Original Research Article

Study of hematological parameters in cases of splenomegaly

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Received: 18-10-2021 / Revised: 16-12-2021 / Accepted: 26-12-2021

Abstract

Background: This was a prospective study carried out in the department of pathology of a tertiary care hospital during a period of one and half years (Nov 2016- June2018). All patients presented with palpable spleen were included in study. Blood samples were collected for complete hemogram, reticulocyte count, sickling test, osmotic fragility and other haematological investigations if needed. Bone marrow examination and serum electrophoresis was done whenever necessary. Grading of splenomegaly was done by Hackett's classification. Data collected was analysed to find out the etiology of splenomegaly and its haematological manifestations. Maximum cases were seen in the age group of 11-20 years (19.23%) with a male preponderance. **Objectives:** To study haematological parameters in cases of splenomegaly in all age groups. To correlate splenomegaly with various hematological parameters and to evaluate hematological and non hematological causes of splenomegaly. **Results:** Total 260 cases of splenomegaly were studied in this present study. Hematological causes of splenomegaly (53.85%) were more common than the non hematological causes (46.15%). Anemia (38.85%) was the most common cause of splenomegaly among the hematological disorders followed by leukemia (11.92%) where as infective etiology (30.77%) was the predominant cause among the non hematological disorders. Hackett's grade I splenomegaly was seen in maximum number of case (38.46%). **Conclusion:** There was no significant correlation between degree of splenomegaly and degree of cytopenia. Increasing splenic size was significantly associated with occurrence of hypersplenism.

Key words: Hematological, non hematalogical, Hackett's classification.

Introduction

Spleen is functionally diverse organ with active roles in immune surveillance and hematopoiesis. The spleen combines the innate and adaptive immune system in a uniquely organized way. Splenomegaly is subject of considerable clinical concern as spleen is not palpable under normal circumstances[1]. Spleen being a part of the reticuloendothelial system, is commonly involved in a wide range of systemic diseases[2]. When palpable, it may be associated with serious disorders from which no age is exempted[1]. A wide variety of diseases can lead to splenic enlargement. The predominant cause of splenomegaly vary with geographical distribution of diseases prevalent in the area[3].

The degree of splenomegaly varies with the disease entity. Most of the chronic conditions like chronic myeloid leukemia, hairy cell leukemia, storage disorders, myelofibrosis, chronic malaria, leishmaniasis lead to massive splenomegaly while in most acute conditions, patient seek medical advice at an early stage with a mild enlargement of spleen[4]. Splenomegaly becomes more significant when associated with hepatomegaly or lymphadenopathy[5]. The etiology of splenomegaly thus differs with the grades of splenomegaly at presentation, the age of the patient, clinical features, and associated signs and symptoms[6].

Splenomegaly, as a symptom or sign, can be evaluated with battery of investigations like hematological, biochemical, cytological, histopathological, serological and radiological.

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Hematologic investigations play an important role in evaluation[7]. This study is an attempt to find out the frequency of various causes of splenomegaly, to study its hematological parameters and to find out role of these hematological parameters as a diagnostic or additional tool in elucidating etiopathogenesis of splenomegaly[5].

Material & methods

This was a prospective study carried out in department of Pathology of a tertiary care hospital during a period of one and half years (Nov 2016- June2018). All the patients admitted in department of Medicine, Surgery, Paediatric and Obstetrics and gynaecology during this period of either gender and of all age groups who clinically presented with palpable spleen was included in this study. Written informed consent was taken for collection of blood samples for various hematological investigations like complete hemogram, bone marrow examination and serum electrophoresis whenever necessary. In cases of uncertain diagnosis bone marrow aspiration and/ or biopsy was done in selected patients. Blood samples were run on fully automated 3 part hematology analyser. Blood smears were stained with fields stain, Leishman's stain, myeloperoxidase (MPO) and studied in detail. Serological tests for Malaria, Dengue, Human immunodeficiency virus (HIV) and Rheumatoid Arthritis Factor were carried out wherever required. Findings of Radiological investigations, such as ultrasonography, 2D Echocardiography, barium studies, CT scan, MRI study were noted in cases, whenever indicated. On the basis of ultrasonography finding hepatomegaly (liver length of >15.5 cm in mid hepatic line) was confirmed[8]. Grading of splenomegaly was done by Hackett's classification[9]. Hackett's grade 1 and 2 were considered as mild splenomegaly, grade 3 as moderate splenomegaly and 4 and 5 were considered as massive splenomegaly. Data collected was analysed to find out the etiology of splenomegaly and its haematological manifestations. Correlation co-

efficient was used to determine the statically significant association between the grades of splenomegaly and degree of cytopenia. Chi square test was applied to found a significant association between increasing spleen size and occurrence of hypersplenism.

