CLINICO-HEMATOLOGICAL CORRELATION OF PATIENTS PRESENTING WITH THROMBOCYTOPENIA.

Pathology

Dr. Ish Pandhi	Consultant Pathologist, Rapid Laboratory, Patiala.
Dr. Gaytri*	Resident, Department of Pathology MMIMSR, Mullana, Ambala * Corresponding Author.
Dr. Sonali Poonia	Resident, Department of Pathology MMIMSR, Mullana, Ambala.

ABSTRACT

Background: Thrombocytopenia is a common clinical problem, found in laboratory results during health examinations. Thrombocytopenia is deficiency of platelets in the blood. Platelets play an essential role in hemostasis, thrombosis and coagulation of blood. The normal platelet count in adult ranges from 150,000 to 450,000/µL. Reduction in platelet number and/or abnormality in platelet function constitutes an important cause of generalized bleeding. Spontaneous bleeding does not become evident until platelet count falls below 20,000 platelets/µL.

Materials and methods: The study was conducted on 100 patients who presented with persistent thrombocytopenia for more than two weeks and was done in Tertiary care hospital. Complete clinical details were recorded. Routine haematological investigations like Complete blood count (CBC) were performed using automated cell counter. Detailed peripheral blood examination (PBF) was done after staining the blood film with May-Grunwald Giemsa (MGG) stain. The bone marrow examination was done in every case and findings were recorded.

Results: A total of 100 cases were included in our study and categorized into neoplastic and non-neoplastic. The most common neoplastic condition were acute leukemia. The most common non-neoplastic conditions were Idiopathic thrombocytopenic purpura followed by megaloblastic anemia. Age distribution of patient varied over a wide range from newborn to 85years of age.

Conclusion: We concluded that thrombocytopenia per se is not a disease but it is an entity which can be seen in a number of clinical problems including neoplastic and non neoplastic diseases. No single investigation can help us to reach the final diagnosis but we require relevant clinical details and a set of investigations to reach the root cause of thrombocytopenia.

KEYWORDS

Thrombocytopenia, Leukemia, Anemia.

INTRODUCTION

Thrombocytopenia is a common clinical problem, found in laboratory results during health examinations. Thrombocytopenia is deficiency of platelets in the blood. Platelets play an essential role in hemostasis, thrombosis and coagulation of blood [1]. The normal platelet count in adult ranges from 150,000 to 450,000/µL [2].Reduction in platelet number and/or abnormality in platelet function constitutes an important cause of generalized bleeding. Spontaneous bleeding does not become evident until platelet count falls below 20,000 platelets/µL.Platelet count in range of 20,000 to 50,000 platelets/µL can aggravate post traumatic bleeding. Bleeding resulting from thrombocytopenia is associated with normal PT (Prothrombin Time) and PTT (Partial Thromboplastin Time) [1]. The wide spread availability of cell counters in clinical laboratories now permits accurate measurement of the mean platelet volume and the extent of heterogeneity in platelet size on the basis of the platelet distribution width. Recently, there have been new insights into the pathogenesis and recognition of various types of thrombocytopenia [3].

MATERIALS AND METHODS

The study was conducted on 100 patients who presented with persistent thrombocytopenia for more than two weeks and was done in Tertiary care hospital. Detailed clinical findings of patients regarding duration of illness, loss of weight, significant family history and any history of drug intake or blood transfusion in the past were taken. This was followed by general physical and systemic examination. Routine haematological investigations like CBC were performed using automated cell counter [4]. The PBF and Bone marrow aspiration slides were processed routinely and stained with MGG stain [5].

RESULTS

A total of 100 cases were included in our study and categorized into neoplastic and non-neoplastic. [Table 1]

TABLE 1: Showing category wise distribution on patients

S. No.	Category	No. of patients
1	Neoplastic	42
2	Non-neoplastic	58
3	Total	100

Age distribution of patient varied over a wide range from newborn to 85years of age [Table 2]

TABLE 2: Showing different age groups

S. No.	Age group	Number of cases
1	0-10	17
2	11-20	17
3	21-30	17
4	31-40	14
5	41-50	10
6	51-60	13
7	61-70	09
8	71-80	02
9	81-90	01
Total		100

Males were more commonly affected than females. In the present study there were 59 male patients (59%) and 41 females (41%) with M:F ratio of 1.44:1 [Table 3].

