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Original Research Article

Evaluation of the Demographic Profiles of Pancytopenia in Paediatric Patients and Correlation of Hematological Parameters with Clinical Findings in Differentiating Causes of Pancytopenia

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Abstract:

Background: Pancytopenia is characterized by simultaneous decrease in all the 3 formed elements of the blood i.e red blood cells, white blood cells and platelets, resulting in anemia, leucopenia and thrombocytopenia. Respectively.

Objectives: To correlate hematological parameters with clinical findings in differentiating causes of pancytopenia.

Materials & Methods: This Prospective study was conducted in the Department of Pathology, Rajendra Institute of Medical Sciences, and Ranchi. The permission to conduct this study was obtained from the central research committee of R.I.M.S.

Results: In PBS, the most common finding was normocytic hypoochromic anaemia in addition to pancytopenia (60% cases). This finding was seen in patients of aplastic anaemia (100% cases), hypersplenism (100% cases) & nutritional deficiency anemia (28.5% of cases). Patients with megaloblastic anemia had macrocytic hypochromic RBCs with hyper segmented neutrophils in the PBS. 71..5% patients with mixed nutritional deficiency patients had dimorphic RBCs in PBS, Patients with aplastic anemia had hypocellular bone marrow aspirate with depressed erythropoiesis, leukopoiesis & megakaryopoiesis. Patients with megaloblastic anemia had hypercellular bone marrow with megaloblastoid changes in erythropoiesis. Patients with hyper splenismand mixed nutritional deficiency patients had mild erythroid hyperplasia in the bone marrow. Acute leukaemia patients had hypercellular bone marrow with predominance of blast cells.

Conclusion: A comprehensive clinical, hematological and bone marrow study of patients with pancytopenia usually helps in identification of the etiology. It is very important to diagnose the cause of pancytopenia early in the disease process, so that adequate intervention could be done on time for the patient.

Keywords: Pancytopenia, Bone marrow aspiration, Megaloblastic Anemia, Nutritional Anemia

Introduction

The primitive hematopoeisis starts in the yolk sac by 2 weeks and switch to definitive hematopoiesis in the fetal liver by 8 weeks. After birth and during early childhood hematopoeisis occurs in the red marrow of the bone. With age hematopoiesis become restricted to skull, sternum, ribs, long bone and pelvis. Yellow bone marrow comprising of fat cells, replaces the red marrow and limits its potential for hematopoiesis.

However, under stress yellow marrow can revert to produce blood cells. From the marrow mature blood cells migrate into the circulations, spleen and other sites. This bone marrow acts as reservoir that responds to ongoing needs for blood cell production. A wide variety of disorders can cause pancytopenia, although the frequency with which each condition is associated with pancytopenia differs considerably. The underlying mechanisms are decrease in hematopoetic stem cell production, marrow replacement by abnormal cells, suppression of marrow growth, ineffective hematopoeisis and cell death, defective cell formation which are removed from the circulation, antibody mediated sequestration and destruction of cells and trapping of cells in hypertrophied and overactive reticulo-endothelial system. [1,2].

Pancytopenia can result from damage to the bone marrow evidenced by low reticulocyte count or

increased destruction of preformed blood cells peripherally with increased reticulocyte count.

The etiology of pancytopenia varies widely in children, ranging from transient marrow suppression by virus to marrow infiltration by life-threatening malignancy. These may also be caused iatrogenically, secondary to certain drugs, chemotherapy or radiotherapy for malignancies. The bone marrow picture may vary depending on the etiology, from normocellular with non-specific changes to hypercellular being replaced completely by malignant cells. According to etiology, degree and duration of the impairment, clinically these can lead to fever, pallor, infection, or serious illness and death. Knowing the exact etiology is important for specific treatment and prognosis.

Primary or genetic causes include Fanconi anemia, dyskeratosis congenita, Swachman's diamond syndrome and amegakaryocytic thrombocytopenia. [3] Acquired cases can be idiopathic or secondary to exposure to radiation, drugs and chemicals (chemotherapy chloramphenicol, sulfa group, antiepileptics etc.), viral infections (cyto megalovirus, Epstein barr, hepatitis B or C, HIV etc), auto immune PNH and marrow replacement disorders (leukemia, myelodysplasia) [4]

Megaloblastic anemia and infections such as enteric fever, malaria, kalazar and bacterial infections can be common cause of pancytopenia in developing countries. [5] Nutritional megaloblastic anemia is also one of the leading causes of pancytopenia in younger children. [6]

Bone marrow profile is useful in the diagnosis of both hematological and non-hematological disorders. For Bone marrow interpretation, the history, clinical feature, bone marrow aspiration, peripheral blood smear, serum Iron, serum ferritin, serum vit B12 and serum folic acid are required.