Selection criteria

Study included all patients admitted in department of medicine, surgery, pediatric and obs. and gynecology who clinically presented with splenomegaly (mild, moderate and massive) in all age groups.

Results

The present study comprised of 260 cases of splenomegaly. The detailed information regarding age, sex, clinical features, grades of splenomegaly and other relevant investigations of all 260 cases were obtained and correlated with hematological parameters. Pediatric age group comprised of 58 cases (22.03%), adolescent 33cases (12.70%) and adults 169 cases (65%). There was a male preponderance with M:F ratio of 1.6:1. As shown in table no. 1 grade II splenomegaly comprising of 65 cases (25%) was predominantly seen in adult age group while grade I splenomegaly was found in pediatric (28 cases, 10.76%) and adolescent (19 cases, 7.30%) age groups. However overall grade I splenomegaly (100 cases, 38.46%) was the most common finding among the total 260 cases of splenomegaly. Fever was the most common clinical presentation seen in 165 cases (63.46%). Cases of splenomegaly associated with hepatomegaly was noted in 125 cases (48.07%), among which congestive splenomegaly was the predominant cause seen in 39 cases (31.2%). There were 27 cases (10.38%) of splenomegaly associated with lymphadenopathy. Out of these 27 cases, splenomegaly with lymphadenopathy and hepatomegaly was seen in 16 cases (6.15%).Hematological causes (53.85%) of splenomegaly were out numbered the non hematological causes (46.15%) in the present study. As shown in table no.2, anemia was the most common cause comprising of 38.85% cases among the hematological disorders followed by leukemia 11.92% cases and other causes were multiple myeloma (1.54%), idiopathic thrombocytopenic purpura(0.77%) and lymphoma(0.77%). Megaloblastic anemia (16.55%) was found in majority of cases followed by dimorphic anemia (10.77%). Acute myeloid leukemia was the most common malignancy comprised of 5.38% cases followed by chronic myeloid leukemia (3.08%) cases and others were acute lymphoblastic leukemia (1.92%) and chronic lymphoid leukemia (1.54%). One 77 years female patient presented with massive splenomegaly was underwent splenectomy. This was diagnosed as a case of low grade B cell Non Hodgkins lymphoma on histopathological examination and immunohistochemistry (figure no.1). One case of lymphocyte rich Hodgkins lymphoma was diagnosed in a 60 years male patient who was presented with moderate splenomegaly and peripheral lymphadenopathy. Infective aetiology was the predominant cause of splenomegaly among the non hematological disorders comprised of 30.77% cases followed by congestive splenomegaly (15%) and one case (0.38%) of systemic lupus erythematosus. Amongst the infective disorders, dengue fever was the commonest cause of splenomegaly seen in 14.61% cases followed by malaria (7.69% cases) and other minor causes like tuberculosis (3.45% cases), enteric fever (2.31% cases), HIV (1.54% cases), leukemoid reaction (0.77% cases) and rubella (0.38% case). Congestive splenomegaly (39 cases, 15%) was the second most common cause among the non hematological disorders comprised of liver cirrhosis 35 cases (13.46%), portal vein thrombosis 3 cases (1.15%) and one case (0.38%) of mitral stenosis with rheumatic heart disease. Bone marrow aspiration was an important investigation to diagnose treatable causes of splenomegaly, hence proved to be diagnostic in 79 cases out of total 82 cases of splenomegaly. Nutritional anemia (67.07%) was the most common indication for the bone marrow aspiration followed by the leukemia (21.95% cases). There were 3 cases of splenomegaly in which no specific abnormality was seen. As shown in the above table no. 3 among the hematological causes (n=140), 90.71% cases of splenomegaly showed decreased Hb. There were 32.8% cases which showed decreased TLC count and 25.7% cases showed increased TLC count. There were 82.14% cases in which platelet count (<1.5lackhs/cumm) was decreased and increased in 4.28% cases. MCV was decreased in 32.14% cases and increased in 38.57% cases. MCH and MCHC were decreased in 56.4% cases and 1.85 % cases respectively. Majority of cases (89.28%) showed decreased RBC count. Among the non hematological causes (n=120), 65.83% cases of splenomegaly showed decreased haemoglobin concentration (table no.4). There were 14.17% cases in which TLC count was decreased and 21.67% cases we associated with increased TLC count. Platelet count was decreased in 82.57% cases (<1.5lackhs/cumm). MCV was decreased in 27.5% cases and increased in 18.34% cases. MCH and MCHC were decreased in 40.83% cases and 13.34% cases respectively. There were 68.33% cases which showed decreased RBC count. However there was no correlation between the size of spleen and degree of anemia and cytopenia (p>0.05). Hypersplenism was diagnosed in 68 cases. Congestive splenomegaly secondary to liver cirrhosis was the major cause (51.47%) followed by megaloblastic anemia (27.94%). Grade II (45.59%) and grade III (33.82%) splenomegaly was observed in maximum cases of hypersplenism followed by grade I (14.70%) and grade IV (5.89%). There was a significant association between increasing spleen size and occurrence of hypersplensim by using Chi square test (p<0.00001). However there is no statically significant association between the grades of splenomegaly and Hb concentration (P-0.134), total leukocytes count (P- 0.555), platelet count (P – 0.925) and RBC count (P- 0.734) by calculating the correlation co-efficient. Twenty patients of hypersplenism were undergone splenectomy. These cases were followed up for 3 months after splenectomy. A good response with increase in haemoglobin, platelet count and total leucocyte count was observed in all the patients (100%) on follow up examination.

