Research Paper

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Clinical Profile of Pancytopenia in Adults

Medical Science

KEYWORDS :
PANCTOPENIA,MEGALOBLASTIC ANEMIA ,BONE MARROW

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ABSTRACT

AIMS AND OBJECTIVES a)To study etiology,clinical features , complications and outcome after treatment of Pancytopenia .

MATERIAL AND METHODS: - The study included 50 patients with Pancytopenia above 12 yrs of age. The patients were followed up after 2 weeks and 1 months interval .

INVESTIGATIONS :- Hemogram Including Hb ,Blood indices ,RDWs, DDLC ,Reticulocyte Count Bonemarrow aspiration + Biopsy ,ESR, USG abdomen Chest X-ray. Wherever indicated Vit B 12 levels ,Sr. LDH levels, Cluster differentiation for cell., Sr. Fe / TIBC Sr., Ferritin, HIV, Bone marrow Culture ,Blood Culture , ANA, ds DNA ,Special Stains for leukemia ,Ham's Test ,Brucella antigen test , Sr ACE level.

OBSERVATIONS Out of the 50 cases, 31 were males and 19 females. The ETIOLOGY in these 50 cases was as follows Megaloblastic anemia 25(50%) Hypoplastic / aplastic anemia 10(20%),Subleukemic leukemia 4(8%) ,Myelodysplasia 3(6%), Hypersplenism 2(4%), Idiopathic thrombocytopenia 2(4%), Tuberculosis 1(2%), Falciparum Malaria 1(2%) ,Myelofibrosis 1(2%) and Metastatic carcinoma 1(2%)Common symptoms were pallor 49, Fever 24,generalized weakness 27,dyspnoea 24.bleeding manifestations 17,pedal edema 7, jaundice 8,ascites 1, loose motions 9,Hepatomegaly 21 ,Splenomegaly 18, Lymphadenopathy 8. Bleeding manifestations like epistaxis, gum bleeding, PV bleeding and petechial rash were common in hypoplastic / aplastic anemia group All the four cases of subleukemic leukemia were showing lymphadenopathy PBS picture Anisocytosis in (58%), NCNC morphology in(34%) and dimorphic picture in (8%) cases. Hypersegmented polyrnorphs was the commonest peripheral blood finding in megaloblastic anemia. Reticulocytosis was increased in 10 out of 50 cases of pancytopenia (20%). The Hb ranged from 2 to 9 gm/dl, platelet counts ranged from 10,000/mm^3 - 1.26 lakh/mm^3 . COMPLICATIONS seen in 37 pts(74%) in the form of UTI, LRTI ,GI and Skin infections ,FUO, GI and Mucosal bleeding, and CCF . RECOVERY good clinical and Hematological recovery was seen in all pt with specific treatment.

Introduction

Pancytopenia is not a disease entity, but a triad of findings of anemia, leucopenia and thrombocytopenia that may result through different mechanisms like destruction of marrow tissue by toxins, radiation (aplastic or hypoplastic marrow), replacement by abnormal or malignant tissue like Hodgkin's and non-Hodgkins lymphoma, multiple myeloma, myelofibrosis, or suppression of normal marrow growth and differentiation like megaloblastic anemia, systemic lupus erythematosus (SLE)4.

In literature there are few comprehensive studies on pancytopenia in India, and the causes of pancytopenia are not well defined. This data, if available, would help in planning the diagnostic and therapeutic approach in patients with pancytopenia 15. . This study was undertaken to diagnose the cases of pancytopenia and to ascertain the cause for it, which would help in initiating early and effective treatment.

AIMS AND OBJECTIVES 1)To study clinical features and complications of Pancytopenia.2)To study etiology of pancytopenia. 3) To study treatment outcome and mortality.

MaterialAND Methods

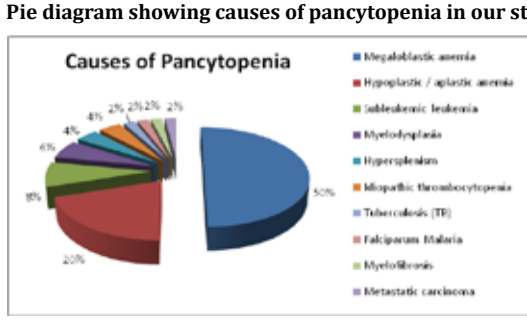
The study included 50 patients above 12 yrs of age. The patients were followed up after 2 weeks and 1 months interval. Anemia :- Male :- < 13.5 gm% Female :- < 12.0 gm%Thrombocytopenia :- < 150 x $10^{9/L}$ Leucopenia :- < 4.5 x 109/L Or

ANC :- < 1000 / cumm Exclusion Criteria :- Bicytopenia , Monocytopenia

Investigations :- Clinical profile governed the investigation for a particular case. Hemogram Including Hb ,Blood indices, RDWs, DLC Reticulocyt Count ,Bone marrow aspiration Biopsy, ESR, USG abdomen and Chest X-ray was done in all patients.. Wherever indicated Vit B 12 level ,Sr.LDHlevels, Cluster differentiation for cell. Sr. Fe / TIBC ,Sr. Feritin ,HIV, Bone marrow Culture ,Blood Culture ,ANA, ds DNA ,Special Stains for leukemia ,Ham's Test, Brucella antigen test and Sr. ACE level were done.