Bone marrow examination is one of the most frequently and relatively safe invasive procedure done routinely in Department of Pathology, RIMS Ranchi. Apart from these tests Flow cytometry is also helpful for evaluation of pancytopenia in children in certain cases.

Materials and Methods:

This Prospective study was conducted in the Department of Pathology, Rajendra Institute of Medical Sciences, and Ranchi. The permission to conduct this study was obtained from the central research committee of R.I.M.S and the Institutional Ethical Committee (IEC). The study period is from July 2017 to June 2018

The nature, methodology and risks involved in the study were explained to the patients and informed consent was obtained. The information collected from the patients and their case records were kept confidential and the patients were given full freedom to withdraw at any point during the study period.

Study population

Pediatric patients of age group 2 months to 18 years with pancytopenia referred to Department of pathology, RIMS for one year period (2017 to 2018) depending upon inclusions and exclusions criteria.

Sample size: A minimum of 100 pediatric patients suspected for pancytopenia was included in the study**.**

Source of data

All the peripheral smears and bone marrow samples received in the hematology section of RIMS, Ranchi was evaluated, and out of which hundred pancytopenic children of age group 2 months to 18 years is included in this study.

Inclusion Criteria:

1. Pediatric patients of age 2 months to 18 years were included.
2. Pediatric patients (2 months to 18years) fulfilling the criteria for pancytopenia wasincluded.

Exclusion Criteria:

1. Recent or ongoing infection, systemic illness
2. Patients with history receiving cancer chemotherapy, radiotherapy, recent bloodtransfusion, and treatment of anemia.
3. Subjects not willing to give consent.

Methodology: After taking particulars (Name, age, sex, address) of the patients,a detailed clinical history including presenting complaints, dietary history and drug history are taken. After that general physical and systemic examination are done with special reference to pallor, status of lymph node, liver & spleen.

Then 2 ml of EDTA (ethylene diamine tetra-acetic acid) anticoagulated peripheral venous blood is collected and processed through SYSMEX-XT2000i automated hematology analyser.

Absolute values including packed cell volume (PCV), mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC) will be calculated forevery patient.

Peripheral blood smear: After that peripheral blood smear is made from fresh non anticoagulated peripheral venous blood and stained by Leishman's stain without any delay.

Bone marrow aspiration study:

Sites of bone marrow aspiration: Anterior iliac crest, posterior iliac crest & Tibia. Commonly

employed needles for marrow aspiration needles are Salah bone marrow aspiration needle.

Statistical Analysis:

All the relevant data so collected are entered in the master chart and analysed using appropriate statistical procedure and software. Statistical analysis of the data is done using Statistical Package for the Social Sciences (SPSS) Software, version 23.0 (IBM). The student's T test is used to compare mean values of quantitative variables. Qualitative variables are analysed by chi square test. Statistical significance will be considered for p values less than 0.05. Values are presented as charts, bar diagrams etc. Results are discussed and correlated with the analysed literature and conclusion is drawn keeping in mind about the limitation of the study

Results

In our study, a total of 100 cases of Pediatric patients with pancytopenia were studied. Out of100cases, 53 patients were male and 47 were female. The mean age of the study population was 12±5.4. Among it, mean age of males was 12±5.76 and mean age offemaleswas12±5.Most of the study population was between in12-18 years both in males and females. It was found that there is no significant statistical difference between the mean age of males and females.

Most of the cases (52%) were in the age group of 12-18 years followed by 26% cases were in the age group 5-12 years. Least number of cases 08% was in the age group of less than1 year. It was found that male are more commonly affected than females in all age groups except 5-12 years groups. There is no significant statistical difference between the age groups of cases.

The most common diagnosis among 100 patients of pancytopenia was Megaloblastic anaemia (38%), followed by aplastic anaemia (30%). The next common diagnosis was Erythroid hyperplasia (11%), followed by mixed nutritional anaemia (07%), & acute leukaemia (5%). The other 3 diagnosis were Hypersplenism (2%), Gaucher's disease (2%) and Normal study (5%).