Table 1: Distribution of grades of Splenomegaly in different age groups (n=260)

Sr. no.	Age groups	Grades of Splenomegaly				
		Grade I	Grade II	Grade III	Grade IV	Total
1	**Paediatric (1month-12yrs)**	28 (10.76%)	18 (6.93%)	10 (3.85%)	2 (0.76%)	58 (22.30%)
2	**Adolescent (13yrs-19yrs)**	19 (7.30%)	8 (3.07%)	5 (1.93%)	1 (0.39%)	33 (12.70%)
3	**Adult (>19-85 yrs)**	53 (20.40%)	65(25%)	39 (15%)	12 (4.61%)	169 (65%)
4	**Total**	100 (38.46%)	91(35%)	54 (20.78%)	15 (5.76%)	260 (100%)

Table 2: Final diagnosis based on haematological parameters in 260 cases of splenomegaly

Final diagnosis	Category	No. of cases	(%)
A. Hematological		140	53.85
1. Anemia (101)	Megaloblastic	43	16.55
	Dimorphic	28	10.77
	Iron deficiency	12	4.62
	Thalassemia major	13	5
	Thalassemia intermedia	1	0.39
	Sickle cell disease	2	0.77
	Autoimmune haemolytic anemia	1	0.38
	Hereditary spherocytosis	1	0.38
2. Leukemia (31)	AML	14	5.38

	CML	8	3.08
	ALL	5	1.92
	CLL	4	1.54
3. Lymphoma (2)	Lymphocyte rich Hodgkin lymphoma	1	0.38
	Low grade B cell Non Hodgkin lymphoma	1	0.38
Plasma cell dyscrasia (4)	Multiple myeloma	4	1.54
5. Others (2)	ITP	2	0.77
B. Non-hematological		120	46.15
6. Congestive (39)	Liver cirrhosis	35	13.46
	Portal vein thrombosis	3	1.15
	Mitral stenosis with RHD	1	0.38
7. Infection (80)	Dengue	38	14.61
	Malaria	20	7.69
	TB	9	3.45
	Enteric fever	6	2.31
	HIV	4	1.54
	Rubella	1	0.39
	Leukemoid reaction	2	0.77
8. Inflammatory (1)	SLE	1	0.38
Total		260	100

Table 3: Haematological findings in haematological causes of splenomegaly (n=140)

Parameters	**Aetiology**					
	Anemia (n=101)	**Leukemia (n= 31)**	**Plasma cell dyscrasia (n= 4)**	**ITP (n=2)**	**Lymphoma (n= 2)**	**Total (n=140)**
1. Hb (gm%)						
11	0	3	0	0	0	3
9-11	5	5	0	0	0	10
7-9	29	9	3	0	0	41
5-7	35	8	0	2	1	46
< 5	32	6	1	0	1	40
2. TLC(/cumm)						
Normal (4-11000/cumm)	47	6	3	1	1	58
Leucocytosis	10	25	0	1	0	36
Leucopenia	44	0	1	0	1	46
3. Platelet count						
Normal (1.5-4.5)	11	5	2	0	1	19
Thrombocytopenia	86	24	2	2	1	115
Thrombocytosis	4	2	0	0	0	6
4. MCV(fl)						
Normal	25	14	2	0	0	41
Increased	41	12	1	0	0	54
Decreased	35	5	1	2	2	45
5. MCH						
Normal	42	18	1	0	0	61
Decreased	59	13	3	2	2	79
6. MCHC						
Normal	81	28	3	1	2	115
Decreased	20	3	1	1	0	25
7. RBC count						
Normal	5	7	0	0	0	12
Decreased	93	24	4	2	2	125
Increased	3	0	0	0	0	3

