ORIGINAL RESEARCH PAPER

Medicine

PANCYTOPENIA A COMMON PRESENTING FEATURE OF MEGALOBLASTIC ANEMIA.

KEY WORDS: Megaloblastic Anemia, Bone Marrow, Pancytopenia.

Binay Kumar Singh* (M.D.) Chief Medical officer,Deptt.of Medicine, ESI PGIMSR, Basaidarapur New Delhi *Corresponding author

Indal Kumar (M.D.), Senior Resident, Deptt.of Medicine, ESI PGIMSR, Basaidarapur New Delhi

ABSTRACT

Objective: Megaloblastic anemia is a common clinical condition, many patients presents as Pancytopenia turned out to be megaloblatic anemia because of Vitamin B12 and folic acid deficiency. There are limited number of studies in Indian subcontinent and few studies are available from the other parts of the worlds on the frequency of various causes of pancytopenia, to Analyze the clinicopathological profile in pancytopenia and its causes.

Methodology : Prospective observational study, on 210 Subjects of pancytopenia older than 13 years, meeting inclusion criteria. The detailed clinical and laboratory workup was done including complete blood count, peripheral smear examination, serum Lactate Dehydrogenase,bone marrow aspiration, biopsy and staining with special stains.

Results : In our study 210 cases of pancytopenia 116 (55.3%) were males and 94(44.7%) females.The majority of the patients were in younger age group 13 - 30 years (64.7%).

Megaloblastic anemia was the most common cause of pancytopenia in 83 (39.52%) , aplastic anemia in 57 (27%), malaria in 17 (8.09%) and hypersplenism in 16 (7.61%) of patients. Acute leukemia, myelodysplastic syndrome, SLE, HBV , multiple myeloma, and sepsis were uncommon.

Conclusion : Megaloblastic anemia and aplastic anemia were amongst the common etiological diagnosis of pancytopenia, comprising 2/3 of all cases. Severe Anemia was more common in megaloblastic anemia. Thrombocytopenia was more common in patients of aplstic anemia, resulting bleeding manifestations.

Introduction : Pancytopenia a common hematological presentation defined as reduction in all three formed elements including erythrocytes, leucocytes and platelets. It is not a disease entity but a triad of findings that may result from a number of disease processes.The defect can be in the bone marrow, periphery or both. Like reduced bone marrow activity, defective or ineffective erythropoiesis and increased destruction of cells by overactive reticulo endothelial system.

Patient of megaloblastic anemia due to folic acid and vitamin B 12 deficiency many times present with pancytopenia[6]. Tropical infectious diseases like malaria can cause transient pancytopenia or it could be persistent in tropical splenomegaly syndrome due to hypersplenism.

The clinical presentation as pancytopenia is different in each disease. Megaloblastic anemia is a common cause of pancytopenia, so evaluation of such patients may help in establishing the etiological diagnosis.

Objective : To Analyze the spectrum of clinical presentation in pancytopenia and identify etiological diagnosis in pancytopenia.

Material and Methodology : A Prospective observational study done in 210 cases of pancytopenia, older than 13 years of age admitted in Medicine ward at a ESI Hospital. Diagnostic criteria for pancytopenia,1.Hemoglobin level <13.5 g/dl in males <11.5 g/dl in females, 2. Leukocyte count <4x10^9/L, 3.Platelet count <150x10^9/L.Patients on chemotherapy, radiation therapy for various malignancy and on whom bone marrow aspiration/biopsy was not done were excluded.

The patients were evaluated in detail clinically as per Performa and laboratory workup,viral markers, immunological tests, hematological profile including complete blood count, red cell indices, peripheral smear, serum lactate dehydrogenase, bone marrow aspiration and biopsy with special stains were carried out.

Results : Two hundred and ten cases of pancytopenia meeting inclusion criteria were enrolled comprising of 116 (55.3%) males and 94(44.7%) females .The majority of the patients with pancytopenia were in younger age group 13 - 30 years (64.7%). Males were more common in 13-20 years age group whereas females were more between 21-30 years.

Megaloblastic anemia was the most common cause of pancytopenia in 83 (39.52%) ,followed by aplastic anemia in 57 (27%), malaria in 17(8.09%) and hypersplenism in 16 (7.61%) of patients(Table 1). Acute leukemia, myelodysplastic syndrome, SLE, HBV , multiple myeloma, and sepsis were also observed.