The mean haemoglobin of the study population was 5.66±1.98gm/dl.

Here it shows that out of 100 cases, 51 cases were found to have with bone marrow hyper cellularity and 10 been mild hypercellular on bone marrow aspiration. Among hypercellular, 29 patients were males and 22 were male. In 30casesbonemarrow aspiration was hypocellular. Among them, 16 cases were males and 14 cases were females. And 9 cases were nor was mocellular on aspiration. It found that gender wise distribution of bone marrow cellularity was not statistically significant.

It was found in bone marrow aspiration that bone marrow erythropoiesis was hyperplastic & megaloblastic in 38 cases of them 25 patients were male and 13 patients were female. The next common finding of depressed marrow was seen in 30 cases. Of them16 were male and 14 were female. The other marrow findings were normoblastic and hyperplastic with few micronormoblast with occasional megaloblast in 8 cases each. The rest findings were normoblastic hypolastic, micronormoblastic hyperplastic and with gaucher cells in 2 case each.

In bone marrow aspiration, leucopoiesis was found to be depressed in 30 patients of them 16 cases were males. In 22 cases leucopoiesis was found to be normal. Giant metamyelocyte were found in 43 cases & blasts were found in only 5 cases. It was found that there is no significant statistical difference of gender wise distribution of these variables.

Bone marrow aspiration showed that, megakaryopoiesis was depressed in 35 patients. Of them, 17 cases were males & 18 cases were female. Megakaryopoiesis was normal in 65 patients, out of which 37 cases were males, and there was no significant statistical difference between males and females.

Out of 38(38%) patients diagnosed as Megaloblastic anaemia 25(65.8%) cases were males and 13(34.2%) cases were females. Aplastic anemia is found in 30 cases. Out of 30(30%) patients 16(53%) cases were males and 14(47%) cases were females. Among 2(2%) cases of hypersplenism, 50% were male and 50%were females. In 7(7%) cases of mixed nutrional anemia, 2 (28.5%) were male and 5(71.5%) were females. Among 5(5%) cases of Acute leukemia 1(20%) was male and 4(80%) were females. There were 11(11%) cases of Erythroid hypeplasia. 6(54.5%) were males and 5(45.4%) were females. And the rest5 (5%) cases were normal study cases. Among them 2(40%) were males and 3(60%) were females. It was found that there is no significant statistical difference of final impression in male and female patients.

Table 1: Showing Age Wise Distribution of Final Impression Among Cases

Age Group	Aplastic anemia	Megalo-blastic anemia	Hyper-splenism	Mixed Nutrional Anemia	Acute Leuke-miaa	Erythroidh yperplasia	Gau-cher's Disease	Nor-mal study	To-tal
0.2-1	2	5	0	1	0	O	0	0	8
1-5	5	4	1	0	2	0	1	2	15
5-12	9	8	0	2	1	5	0	1	26
>12	14	21	1	4	2	6	1	2	51
Total	30	38	2	7	5	11	2	5	100

The most common cause of pancytopenia, i.e Megaloblastic anemia is most common in the age group of 12-18 yrs while least common is in the group of 1-5year. Similarly Aplastic anemia is common in the age group of 12-18 years while least common in the age group of 2 months- 1 year. There is no significant statistical difference between the age groups of cases.

Table2: Distribution of Chief Complaints According To Final Impression

	Fever	Malaise	Abd Distensio N	Petechial Rash	Bleeding	Total
A.A	11	6	4	4	5	30
M.A	20	8	5	2	3	38
H.S	1	0	1	0	0	2
MNA	4	2	1	0	0	7
AL	0	3	2	0	0	5
EH	7	3	1	0	0	11
Gauchers	0	1	1	0	0	2
Normal	3	0	2	0	0	5
TOTAL	46	23	17	6	8	100

Table 3: Distribution of Salient Examination Findings among Final Impressions

Variables	Pal-lor	Pallor + Spleno-megaly	Pallor + Hepa-tomegaly	Pallor + Hepatosple-nomegaly	Pallor +Lymph adenopa-thy	Pallor+Lymph Denop-thy+Hepatospleno megaly	To-tal	P Val ue
AA	21	3	1	5	0	0	30	
MA	29	6	2	1	0	0	38	
HS	0	2	0	0	0	0	02	
MNA	5	1	0	0	1	0	07	
AL	0	0	3	0	0	2	05	
EH	5	2	1	3	0	0	11	
Gauchers	0	0	0	2	0	0	02	
Nor Mal Stud Y	3	2	0	0	0	0	05	<0.
Total	63	16	6	10	1	2	100	01

