ORIGINAL ARTICLE

Etiologic Spectrum and Clinical Features of Pancytopenia: A Hematological Study in a Tertiary Care Hospital at Quetta

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ABSTRACT

Objective: To determine the clinical profile, etiological spectrum and bone marrow findings of patients presenting with pancytopenia.

Patients and Methods: This was the cross sectional observational study conducted in the Department of Pathology, Hematology Section, Bolan Medical Complex, Teaching Hospital Quetta spanning over a period of five years from January 2009 to January 2014. Four hundred and two patients fulfilled the criteria of pancytopenia. Routine complete blood count (CBC), peripheral blood smear (PBS) and bone marrow aspirations (BMAs) done on all patients. Bone marrow trephine biopsies (BMTBs) were done where needed. These procedures were performed according to standard methods. SPSS-11 was used to analyze the data.

Results: Out of 402 patients 32.8% were of megaloblostosis, 25.4% hypocellular marrow, 11.4% normocellular marrow, 5.2% acute lymphoblastic leukemia (ALL) and visceral leishmaniasis (VL) each, 4.5% mixed deficiency anemia (MDA), 0.8% acute myeloid leukemia (AML), malaria 2.7%, idiopathic thrombocytopenic purpra (ITP) 2.8 and 1.5% hypersplenism. Male to female ratio was 1.4:1. The commonest presenting complaint was pallor (69.52%), fever (27.20%) bleeding manifestations (15.6%), bleeding with fever (9.9%) and others.

Conclusion: Complete blood count, peripheral blood smear and bone marrow aspiration and in some cases bone marrow trephine biopsies are of paramount importance in diagnosing patients with pancytopenia. As a large number of pancytopenic patients are having benign and reversible causes, an early and prompt diagnosis is mandatory for the purpose of making appropriate therapeutic decisions.

Key words: Pancytopenia, Etiologic Break-up, Bone marrow examination

INTRODUCTION

Pancytopenia is a reduction in all three formed elements of blood to the level below the lower normal limit leading to simultaneous presence of anemia, leucopenia and thrombocytopenia. Thus, it is not a disease entity by itself, but rather a triad of findings[1]. It is regularly encountered in hematology practice[2]. As far as causes of pancytopenia are concerned there may be inherited causes of bone marrow failure like Fanconi anemia, Dyskeratosis congenital, Shwachman–Diamond syndrome, congenital amegakaryocytic thrombocytopenia and hemophagocytic lymphohistiocytosis. Mostly multiple gene defects are responsible for the development of these disorders[3]. Beside these, other common causes secondarily producing pancytopenia are decrease in hemopoietic cell production in bone marrow e.g. by infection, toxins, malignant cell infiltration or suppression, or can have normocellular or even hypercellular marrow without any abnormal cells[4]. Ineffective hematopoiesis with cell death in marrow, formation of defective cells which are rapidly removed from circulation, sequestration and/ or destruction of cells by action of antibodies or trapping of normal cells in a hypertrophied and over reactive reticuloendothelial system[5].

The aim of this study was to determine the clinical profile, etiological spectrum and bone marrow findings of pancytopenic patients. The study focused on identifying easily treatable and reversible causes of pancytopenia[6]. The data will help in planning the diagnostic and therapeutic approach to patients with pancytopenia. Bone marrow examination is an established diagnostic modality in the evaluation of various causes of these disorders[7].

PATIENTS AND METHODS

The cross sectional observational study was under taken at the Hematology Section, Department of

Pathology, Bolan Medical Complex Teaching Hospital, Quetta (Baluchistan) from January 2009 to January 2014. Patients of all age groups and of both sexes were included. Case selection was based on cases referred by clinicians from different medical and oncology wards of Bolan Medical Complex Teaching Hospital Quetta to Hematology Section for bone marrow aspiration and trephine biopsies supported by Laboratory evidences, which included peripheral blood count and smears, hemoglobin (Hb), total leukocyte count (TLC), and platelet count (PLT). All patients with Hb <10 Gm/ dl, TLC <4000/ µl, and PLT <100,000/ µl were included in study[8]. Patients on myelotoxic chemotherapy were excluded. Two milliliters of EDTA (Ethylene diamine tetra acetic acid) anticoagulated blood was collected and processed through automated hematology analyzer and hematological parameters were obtained, which included Hb, red blood cells (RBC) count, TLC. Differential leukocytic count (DLC), PLT, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC). Erythrocyte sedimentation rate (ESR) was estimated in all cases by Westergren's method. Peripheral smear was stained by Leishman stain for all the cases and examined in detail. Bone marrow aspiration was subsequently carried out under aseptic percutaneous technique after obtaining consent from the patient. Bone marrow biopsies were done where needed. SPSS-11 was used to analyze the data.

RESULTS

A total of 402 patients of peripheral pancytopenia were analyzed. The mean age of patients was 23.77±18.41 years. Two hundred thirty two (57.71%) were male and 170 (42.28%) were female. Male to female ratio was 1.4:1. The commonest presenting complaint was pallor in 276 (68.65%), fever 108 (26.86%), bleeding manifestations in 62 (15.42%), and bleeding with fever in 40 (9.95%) cases (Table 1). Generalized weakness was, one of the commonest symptom seen. Similarly splenomegaly, hepatomegaly and lymphadenopathy were the most frequent signs and physical findings observed in patients in descending order (table 2). The most common cause of pancytopenia was megaloblastosis in 132 (32.83%) cases followed by hypocellular marrow 102 (25.37%), normocellulr marrow 46 (11.44%), acute lymphoblastic leukemia 21 (5.22%), VL 21

