gm/dL in males; 11.5 gm/dL in females.

Total leucocyte count less than 4000 /cmm.

Platelet count less than $1, 50,000$ /cmm.

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 from 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 were in the age group of 15 to 24 years (42%) and three cases were in the age group of More than 65 years (3%). Out of 110 patients, 55 patients (50%) were males and 55 patients (50%) were females. Accounting a ratio of male to female was 1:1.

The commonest symptom was shortness of breath (47%) followed by fever (20%), bleeding manifestations (14%), yellowish discoloration (11%), easy fatigability (3%). Pallor was universally present in all the patients followed by splenomegaly (37%), icterus (35%), hepatomegaly (19%) and lymphadenopathy (5%).

Seventy five percent (75%) of patients had hemoglobin value less than or equal to 6 gm%. Majority 36% had total leucocyte between 2100 to 3000 cells/cmm followed by 34% had between 3100 to 4000 cells/cmm. Patients (58%) 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 (62%) of the patients had dimorphic blood picture on peripheral smear followed by Microcytic hypochromic picture (20%). Majority (79%) of the patients had hypercellular bone marrow fig.1 followed by hypocellular (14%) and norm cellular marrow (8%).

The most common cause of pancytopenia was Megaloblastic anemia (53%) followed by Nutritional anemia (16%), aplastic anemia (9%) and Leukemia's (7.4%). In majority of patients of megaloblastic anemia bone marrow is hypercellular (96.5%). Majority of patients in megaloblastic anemia had iron stores 1+ (50%) when graded after perls stain.

Out of total 110 cases 10 cases were Aplastic anemia figure. 2. Out of 10 cases 4 cases had clinically significant history. These are listed below

1. 28 yrs. Female, known case of Plummer Vinson syndrome.
2. 59yrs. Male, known case of ITP.

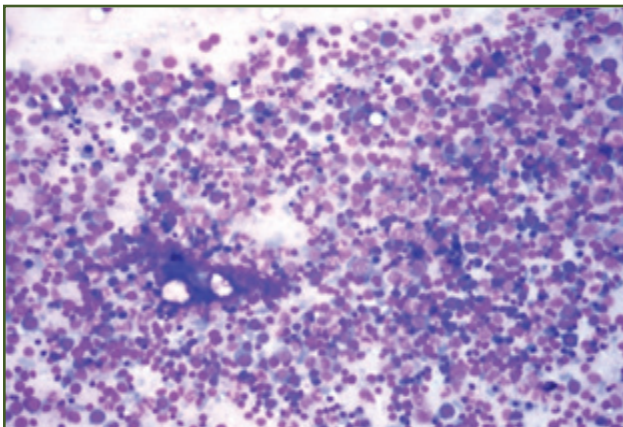


Fig.1: Picture Showing Hypercellular Marrow.

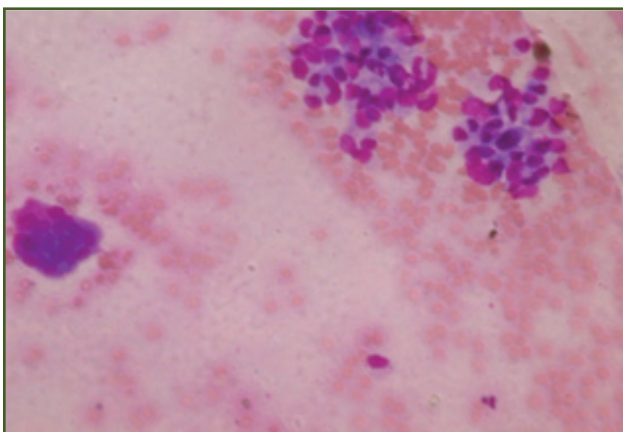


Fig. 3: Bone Marrow Aspiration Smears Showing Deposition of Small Round Cells.

3. 58yrs, female, known case of myasthenia gravis.
4. 23 yrs. Female, known case of RVD on Zidovudine.

Eight(7.40%)out of one hundred ten patients of pancytopenia were due to malignancy of hematolymphopoietic system involving the marrow. All the cases were acute leukemia's. 5(62%) out 8 were of myeloid series, 3(38%) out of 8 were of lymphoid series. Seven (6.30%) out of one hundred ten patients of pancytopenia were due to hypersplenism. The commonest age of presentations was between 25-34 yrs. 4 (3.60%) out of 110 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%

Three (2.70%) out of one hundred ten cases of pancytopenia were cases of metastatic deposits involving the bone marrow figure 3&4. The commonest indications for trephine biopsy were to investigate Hypo plastic marrow and dry tap in our institution table.2.