Table 4: Haematological findings in non- haematological causes of splenomegaly (n=120)

Parameters	**Aetiology**				
	Infection(n= 80)	**Inflammtory (n= 1)**	**Congestive (n= 39)**	**Undetermined (n= 0)**	**Total (n=120)**
1. Hb (gm%)					
11	12	0	7	0	19
9-11	17	0	5	0	22
7-9	14	0	24	0	38
5-7	14	0	20	0	34
< 5	2	1	4	0	7
2. TLC (/cmm)					
Normal	55	0	22	0	77
Leucocytosis	17	1	8	0	26

Leucopenia	8	0	9	0	17
1. Platelet count					
Normal (1.5-4.5)	16	0	5	0	21
Thrombocytopenia	64	1	34	0	99
Thrombocytosis	0	0	0	0	0
2. MCV(fl)					
Normal	44	1	20	0	65
Increased	9	0	13	**0**	**22**
Decreased	27	0	6	0	33
3. MCH					
Normal	45	1	25	0	71
Decreased	35	0	14	0	49
4. MCHC					
Normal	69	1	34	0	104
Decreased	11	0	5	0	16
5. RBC count					
Normal	38	0	0	0	38
Decreased	42	1	39	0	82
Increased	0	0	0	0	0

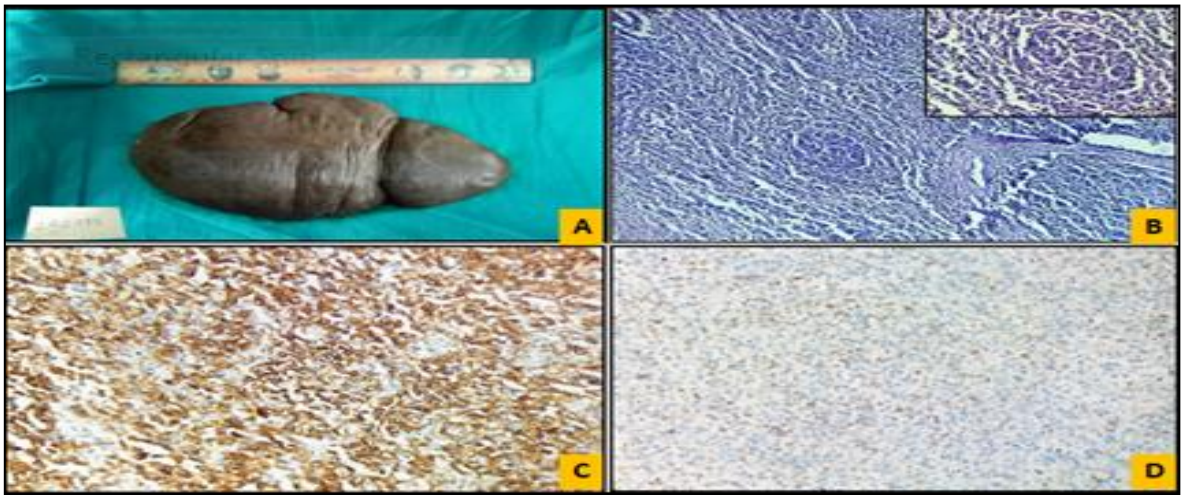

Fig 1- Gross specimen showing massively enlarged spleen in a case of low grade B cell Non-Hodgkin lymphoma (A). Photomicrograph of a case of low grade B- cell Non Hodgkin lymphoma showing effacement of architecture by malignant lymphoid cells arranged in marginal zone pattern (400X). Inset shows central zone of small lymphoid cells and outer zone of medium sized cells (400X) (B). Photomicrograph of a case of low grade B- cell Non Hodgkin lymphoma showing CD 20 positivity (400X) (C). Photomicrograph of a case of low grade B- cell Non Hodgkin lymphoma showing focal positivity for Bcl-2 (400X)(D).