Among Megaloblastic Anemia 15.7% had splenomegaly in addition to pallor. Among Aplastic Anemia 16.6% had hepatosplenomegaly in addition to pallor. 14.2% cases of Mixed Nutrional Anemia had splenomegaly and another 14.2%% had lymphadenopathy in addition to Pallor. Here the table shows 100% cases had pallor on general physical examination. In ion to pallor.60% of acute leukemia had hepatomegaly and 40% had lymphadenopathy in addition to hepatosplenogaly and pallor. All cases of hypersplenism had splenomegaly and all cases of gaucher's disease had hepatosplenomegaly in addition to pallor. Here the table shows 100% cases of aplastic anaemia, 100% cases of hypersplenism 100% cases of Erythroid hyperplasia and 28.5% cases of mixed nutritional anaemia had normocytic hypochromic RBCs on peripheral blood smear. All the patients with megaloblastic anaemia and Gaucher's disease had macrocytic hypochromic RBCs. 5 (71.5%) patients of mixed nutritional anaemia showed dimorphic RBCs. Acute leukaemia patients had occasional blasts in peripheral blood smear. It was found that these findings were statistically significant.

Table 4: Distribution of Bone Marrow Cellularity According To Final Impression

Variables	Hypo Hyper Mild Normo Total P value Hyper Cellular	
AA	30 0 0 0 30	
MA	0 32 5 1 38	
HS	0 0 1 1 2	
MNA	0 3 2 2 7	
AL	0 5 0 0 5	<.001
EH	0 10 0 1 11	
Gaucher's	0 1 1 0 2	
Normal Study	0 0 1 4 5	
Total	30 51 10 9 100	

100% patients of Aplastic anaemia patients had depressed erythropoiesis, leucopoiesis and megakaryopoiesis. There was relative mild increase in lymphocytes in the marrow. All cases of Megaloblastic anaemia showed hyperplastic and megaloblastoid changes in erythropoiesis with normal leukopoiesis and megakaryopoiesis. Patients with Mixed nutritional deficiency had hyperplastic erythropoiesis. Few of the erythroid precursors were micronormoblastic in appearance with presence of occasional megaloblasts. They had normal leukopoiesis and megakaryopoiesis. All patients with Hypersplenism had hyperplasic and normoblastic erythropoiesis, their leukopoiesis and megakaryopoiesis being normal. 3 patients of acute leukaemia showed more than 80% blasts in the bone marrow. Their erythropoiesis and megakaryopoiesis were depressed. The patient with Erythroid hyprplasia had either normoblastic hyperplastic or micronormoblastic hyperplastic erythropoiesis, with normal leukopoiesis and megakaryopoiesis. Gaucher's disease showed hyperplastic and megaloblastoid changes in erythropoiesis with normal leukopoiesis and megakaryopoiesis, with presence of Gaucher cells (Glycolipid laden macrophages). Therest 5cases had normal erythropoiesis, leukopoiesis and megakaryopoiesis It was found that all these findings are statistically significant.

Table 5: Distribution of mean Vitamin B12, mean folic acid & mean Iron and mean ferritin level according to final impression

	Mean Serum Iron(ug/dl)	Mean Serum Ferritin(ng/ml)	Mean Serum Vitb12 (Pg/ml)	Mean Serum Folic acid (ng/ml)
AA	159±76.5	462±354	355.9±152.3	7.23±4.56
MA	149±85.2	373±299.1	101.7±63.9	2.91±1.74
HS	71±12.7	72.5±7.7	293.5±62.9	7.9±0.42
MNA	18±7.02	9.28±3.14	142.28±43.16	2.86±0.9
AL	116±57.7	259±108.64	415.4±379.75	5.8±2.02
EH	89±17.4	493±348.33	197.2±21.42	3.9±1.72
Gaucher Disease	122±14.1	318±13.43	168.5±139.3	4.15±0.91
Normal Study	74.6±28.9	236.4±35.35	242.8±111.47	4.06±0.47
P Value	<0.01	<0.01	<0.01	<0.01

Discussion

There are varying reports on the underlying etiology of pancytopenia from various parts of the world. In a study in France by Imbert et al. 213 consecutive adult pancytopenic patients were reviewed and underlying malignant myeloid disorders were found in 42% of their cases and various malignant lymphoid disorders in 18%, followed by aplastic anemia in 10%.