OBSERVATIONS

Pie diagram showing causes of pancytopenia in our study



AGE AND SEX DISTRIBUTION

The age range of patients in our study was 12 years to 69 years. Commonest age 21-30 years ,31 were males and 19 females. Slight male preponderance was seen. The overall male to female ratio was 1.63:1 . (30%) belonged to third decade, 20% second decade and 18% third decade.

CLINICAL FEATURES OF PANCYTOPENIA

-Progressive pallor, generalised weakness, fever, dyspnoea were the commonest clinical features in this group. Hepatomegaly was seen in 11 cases (44%) and splenomegaly in seven cases (28%) of megaloblastic anemia.

PERIPHERAL BLOOD FINDINGS

Anisocytosis of varying severity was the commonest morphologic type (58%) followed by normocytic normochromic (34%) and dimorphic picture (8%) in the decreasing order of frequency.**Normocytic normochromic anemia** was common finding in all other causes of pancytopenia except for megaloblastic anemia and myelofibrosis where anisocytosis was common accounting for 22 cases (88%) and one case (100%) respectively. In myelofibrosis, it was showing characteristic tear drop red cells. **Hypersegmented polyrmorphs** was the commonest peripheral blood finding in megaloblastic anemia. **Reticulocytosis** was seen in 10 out of 50 cases of pancytopenia(20%)

HEMOGLOBIN LEVEL -The hemoglobin levels of patients in our study ranged from 2 to 9 gm/dl 19 cases (38%) had hemoglobin levels between 3 to 5 gm/dl suggesting severe degree of anemia at the time of presentation as pancytopenia.Hemoglobin levels were more severely reduced in hypoplastic / aplastic anemia group.

LEUCOCYTE COUNTS

The total leucocyte counts of patients in our study ranged from 1000-4000/mm3 Maximum number of cases i.e. 50% cases fell in 3000-4500/mm3 range of total leucocyte count. The total leucocyte count between 1000-2000/mm3 were seen more commonly in hypoplastic/aplastic anemia (80%) and subleukemic leukemia (25%) groups.

PLATELET COUNT DISTRIBUTION IN VARIOUS CAUSES OF PANCYTOPENIA

The platelet counts of patients in our study ranged from 10,000/mm3 - 1.26 lakh/mm3 Majority i.e. 23 cases (46%) had platelet counts between 50,000/mm3 - 1 lakh /mm3 . 8% of the patients had platelet counts below 20,000/mm3 and all these patients were from hypoplastic/aplastic anemia group.

BONE MARROW FINDINGS

Out of 50 patients bone marrow study was done in 47 patients ie 94%. In remaining 3 (6%) patients cause of pancytopenia were obvious (Hypersplenism and Falciparum Malaria) so bone marrow examination was avoided.

Out of 22 cases of pure megaloblastic anemia, iron was increased in 18 cases (8l.81 %) Out of three cases of dimorphic anemia, iron was reduced in two cases (66.66%),Reticulin was normal in all cases except for myelofibrosis, in which it is increased upto grade 3. Out of 25 cases, 22 cases (i.e. 88%) showed pure megaloblastic anemia of varying severity whereas three cases (12%) showed dimorphic anemia, i.e. combination of iron deficiency and megaloblastic anemia in varying proportions. Of the **eight cases of hypoplastic anemia**, one case had a history of pulmonary tuberculosis and whose bone marrow biopsy showed hypoplasia along with granulomatous inflammation. Of the **two cases of aplastic anemia**, one patient was coal tar worker for the last 20 years .

COMPLICATIONS

Out of 50 patients, 37 patients (74%) showed complications related with pancytopenia. Out of those 37 (74%) patients, 22 (44%) complications were infective, bleeding was seen in 13 (26%) and 2 (4%) cases had CCF.In infections, most common were FUO - 6 (12%) and GI infections - 5 (10%) and in bleeding, mucosal bleeding was common followed by GI bleeding.