TABLE 3: Showing sex distribution of patients

S. No.	Sex	No of patients
1	Male	59
2	Female	41
Total		100

The most prevalent clinical feature was generalized weakness (95%) followed by fever which constituted 66% of the cases. However breathlessness, alcohol ingestion and drug intake formed the minor group (2% each). [Table 4]

TABLE 4: Showing clinical presentation in patients of thrombocytopenia

S. No.	Clinical presentation	Number of cases
1	General weakness	95
2	Fever	66
3	Petechiae/ Purpura/ Bruise	31
4	Bleeding	15
5	Menorrhagia	4
6	Organomegaly	24
7	Lymphadenopathy	6
8	Icterus	11
9	Bony tenderness	4
10	Drug intake	2
11	Alcohal	2
12	Breathlessness	2

Most common neoplastic condition was acute leukemia. The non-neoplastic conditions were Idiopathic thrombocytopenic purpura followed by megaloblastic anemia. Other neoplastic cases were Chronic myeloid leukemia, Plasma cell dyscrasia, Myelofibrosis, Non-Hodgkin's lymphoma, Myelodysplastic syndrome and Non-neoplastic diagnosed conditions were Dengue, Viral infections, Radiotherapy induced thrombocytopenia, Drug induced thrombocytopenia. [Table 5]

TABLE 5: Showing Neoplastic and Non-neoplastic diagnosis

S. No.	Diagnosis	Number of cases
	Neoplastic	
1	Acute myeloid leukemia	19
2	Acute lymphoblastic leukemia	17
3	Plasma cell dyscrasia	02
4	Chronic myeloid leukemia	01
5	Myelodysplastic syndrome	01
6	Non- Hodgkin's lymphoma	01
7	Myelofibrosis	01
	Non- neoplastic	
8	Idiopathic thrombocytopenic purpura	21
9	Megaloblastic anemia	19
10	Aplastic anemia	05
11	Dengue	07
12	Viral infections	02
13	Radiotherapy induced thrombocytopenia	01
14	Drug induced thrombocytopenia	02
15	Thrombotic thrombocytopenic purpura	01
Total		100

Total leucocyte count varied from 1200 to 1.1 lac/µL, with lowest in case of aplastic anemia and highest in a case of chronic myeloid leukemia (CML) in blast crisis respectively. [Table 6]

TABLE 6: Showing total leucocyte count in patients

S. No.	Total leucocyte count/µL	No. of patients
1	Normal (4,000 – 11,000)	51
2	Increased (>11,000)	36
3	Decreased (<4,000)	13
Total		100

Lowest platelet count of 2000/µL was seen in 3 years old female patient suffering from dengue who presented with petechial spots and high grade fever and bleeding PR followed by second lowest count of 3000/µL in patients of ITP and TTP. Patients with severe megaloblastic anemia presented with low platelet count ranging from 7000/µL to 98,000/µL and those suffering from viral infections and dengue ranged from 2000/µLto 77,000/µL. Platelet count of 5000/µL to 98,000/µLwas recorded in cases of acute leukemia. [Table 7]

TABLE 7: Showing platelet count

S. No.	Platelet count/µL	No. of patients
1	0-20,000	44
2	21,000- 40,000	22
3	41,000-60,000	14
4	61,000-80,000	09
5	81,000-1Lac	10
6	>1lac -<1.5 Lac	01

The most common blood picture was microcytic hypochromic, followed by normocytic normochromic picture. Inclusions as basophilic stippling and piokilocytes as ovalocytes, target and tear drop cells were seen patients suffering from megaloblastic anemia. [Table 8]

TABLE 8: Showing RBC morphology

S. No.	RBC morphology	No. of patients
1	Normocytic normochromic	26
2	Microcytic hypochromic	39
3	Macrocytic	12
4	Dimorphic	23
5	Poikilocytes	15
6	Inclusions	03

In most of the patients the size of the platelets was normal. Megathrombocytes (giant platelets) were noted in patients with megaloblastic anemia, chronic myeloid leukemia, myelofibrosis and microthrombocytes (microplatelets) noted in myelodysplastic syndrome. [Table 9]

TABLE 9: Showing platelet size

S. No.	Platelet size	No. of patients
1	Normal	81
2	Giant platelets	18
3	Microplatelets	01

DISCUSSION

In our study the age of patient ranged from 2-85 years. Cytopenias were observed more in males (59) than females (41), with male to female (M:F) ratio of 1.44:1. Age and sex distribution was compared with other studies of Gayathri and Rao et al [6] were 1.2:1 and KhungerJM et al [7] were 1.2:1.