In a study from Zimbabwe comprising 134 patients with pancytopenia, megaloblastic anemia was the most frequent cause, followed by aplastic anemia and acute leukemia in their cohort of pancytopenic patients. [6]

Jha et al. [7] from Nepal studied the causes of pancytopenia in 148 patients. The commonest etiology of pancytopenia in their study was hypoplastic bone marrow seen in 43 cases (29%), followed by megaloblastic anemia in 35 cases (23.6%) and hematological malignancy in 32 cases (21.6%). In children, hypoplastic bone marrow (38.1%) and in adults' megaloblastic anemia (30.2%) was the commonest etiology reported by them.

Studies from India on etiology of pancytopenia are limited and have shown variable causes, depending on the referral population and nutritional status of the study area. Etiological profile of adult pancytopenic patients was studied by Varma et al. [8] and Kumar et al. [9] Tilak et al [10] and Khunger et al. [11] included children along with adults while doing a clinico-hematological analysis of 77 and 200 pancytopenic patients, respectively;

In children, Bhatnagar et al., [12] who retrospectively analyzed 109 pediatric patients presenting

with pancytopenia, found megaloblastic anemia as the single most common etiological factor causing pancytopenia in 28.4% children, followed by acute leukemia and infections in 21% patients each, and aplastic anemia in 20% cases. Gupta et al. [13] reviewed 105 children aged 1.5-18 years with pancytopenia. In their study, aplastic anemia was the most common cause of pancytopenia (43%), followed by acute leukemia (25%). Infections were the third most common cause of pancytopenia of which kala-azar was the most common. Megaloblastic anemia was seen in 6.7% children by them. Fever and progressive pallor were the most common presenting complaints in their cohort, being present in 81.4%, followed by bleeding manifestations in 72.9%.

In present study, the most common underlying etiology is Megaloblastic anemia seen in 38 (38%), followed by Aplastic anemia in 30 (30%) pancytopenic children. Acute leukemiais seen in 5 (5%) children. Other causes were mixed nutrional anemia (07%), Erythroid hyperplasia (11%), and gaucher disease (2%). In the present study, most of the study population (52%) was in the age group 12 – 18 years with mean age of 12±5.4years. Bahl D et al and Khod ke et al in their studies showed the commonest age group was in 2nddecade. In the present study out of 100 patients, 54 were male patients, making the male female ratio 1.7:1. In various studies conducted on pancytopenia, male preponderance was noted like male female ratio was1.52:1instudybyAmieleena Chhabra et al, 1.3:1by Khodke et al, and 1.79:1 by Bhatnagar et al.

The most common presenting chief complaint was Fever, which was present in 45% of cases. The second most common was Malaise (present in 23% of cases), followed by abdominal distension (17%ofcases). The other chief complaints were bleeding (8%), and rashes (7%). Naseem et al, Rathod et al in their studies also found Fever as the most common symptom. In the study conducted by Bhatnagar et al bleeding was the most common symptom.

In the present study 100% of the study population presented with pallor, in addition 16% had pallor with splenomegaly, 7% had hepatosplenomegaly & 10% had hepatosplenomegaly in addition to pallor and 2% had lymphadenopathy. Naseem et al in their studies found Pallor (59%) as the most common sign followed by hepatomegaly in 51% and splenomegaly in 37%. In the present study, the mean haemoglobin of the study population 5.66±1.98gm/dl. The mean total leukocyte count was 2921±925/cu.mm. and the mean platelet count was 55907±26581/cu.mm. Santra G et al. in their study found mean haemoglobin concentration of 5.90 ± 1.90 g/dl, mean total leukocyte count 2,633/mm3 and mean platelet count 45.20 ± 38.60 $\times 10^3$) /mm3.

Acute Leukemia

Acute leukaemia was found in 5% patients in our study, compared to 2.0% reported by Khodke et al., 26.6% reported by Naseemet al. 16 & 25% found by Gupta et al. in their studies. 4 cases (80%) were of B cell leukemia and 1(20%) case was of T cell leukemia. 4 of them were female patients in our study.2 of them were in the age group1–5 years & the other 2 in the age group of 12 –181 in the age group of 5-12years. 3 cases presented with fever and rest of the 2 patients presented with abdominal distension. 60% of acute leukemia had hepatomegaly and 40% had lymphadenopathy in addition to hepatosplenogaly and pallor. PBS showed occasional three or four blast cells along with pancytopenia. Bone marrow aspiration revealed hypercellular bone marrow with predominance of blasts (more than 80%).