Commonest symptom was easy fatigability(68.9%) in the study group. The other common symptoms were fever(64.2%). Bleeding manifestation was seen in (27.6%) cases, epistaxis was most common bleeding manifestation., signs of bleeding in 27% , icterus in 20% , lymphadenopathy in 8% , hepatomegaly was found in (43.8%) and splenomegaly in (42.8%) of patients.

Megaloblastic anemia and aplastic anemia were the two most common etiological diagnosis were observed, comprising (66.66%) 140 cases. (Table 2).

The physical signs of the patients with megaloblastic anemia in the study shows that 80/83 cases had pallor, 22/83 cases had icterus, 40/83 cases had hepatomegaly, 32/83 cases had splenomegaly. Hepatosplenomegaly was one of the significant finding on examination of these patients (Table 2).

The laboratory evaluation of patients of Megaloblastic shows that hemoglobin level varied between as low as 1.6 gm to 12 gm%, the mean level of 4.49±2.11 gm%, in megaloblastic anemia. Total leukocyte count in megaloblastic anemia varied between 340 to 3970/cumm with mean value 2692±836.82 and 1100 to 3690/cumm in aplastic anemia. Platelets was low in aplastic anemia with 3000/cumm, when compared to megaloblastic 4000/cumm. Megaloblastic patients have high Mean Corpuscular Volume (MCV) values,the average level was 111±8.96. Serum lactate dehydrogenase(LDH) varied between 700 to 1580 with an average of 983 (Table2).

Sixteen of the cases attributed to hypersplenism. These patients had moderate to large splenomegaly, bone marrow aspiration showing hypercellular marrow. Most of the patients were having chronic liver disease and portal hypertension, two of them had tropical splenomegaly.

Eight cases of myelodysplastic syndrome(MDS) presented with pancytopenia. Easy fatigability, and fever as their main presenting complaint.Pallor was seen in all patients, three patients also had splenomegaly. Four of these were diagnosed as MDS, RAEB (Refractory Anemia with Excess Blasts), two as MDS,RA(Refractory Anemia) and rest two as MDS unclassified .

Discussion: In our study 116 (55.3%) were males and 94(44.7%) females. Male preponderance was noted in all groups Most of the patients were in second and third decade.The mean age in the present study was 32.97 years, which is in concordance with **Kumar et al**[2] where mean age was 30.6 years. In a study done by **Tilak et al**,[2] 32.47% of patients were seen under 20 years of age, this was because they also included pediatric patients in their study.

In our study we noted various etiological diagnosis of pancytopenia, but the two common causes seen were megaloblastic anemia (39.5%), aplastic anemia (27.1%)followed by malaria (8%) and hypersplenism(7.6%).Others disease like acute leukemia,MDS, SLE, HBV also observed. Multiple myeloma and sepsis were also noted in very few cases.

Megaloblastic anemia was the most common cause of pancytopenia in 83 (39.6%) patients. Peripheral smear in all the cases showed macrocytes. Mean corpuscular volume (MCV) was elevated in most of these patients with mean value of 111± 8.96 and 40/83 of them had hypersegmented neutrophils.Serum LDH varied between 700 to 1580 with an average mean of983±196, p value<0.0001 (Table 2).

Similar results have been reported in hematological study from other Indian centers. **Kale et al**, [1] from Mumbai in a study of 65 pancytopenia patients detected megaloblastic anemia in 25.4% of cases. **Senet l**, [3] from Rohtak found megaloblastic anemia in 39% of the 191 patients studied. **Tilak et al**, [2] quotes an incidence of 68 % whereas **Kumar et al,**[4] gives an incidence of 22.3% for megaloblastic anemia. **Khunger JM et al**[5] studied 200 cases in Sufdarjung hospital Delhi found 72% of cases with megaloblastic anemia. **Jha A et al**[6] from Nepal found 30.18% of cases had megaloblastic anemia**. Kishorekhodkeet al**[7] from Dr RML Hospital New Delhi found that in 50 cases of pancytopenia 44% were due megaloblastic anemia. This high incidence can be attributed to the nutritional deficiency common in our country.A study done in Israel did not find megaloblastic anemia as a very common cause of pancytopenia.

Comparing the hemoglobin level in the four major groups of pancytopenia, the mean hemoglobin level in megaloblastic anemia group was (4.49±2.11gm%),which is lower than the other groups. Similar results were noted **Kumar etal**,[4] where hemoglobin level noted was 4.6 gm%.

Aplastic anemia was the second common (27.14%) cause of pancytopenia .This is comparable with the above mentioned studies, however aplastic anemia was most common cause of pancytopenia in studies by **Vermal et al**[7] and **Hossain et al**[8] .