TREATMENT OUTCOMES -During hospital stay and during one month follow up there was no mortality . All patients (100%) showed symptomatic improvement. Patients with Megaloblastic anemia, TB & Falciparum Malaria showed complete clinical as well as hematological improvement but in the rest of the patients mild pancytopenia persisted during follow up. **.**

DISCUSSION

The commonest cause for pancytopenia in our study was megaloblastic anemia which is consistent with those of Tilak V, et al and Khcdke K. et al in their study of 77 and 50 cases of pancytopenia respectively 15,4. This was followed by aplastic anemia which is the commonest cause in the studies of Kumar R et al and Niazi M. et a1 8,2. .

Age and Sex distribution of cases studied

The age range in our study was 12 years to 69 years. The maximum number, i.e. 37 cases (74%) occurred below the age of 40 years with majority, i.e. 28 cases (56%) occurring in second and third decade, the commonest age group for presentation being between 21-30 years .. A slight male preponderance was seen. The overall male to female ratio was 1.63: 1. Other studies also have reported similar results (7) of younger age group with 60% of cases occurring below 30 years of age.

LABORATORY DATA AND CLINICAL FEATURES ESPECIALLY IN MEGALOBLASTIC ANEMIA In the present study progressive pallor was the most common clinical feature and it was found in almost every case. Generalised weakness (48%), Fever (54%) and dyspnoea (48%) were the other common presenting features. Bleeding manifestations were seen in 34% cases. Hepatomegaly was present in 42% cases while splenomegaly was seen in 34% cases. (7,2).

In the present study, anisocytosis of varying severity was the commonest morphologic type (58%) followed by normocytic normochromic (34%) and dimorphic anemia (8%) . Hypersegmented polymorphs were in 48% cases, circulating immature cells in 14% cases, relative lymphocytosis in 24% and reticulocytosis in 20% cases. Tilak V. et al have also reported commonest morphologic type as anisocytosis in 64% cases of pancytopenia. They have also reported hypersegmented polymorphs in 45% cases, circulating immature cells in 1.29 % cases, relative lymphocytosis in 14.28% and reticulocytosis in 7.79% cases in their study of 77 cases of pancytopenia (15). Khodke K. ct al have also reported anisocytosis in 60% cases of pancytopenia representing the commonest morphologic type. They have also reported hypersegmented neutrophils in 40% cases, circulating immature cells in 4% cases, relative lymphocytosis in 10% cases and reticulocytosis in 6% cases, in their study of 50 cases of pancytopenia (77.)

In the present study, 19 cases (38%) had hemoglobin levels between 3 to 5 gm/dl, suggesting severe degree of anemia at the time of presentation. 25 cases (50%) had total leucocyte count ranging from 3000-4500/mm3. Only nine cases (18%) had it below 2000/mm3. 23 cases (46%) had platelet counts between 50,000- 1 lakh/mm3 and only four cases (8%) had platelet counts below 20,000/mm3.

In our study, 20 cases (80%) of megaloblastic anemia had hemoglobin level ranging from 3 to 7 gm/dl suggesting moderate to severe degree of anemia. Anisocytosis was seen in 88% of cases. 16 cases (64%) of megaloblastic anemia had TLC ranging from 3000-4000/mm3. 18 cases (72%) had mild to moderate thrombocytopenia (Platelet counts above 50,000/mm3. Only one case showed reticulocytosis. Hypersegmented polymorphs were seen in 23 cases (92%) of megaloblastic anemia. Thus, our observation suggest that leucopenia and thrombocytopenia in megaloblastic anemia are usually milder than anemia and that the reduction in leucocytes and platelets, increases with the severity of the anemia. And also that megaloblastic anemia is a common cause of macrocytic pancytopenia and by far the most readily treatable cause.

HEMOGLOBIN, PERIPHERAL SMEAR AND PLATELET COUNT IN OTHER CAUSES OF PANCYTOPENIA—

Out of 10 cases of **hypoplastic/aplastic anemia** group, seven cases (70%) had hemoglobin level below 5 gm/dl suggesting severe degree of anemia. . Normocytic normochromic morphology was seen in seven cases (70%). Reticulocytosis was seen in four cases (40%). In aplastic anemia, reticulocyte count is normal or low, however, a relatively high reticulocyte count is a good prognostic factor 4,8,,13,9. which was found in our four cases. Eight cases (80%) had TLC ranging from 1000 to 2000/mm3 with relative lymphocytosis in five cases (50%). Out of the ten cases, four cases (40%) had platelet count below 20,000/mm3. Additional four cases had platelet count between 20,000 to 50,000/mm3. Progressive pallor (100%), fever (70%) and bleeding manifestation (60%) were the commonest presenting features indicating towards severity of anemia and thrombocytopenia. (2)

Out of the four cases of **subleukemic leukemia** three cases (75%) had hemoglobin level below 5 gm/dl. Two cases showing normocytic normochromic RBC morphology with low to normal reticulocyte count. Two cases had TLC ranging from 3000-4500/mm3. The remaining two cases had TLC below 3000/mm3. All the four cases had platelet count between 20,000 to 50,000/mm3. Progressive pallor, fever and bleeding manifestations were the commonest presenting features, all indicative of

a severe type of anemia. Kumar R. et al . (8)

8~ reported 20 cases of acute leukemia in a study of 166 pancytopenia patients; majority of them had their hemoglobin levels between 2.6 to 6 gm%, mean being 4 gm%. Total leucocyte counts were between 650-3200/mm3, the mean being 2200/mm3 and the platelet counts were between 18,000-96,000/mm3, mean being 52,000/mm (3,15).