Most common clinical presentation was generalised weakness followed by fever (66%), bleeding tendencies – petechiae/ purpura/ bruise (31%) and bleeding (15%). Similarly, Santra and Das et al [8] found weakness in 45%, fever in 50.4% and bleeding tendencies in 41.4% cases.

In present study of peripheral smear microcytic hypochromic was predominant finding. Microcytic hypochromic RBC's were seen in 39% cases followed by normocytic normochromic RBC's (26%). Macrocytic picture were seen in 12% and dimorphic picture was seen in 23%. Other study of Yadav A et al [9] showed similar finding in peripheral smear, microcytic hypochromic RBC's in 27.22% cases followed by normocytic normochromic RBC's in 26.6% cases, macrocytic picture were seen in 25% cases and dimorphic picture was seen in 20.56% cases. The peripheral blood film examination and CBC results (from hematology analyzer) correlated well with bone marrow findings in most of the cases.

In present study there was 36% incidence of acute leukemia (19% incidence of acute myeloidleukemia and 17% incidence of acute lymphoblastic leukemia) compared with 32% reported by Kumar Ret al [12] and Khunger JM et al [7] reported 29% incidence of acute leukemia.

Out of 100 cases of thrombocytopenia;ITP was found in 21 cases, Both PBF and CBC findings, especially platelet parameters (MPV), correlated well with bone marrow findings in some patient . All the cases showed peripheral isolated thrombocytopenia with increased megakaryocytes .

Megaloblastic anemia was seen in 19 patients. Bone marrow study showed erythroid hyperplasia with pronounced megaloblastic change. Giant stab forms and related megaloblastic changes in megakaryocytes were also seen. Peripheral thrombocytopenia was associated with characteristic CBC and peripheral smear findings.

Acute leukemia was seen in 36 patients (ALL – 17 and AML- 19). In these cases, thrombocytopenia was associated with anemia and leukocytosis with many blast cells (myeloblasts in AML and lymphoblast in ALL).

One patient of chronic myeloid leukemia (chronic phase) on follow up developed blast crisis (myeloid) during this period of our study and developed thrombocytopenia. The marrow in this case was cellular with myeloblasts> 20% and markedly decreased megakaryocytes.

One case of myelofibrosis with thrombocytopenia were also observed. In this case, peripheral thrombocytopenia was associated with leucoerythroblastic blood picture on PBF with hypoplastic/aplastic bone marrow. Fibrosis was highlightened on reticulin stain.

5 cases of aplastic anemia presented with thrombocytopenia. All these cases showed pancytopenia on PBF with hypocellular bone marrow with increased fatty tissue.

One patient of MDS also presented with thrombocytopenia with leukocytic precursors. The marrow in this patient was hypercellular with erythroid hyperplasia, and showed features of dysmegaka ryopoiesis and dyserythropoiesis.

7 cases of dengue and 2 cases of viral infections presented with thrombocytopenia. The PBF in these cases showed thrombocytopenia along with many activated lymphocytes. Serology was done for conformation.

If clinical details are complete, CBC parameters (from hematology analyzer) along with careful examination of PBF in these patients are very useful in predicting the diagnosis in most of the patients and in these cases, invasive procedures like bone marrow aspiration and bone marrow trephine biopsy can be avoided/deferred.

We also found out that bleeding is not a very common manifestation in thrombocytopenia, and moreover few patients with very low platelet count (less than 20,000/µL) had no bleeding manifestation.

Platelet transfusion is not necessary in patients of thrombocytopenia who presented without any bleeding manifestations and some patients of dengue with low platelet count but without any form of bleeding recovered spontaneously.

Parameters like serum vitamin B12 and red cell folate levels, if possible, can be of great help in megaloblastic anemia.

CONCLUSION

Hence, we conclude from our study that clinical history, complete examination of the patient along with routine hematological investigations including PBF and CBC combined with bone marrow aspiration and bone marrow trephine biopsy in certain cases, biochemical, radiological and serological examination are important in diagnosing the cases presenting with thrombocytopenia either isolated or combined with other cytopenias.

Hence, in all the cases of thrombocytopenia, detailed clinical examination should be done after taking complete history and these patients should be subjected to CBC and PBF examination which will provide clue to the underlying disorder and one can plan accordingly for further investigations if necessary like bone marrow aspiration and bone marrow trephine biopsy and other related investigations.

This protocol will help in providing early diagnosis, treatment and also minimize patient's stay in hospital, cost and above all patient's agony.

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