Bleeding is a common early symptom of aplastic anemia, p value <0.0001 (Table 2). In the present study 38 out of 57 (66.6%) cases had bleeding manifestation at presentation. On comparing the platelet count in the four major diseases causing pancytopenia it was noted that the platelet count was lowest in aplastic anemia group. Mean platelet count in this group was 38,000/cumm. Similar results have been documented by **Kumar et al**.[4]

In the present study 19 (9.04%) of cases of pancytopenia were due to malaria. **V Gupta et al** [9] found malaria to be responsible for pancytopenia in 2.9% of the cases. The incidence of malaria was high in the present study when compared to **V Gupta etal**,[9] none of the other studies mentioned above had malaria as one of the cause. This could be seen in view of prevalence of malaria in the region.

Conclusion: Megaloblastic anemia was most common etiological diagnosis of pancytopenia. Severe Anemia was more common with high mean corpuscular volume and high serum lactate dehydrogenase levels in megaloblastic anemia. thrombocytopenia was also observed but bleeding manifestation were less as compare in patients of aplastic anemia.

Tables:

Table 1: Pancytopenia and its various causes.

S.No.	Etiology	No of Cases n=210	Percentage (%)
1	Megaloblastic Anemia	83	39.52
2	Aplastic Anemia	57	27.14
3	Malaria	17	8.09
4	Hypersplenism	16	7.61
5	Acute Leukemia	12	5.7
6	MDS	8	3.8
7	Lymphoproliferative Disorder	4	1.9
8	SLE	3	1.4
9	HBV	4	1.9
10	Multiple Myeloma	2	0.95
11	Sepsis	1	0.4
12	No Cause	3	1.4
	Total	210	100%

TABLE -2 Profile of megaloblastic anemia in comparision with aplastic anemia

S. No.	Clinic-pathological parameter	Megaloblastic anemia, n = 83	Aplastic anemia, n= 57	P value
1	Easy fatigability	69 (84.1)	39 (68.4)	0.300
2	Pallor	80 (97.5)	52 (91.2)	0.932
3	Fever	47 (57.3)	26 (45.6)	0.1754
4	Pedal Edema	11 (13.4)	5 (8.7)	<0.0001
5	Bleeding manifestation	5 (6.09)	38 (66.6)	<0.0001
6	Icterus	22 (26.8)	2 (3.5)	0.0005
7	Lymphadenopathy	0 (0)	5 (8.7)	0.0070
8	Hepatomegaly	40 (48.7)	13 (22.8)	0.0024
9	Splenomegaly	32 (39.0)	0(0)	<0.0001
10	Hb(gm/dl)	4.49±2.11	5.46±2.77	0.0202
11	TLC (/cu mm)	2692±836.82	2294.9±780.9	0.0053
12	Platelet(l/cumm)	0.57±0.29	0.38±0.31	0.0003
13	MCV	111±8.96	88.24±11.15	0.0588
14	LDH	983±196	289.85±126.5	<0.0001

References

1. Kale P, Shah M, Sharma YB, Pathare AV, Tilak GH, Pancytopenia with cellular marrow- a clinical study. J AssocPhys India 1991 ; 39:926.
2. Sen R, Bali R. Pancytopenia : Causes and their frequency of distribution. India J Hematol Blood Transf 1996;14:44-45.
3. Tilak V, Jain R. Pancytopenia – A clinico-hematological analysis of 77 cases. India J PatholMicrobiol 1999;42(4):399-404.
4. Kumar R,Kalra SP. Pancytopenia – A six year study. J Assoc Physicians India 2001;49:1078-81.
5. KhungerJM,Arulselvi S ,Sharma U,Ranga S, TalibVH,Pancytopenia –a clinicohematological study of 200 acses.Indian J PatholMicrobiol ,2002 Jul; 45 (3):375-9.
6. JhaA,SayamiG,AdhikariRC,PantaAD,JhaR,Bone marrow examination in cases of pancytopenia. JNMA J Nepal Med Assoc.2008Jan–Mar;47(169) :12-7.
7. Kishore Khodke,SMarwah,GBuxi,R B Yadav,N K Chaturvedi,Journal ,Indian AcademyOf Clinical Medicine.Vol 2, No.1 and 2 ,Jan-Jun 2001.
8. VermaN,DashS.Reappraisal of underlying pathology in adult patient presenting with pancytopenia.Trop Geog Med 1992;44:322-7.
9. V Gupta, S Tripathi, V Tilak, BD Bhatia - A study of clinico-haematological profiles of pancytopenia in children Tropical doctor, 2008 ; Vol 38, Issue 4, 2008.