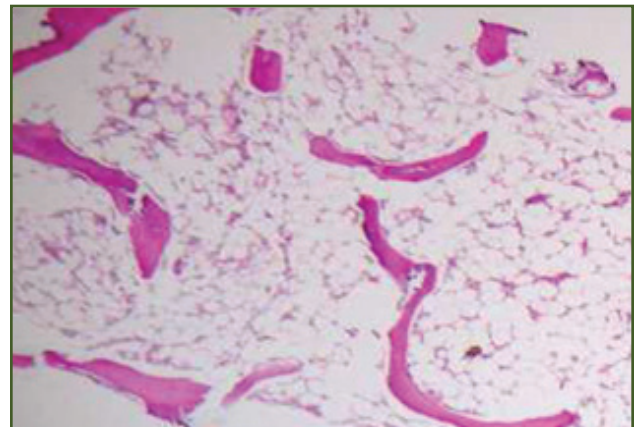


Fig. 2: Bone Marrow Biopsy of Aplastic Anemia

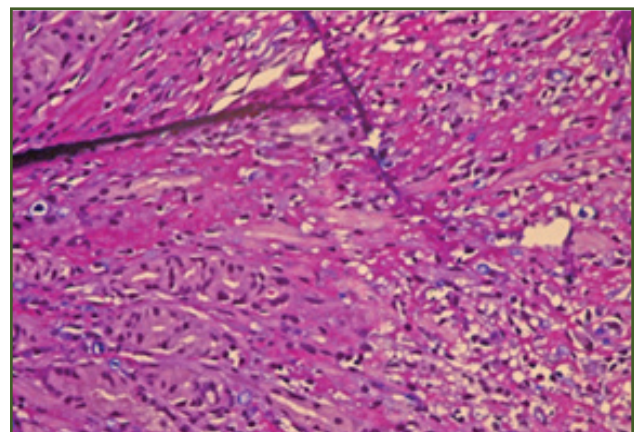


Fig. 4: bone marrow biopsy showing metastatic deposits of Adenocarcinoma(alcian blue stain).

Table 1: list of cases with metastatic deposits in bone marrow

Age (yrs.)	sex	BM NO.	Biopsy No.	P.s	aspiration	Biopsy Impression
17	male	59/12	1625/12	Normocytic/Hypochromic	Dry tap	Metastatic deposit of spindle cells. Advised IHC
30	male	109/13	2949/13	Microcytic/Hypochromic	Dry tap	Metastatic deposits of Round cells ?NHL Advised IHC
50	male	110/13	3225/13	Normocytic/Hypochromic	Dry tap	Metastatic deposits of Adenocarcinoma

Table 2. Number of patients undergone Trephine Biopsy and their indications.

Indication for trephine biopsy	Number of patients
Hypo plastic marrow	7
Dry tap	6
Rule out granuloma	1
Malignancy	3
Total	17

Discussion

In the present study out of 110 cases studied the most common cause was Megaloblastic anemia (53%) followed by Nutritional anemia (mixed) (16%), aplastic anemia. The commonest cause of pancytopenia, reported from various studies throughout the world has been aplastic anemia. This is in sharp contrast with the results of present study where 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 (68%) red blood cell morphology was dimorphic with anisopoikilocytosis. In majority of patients the reticulocyte count fall in range of 0.1-2%. Erythroid hyperplasia with megaloblastic maturation was seen in all the patients.

Hypersplenism (19 %) was the second most common cause of pancytopenia as studied by Osama Ishtiaq et al.⁹, (12 %) due to portal hypertension, (5 %) due to chronic malaria and (4 %) were undiagnosed. In present study Seven (6.30%) out of one hundred ten patients of pancytopenia were due to hypersplenism. The commonest age of presentations was between 25-34 yrs. (43%) with overall female predilection.

Gagandeep Kaur et al.¹⁰ in their study studied 784 bone marrow aspirations performed during a 69 months period, 9(1.1%) patients showed metastatic bone marrow involvement. In present study Three (2.70%) out of one hundred ten cases of pancytopenia were cases of metastatic deposits involving the

bone marrow. One case was adenocarcinoma, others needed Immunohistochemistry evaluation.

Conclusion

The etiological spectrum of pancytopenia is diverse. The present study reveals megaloblastic anemia is the commonest cause in Indian scenario where 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 anemia's 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. Thus both procedures are complimentary and help in providing a prompt and precise diagnosis in the Setting of pancytopenia.

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Competing Interests

None declared

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