Table 1: Presenting complaints

Presenting complaint	No.	%
Easy Fatigability	276	68.65
Fever	108	26.86
Bleeding manifestation	62	15.42
Fever with bleeding	40	9.95
Bony Tenderness	16	4.00
Pallor with fever	13	3.23
Dyspnoea	11	2.73
Weight loss	9	2.23
Jaundice	6	1.5
Rigors	4	1.00

Table 2: Physical findings

Physical findings	No.	%
Pallor	276	68.65
Lymphadenopathy	14	3.5
Splenomegaly	67	16.66
Hepatomegaly	05	1.24
Hepatosplenomegaly	34	8.45
Lymph node + organomegaly	05	1.24

Table 3: Etiologic association of pancytopenia cases n= 402

Etiologic break-up	No.	%
Normocellular marrow	46	11.44
Malaria	11	2.73
Megaloblastosis	132	32.83
AML	8	2.0
ALL	21	5.22
Hypocellular marrow	102	25.37
MDA	18	4.47
ITP	11	2.73
VL	21	5.22
Iron deficiency Anemia	3	0.75
Matastasis	5	1.24
Myeloid Hyperplasia	3	0.75
Storage disorders	1	0.24
Myelofibrosis	2	0.5
Megakaryocytic Hyperplasia	2	0.5
Multiple myeloma	1	0.24
Diagnosis undetermined	1	0.24
Erythroid Hypoplasia	1	0.24
Erythroid Hyperplasia	3	0.75
Bone Marrow hyperplasia	3	0.75
VL with HIV	1	0.24
Hyperspleniam	6	1.5

(5.2%) each and MDA 18 (4.47%). The other causes of pancytopenia were malaria, ITP, AML, hypersplenism, marrow matastasis, myeloid hyperplasia, iron deficiency anemia, erythroid hyperplasia, bone marrow hyperplasia, mylofibrosis, megakaryocytic hyperplasia, storage disorders, multiple myeloma, erythroid hypoplasia, visceral leishmaniasis with HIV (co-infection) and a single case undetermined etiology (Table 3). The mean Hb in all cases of pancytopenia was 6.51±2.12 Gm/ dl, Mean TLC was 2.44±0.41/ µl and Mean platelet count was 42.08±30.6/ µl.

DISCUSSION

Pancytopenia is a serious hematological disorder which warrants further investigations to establish the etiology. Most of the disorders associated with pancytopenia are diagnosed through Bone marrow aspiration and trephine biopsy[9] which is regarded as first line and key investigation. The mechanism by which pancytopenia develops appears to be either associated with decrease in hemopoietic cell production, as a result of destruction of the marrow tissue by toxins, replacement by abnormal or malignant tissue or through suppression of normal growth and differentiation.

In the present study easy fatigability (68.55%) was the commonest symptoms followed by fever (26.86%) and bleeding manifestations (15.42%). In a study Khodke et al[10] reported that fever was the commonest symptoms followed by weakness (30%) and bleeding manifestations (20%). In another study Niazi and Raziq[8] reported that weakness (68.2%) were the commonest symptoms, followed by fever (47.7%) and bleeding manifestations (33.7%). Pallor (68.65%) was the most common sign followed by splenomegaly (16.66%) and hepatosplenomegaly (8.45%). In studies done by Khodke et al[10] and Niazi and Raziq[8] reported that pallor and hepatosplenomegaly were the commonest signs as in the present study.

A diverse variety of disorders can cause pancytopenia. The prognosis depends on severity of pancytopenia and on the nature of underlying cause. Causes of pancytopenia differ in different studies conducted in different countries[10-18] due to difference of prevalence of various disorders in communities. The commonest cause of pancytopenia in the present study was megaloblastic anemia (32.83%). Bone marrow aspiration was sufficient to establish the diagnosis in majority of megaloblastic anemia cases. Hypercellular and normocelluar marrow was observed and dyserythropoietic changes were seen in few of cases with megaloblastosis. Shift to right was seen in neutrophils in substantial number of cases. Increased incidence of megaloblastic anemia correlated well with the high prevalence of nutritional anemias and poor socio-economic status of the patients. Chronic diarrheas–Rota virus infection in children causes folate deficiency.

Findings of Tilak and Jain[14], Savage et al[15], Khodke et al[10] Khunger et al[13] and Gayathri & Rao[17] agree with the findings of the present study. The incidence of megaloblastic anemia in other studies varied from 0.8% to 68%[8-10,13-18-19]. Systemic lupus erythematosus should be included in the differential diagnosis of every adolescent with pancytopenia. An accurate diagnosis with the appropriate therapy is vital and can cause lasting reversal of this condition[20].

The second most common cause of pancytopenia in the present study was hypoplastic marrow (25.37%). The incidence of aplastic anemia quoted from West is (10-25%).[10,11] Bone marrow trephine biopsies were performed to confirm the diagnosis. In studies conducted in different places of subcontinent, the incidence of hypoplastic marrow ranges between 7.7% to 43%[1-3,5-11].

The 3rd common cause in the present study was acute lymphoblastic leukemia especially in children and visceral Leishmaniasis (5.22%) each. One case of HIV positive with Leishmaniasis was detected (0.24%). Bone marrow smears were flooded with LD bodies especially in macrophages. Significant number of patients in this category came from Afghanistan. The easy availability of over the counter drugs without prescription may be playing an important role in it.

CONCLUSION

The varied causes of pancytopenia can be attributed to the geographic area, genetic differences, and stringency of diagnostic criteria, and concludes that bone marrow examination is playing a pivotal role in diagnosing the various etiologies of pancytopenia. As a large number of pancytopenic patients have a benign and reversible etiology, the early and prompt diagnosis may be life saving, avoiding the battery of tests and in the wake alleviating misery and financial burdon on the patients.

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