In the present study, we had **three case of MDS**. All were having hemoglobin below 5 gm/dl, suggesting severe degree of anemia. Two cases (66.66%) showed normocytic normochromic morphology and reticulocytosis. All the three cases of myelodysplasia had TLC ranging from 3000-4500/mm3 with two cases showing circulating immature cells upto myelocytes. All the three cases of MDS had platelet count ranging from 50,000 to 1.5lakhs/mm3. Progressive pallor, bleeding manifestations, fever, dyspnoea were the commonest presenting features..

BONE MARROW EXAMINATION:
We performed bone marrow aspiration and bone marrow biopsy in 47 cases of pancytopenia in the present study. In remaining 3% of patients cause of pancytopenia was obvious (Hypersplenism and Falciparum Malaria).

In the present study, the commonest cause of pancytopnenia was megaloblastic anemia. Out of 50 cases of pancytopenia, 25 cases (50%) were of megaloblastic anemia. Pancytopenia in megaloblastic anemia appears to be commoner from various series - 68%, 44%, 47%, 25.4%, 64%, and 39% reported by Tilak V. et al, Sarode et al, Mikibi et al, Kale et ai, Ng SC et al and Sen et al respectively 15,13,6,9,14.

Out of 25 cases, 22 cases (88%) showed pure megaloblastic anemia of varying severity whereas three cases (12%) showed dimorphic anemia, i.e. combination of iron deficiency and megaloblastic anemia in varying proportions. Sen R. et al too reported 75 cases of pure megaloblastic anemia and 36 cases of mixed vitamin B12 / folate and iron deficiency (.14)

Pancytopenia due to megaloblastosis is albeit, transient, and easily reversible with appropriate treatment. Thus megaloblastic anemia should always be considered in the evaluation of pancytopenia in Indian setting. Out of 50 cases, **10 cases (20%) were hypoplastic/aplastic anemia** group. Of these one had TB and the other was a coal tar worker. Out of the 50 cases of pancytopenia, four cases (**8%) were of subleukemic leukemia**. Out of these four cases, two were of ALL-L1 type. The remaining two were of AML .Other studies have shown incidence between 12-14.5%15,14,10. **Three patients (6%) were of myelodysplasia..** We applied arbitrary criteria described by Jacobs A and labelled these cases as **refractory anemia** and put on therapeutic trial of hydroxocobalamin and folic acid for 21 days. Kumar R. et al and Khodke K. et al have reported 3.6% and 2% cases of MDS as a cause of pancytopenia in their respective studies 7,8. **Two cases had (4%) ITP**. One case was ICS with TB. In one case of pancytopenia due to **myelofibrosis.** Aspiration was a dry tap. But bone marrow biopsy revealed increased reticulin fibrosis of grade 3(15). one case was **Prostatic Carcinoma** metastasis the bone marrow presenting with pancytopenia. we had a **single case of falciparum malaria** in the present study. The patient was put on antimalarial treatment immediately after diagnosis. (1,5)

In our study out of 50 patients, 37 patients (74%) showed complications related with pancytopenia. Out of those 37 (74%) patients, 22 (44%) complications were infective, bleeding was seen in 13 (26%) and 2 (4%) cases had CCF. In infections, most common were FUO - 6 (12%) and GI inefections - 5 (10%) and in bleeding, mucosal bleeding was common followed by GI bleeding.

During hospital stay and during one month follow up mortality was nil. All patients (100%) showed symptomatic improvement. Patients with Megaloblastic anemia, TB & Falciparum Malaria showed complete clinical as well as hematological improvement but in the rest of the patients mild pancytopenia persisted during one month follow up.

CONCLUSIONS: -
With the help of detailed clinical history, physical examination and hematological investigations, causes of pancytopenia can be diagnosed and causes can be ascertained. Megaloblastic anemia due to vitamin B12 / folate deficiency, particularly nutritional in origin seems to reflect the higher prevalence of pancytopenia in indian subjects should be searched for thoroughly since it is treatable, putting hypoplastic/aplastic anemia in second position, which is the leading cause for pancytopenia in western country.

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