Discussion

Splenomegaly in a symptomatic patient is of considerable clinical significance. One must investigate a case of splenomegaly as many of the conditions causing splenomegaly are treatable[4]. Cases of nutritional anemia and infections can also be treated with medical line of treatment. Nadim et al have shown regression in splenic size with correction of iron deficiency[4]. In present study we have come across 5 cases of iron deficiency anemia which had shown features of hypersplenism. Given the multitude of functions of spleen, it is not surprising that splenomegaly occurs in variety of conditions. However careful clinical evaluation and routine hematological investigations provide answers in of many of these conditions. This is exemplified in observations in present study which showed very few cases of infective pathology. Similarly cases of enteric fever, or septicemia which had splenomegaly were diagnosed by other pertinent investigations and were not referred for hematological work up. Only those cases of splenomegaly were evaluated which were referred to us by clinicians for extensive hematological workup, especially bone marrow examination. In the present study males were affected more than the females. Similar findings have been reported by by Deepti et al (2016), Chandanwale et al (2015), Timite-Konan M. et al (1992) and Humaira et al (2016)[1,5,10,11]. Amongst the total 260 cases of splenomegaly, pediatric cases comprised of 22.30% and similar observations were made by Ali et al (2004) and Sundaresan et al (2005) [12,13]. Adolescent age group comprised of 12.7% cases and adult age group 65% cases and these findings are in concordance with the study done by Sundaresan et al(2005) and Bhatija et al(2016) [13,14]. The most common grade of splenomegaly was mild (Grade I and II, 73.46%) followed by moderate (Grade III, 20.77%) and massive (Grade IV, 5.76%) splenomegaly. This was comparable to a study done by Hussain et al and Nadeem et al[2,4]. Fever was the most common clinical feature seen in 63.46% cases and similar findings were noted by by Deepti et al and Nadeem et al[1,4]. Associated hepatomegaly was found in 48.07% cases and similar observation was made by Kulkarni et al and Ali et al(2004) in their study[3,12]. In this study 10.38% cases were associated lymphadenopathy and similar findings were noted by the Ali et al (2004) and Bhatija et al(2016)[12,14]. Multiple organomegaly (splenomegaly+hepatomegaly+ lymphadenopathy) was seen in 6.15% cases in the present study. These cases were thalassemia major and bacterial infections. Thus occurrence of multiple organomegaly is an important feature of infections and hematological disorders. Similar findings were also noted by other authors[4,12,15]. This consideration should help in clinical decision of etiology of splenomegaly. Hematological causes of splenomegaly (53.85%) were dominant over the non hematological causes of splenomegaly and similar findings

have been reported by Chandanwale et al, Ali et al and Bhatija et al [5,12,14]. Anemia was found as the predominant cause of splenomegaly among the haematological causes and similar observations were made by Chandanwale et al and Bhatija et al[5,14]. Leukemia as a cause of splenomegaly was noted in 22.14% cases and these findings are in concordance with the study done by Chandanwale et al[5]. Infective causes of splenomegaly (66.67%) were predominant among the non-hematological disorders and similar observation was noted by Bhatija et al[14]. Congestive splenomegaly noted in 32.50% which is in accordance with the study done by Bhatija et al[14]. Megaloblastic erythropoiesis was diagnosed in maximum number of cases (32.92%) on bone marrow aspiration. However in the present study 9.76% cases of iron deficiency and 4.88% cases of acute lymphoblastic leukemia and 9.76% cases of acute myeloid leukemia were reported on bone marrow aspiration and these findings are in concordance with the study done by Varsha et al [6]. Congestive splenomegaly was found in 47.06% cases of hypersplenism and similar findings were noted by Sundaresan et al (2005)[13]. There was a significant association between increasing spleen size and occurrence of hypersplenism in this study and similar observations were made by Kulkarni et al , Sundaresan et al and Bhatija et al[3,13,14]. However there was no correlation between splenic size & degree of anemia and cytopenia and these findings are in concordance with the studies done by Deepti et al , Sundaresan et al and Bhatija et al[1,13,14]. Splenectomy was performed in 20 patients. There was an improvement in all hematological parameters and similar results were noted by Kulkarni et al, Chandanwale et al, Sundaresan et al and Bhatija et al[3,5,13,14].

Conclusion

Any case of splenomegaly should always be investigated thoroughly as most of the cases are treatable. Hematological parameters in any patient with enlarged spleen are utmost important as a diagnostic or additional tool in elucidating the etiopathogenesis of splenomegaly.

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Conflict of Interest: Nil Source of support: Nil