Hypersplenism

In this study only 2 (2%) cases presented with hypersplenism. Rathod et al in their study also found only 2.5% case of hypersplenism. While the studies conducted by Jha et al found 6.25% of hypersplenism cases.50% of patients with hypersplenism presented with abdominal distension. Male to female ratio was 1:1. 50% of the patient presented with abdominal distension. All the patients had pallor with enlarged palpable spleen at presentation. In PBS all the patients of hypersplenism had normocytic normochromic RBCs. Bone marrow aspiration was mildly hypercellular to normocellular with normoblastic and hyperplasic erythropoiesis. Leukopoiesis and megakaryopoiesis were within normal limits. Thus, the commonest causes of pancytopenia reported by different studies throughout the world have been, megaloblastic anemia aplastic anemia and leukemia. Below table summarizes the salient findings of various studies on pancytopenia.

We found that the routine hematological parameters were non-specific and showed a significant overlap among the major causes of pancytocytopenias. However, the peripheral blood films were valuable in pointing toward the cause in patients with megaloblastic anemia and leukemia. Bone marrow aspirate was found to be sufficient for diagnosis in most cases of acute leukemia and Megaloblastic anemia.

Conclusion

A comprehensive clinical, hematological and bone marrow study of patients with pancytopenia usually helps in identification of the etiology. It is very important to diagnose the cause of pancytopenia early in the disease process, so that adequate intervention could be done on time for the patient

References

1. Islam A, Glomski C, Henderson ES. Endothelial cells and hematopoiesis: a light microscopic study of fetal, normal,and pathologic human bone marrow in plastic emedded sections. Anat Rec 1992; 233:440–52.
2. Rosse C, Kraemer MJ, Dillon TL, McFarland R, Smith NJ. Bone marrow cell populations of normal infants; the predominance of lymphocytes.J Lab Clin Med 1977; 89:1225–40.
3. Pizzo PA, D' Andrea AD. The pancytopenias in: Behrman RE, Kleigman RM, Jenson HB. Nelson textbook of pediatrics. 17th ed. Philadelphia: sanders; 2003;1642-6
4. Alter BP. Bone marrow failure syndromes in children. Pediatr Clin North Am 2002; 49:973-88.
5. Bhatnagar SK, Chandra J, Narayan S, Sharma S, Singh V, Dutta AK. Pancytopenia in children: etiological profile. J TropPediatr 2005; 51:236-9
6. Katar S, Nuri Ozbek M, Yaramisa A, Ecer S, Nutrional megaloblastic anemia in young Turkish children is associated with vitamin B12 deficiency and psychomotor retardation.J Pediatr Hematol Oncol 2006;28:559-6
7. Wickramasinghe SN. Bone marrow. In: Histology for Pathologists. 3rd edn. Mills SE. (ed). Philadelphia: Lippincott Williams & Wilkins; 2007:800–36.
8. Yadav BS. Verma Kiyawat P. Clinical profile of pancytopenia: a tertiary care experience. International Journal of Bioassays.2014 Dec31;4(01):3673
9. Habib ur Rahman, Fazil M Khan FM. The etiological pattern of pancytopenia in children upto 15 years. Pak Armed Forces Med J 2003; 53:183-7
10. Friebert SE, Shepardson LB, Shurin SB, Rosenthal GE, Rosenthal NS. Pediatric bone marrow cellularity: are we expecting too much? J Pediatr Hematol Oncol 1998; 20:439–43.
11. Sturgeon P. Volumetric and microscopic pattern of bone marrow in normal infants and children: III. Histologic Pattern. Pediat- rics 1951; 7:774–81.
12. Sturgeon P. Volumetric and microscopic pattern of bone marrow in normal infants and children. I. Volumetric pattern. Pediat- rics 1951; 7:577–88.
13. Ogawa T, Kitagawa M, Hirokawa K. Age-related changes of human bone marrow:a histometric estimation of proliferative cells, apoptotic cells, T cells, B cells and macrophages. Mech Ageing Dev. 2000; 117:57–68.