ORIGINAL ARTICLE

Clinical Features and Frequency of Immune Thrombocytopenia in Hospitalized Pediatric patients: A study based on Bone Marrow Aspiration

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ABSTRACT

Aims: To see frequency along with clinically significant symptoms and signs of immune thrombocytopenia (ITP), in hospitalized pediatric patients below fifteen years at Mayo hospital Lahore, a tertiary care teaching hospital.
Settings: Clinical laboratory of children Department, at Mayo hospital Lahore during Feb 2009 to January 2013.
Design: Study was retrospective.
Methods: Hospital files of all pediatric patients of less than 15 years of age with confirmed conclusion of suffering from ITP, were reviewed in detail in reference to detailed history of illness, detailed physical examination, first complete blood counts (CBC) report along with descriptive peripheral blood picture and marrow aspiration report. Complete blood counts and bone marrow aspiration was done in all patients.
Results: During this period of study, six hundred seventy eight bone marrow aspirations / biopsies were carried out. Malignant blood disorders were diagnosed in two hundred thirty six (34.80%) children. Remaining four hundred forty two (65.20%), children were having benign hematological disorders. Out of 442 children declared as suffering from benign blood disorders fifty eight (13.10%), children were finally diagnosed as suffering from immune thrombocytopenia.. The commonest Presenting clinical features in these children were petechial hemorrhages (90.0%), bruises (73.7%.
Conclusion: Immune thrombocytopenia (ITP), a commonly diagnosed benign hematological disorder in children, typically presents with few clinical features. In majority of cases it is a simple straight forward diagnosis successfully achieved by clinically presenting features, physical examination, complete blood counts report, peripheral blood smear findings and authenticated bone marrow aspiration report.
Keywords: Immune thrombocytopenia, Epistaxis, Petechiae.

INTRODUCTION

Immune thrombocytopenic purpura (ITP) is a clinically important hematological pathology. It is quite frequently seen in pediatric as well as in adult patients when their suspicious clinical presentation demands CBC report and finally their complete blood counts (CBC) report show thrombocytes count falling below $100x10^9$/L. This decrease in platelets count is immunologically mediated. Thrombocytes are produced normally in bone marrow and afterwards are being destroyed either in peripheral blood or within the bone marrow by antibodies produced as auto-antibodies[1]. In children ITP is a self-limiting disorder whereas it may exhibit a chronic course in adults[2]. Interestingly underlying pathogenesis may be remarkably different in two age groups.

An international working group (IWG), on ITP released a declaration that ITP abbreviation should be taken as immune thrombocytopenia. Idiopathic and purpura words must be avoided, as it is proved by massive data collection that in majority of pediatric and adult patients purpuric spots are absent, even under the circumstances when these patients show visible petechiae and bruises[3]. Some of the authors have used autoimmune thrombocytopenia for ITP.

Two main categories of immune thrombocytopenia are primary and secondary ITP. Researchers working on pathophysiology of ITP have finally declared that decreased platelet counts in primary ITP is due to destruction of platelets by auto-antibodies either in peripheral blood or in bone marrow[4]. Other less documented mechanisms involved in thrombocytopenia are defective megakaryocytopoiesis[5]and T-cells mediated platelets destruction[6]. In some of the ITP patients, all three above mentioned mechanisms are operating to a variable degree. In secondary immune thrombocytopenia, underlying primary pathology is blamed for thrombocytopenia, as seen in systemic lupus erythematosus (SLE), rheumatoid arthritis, infection with H. pylori and HIV[7].

Eighty percent of pediatric patients suffering from ITP show remission in 6-12 months[8]. Among ITP diagnosed children, 80% turn out to be of primary whereas 20% as secondary ITP cases[9]. Platelets auto-antibodies are detected in about 20% cases only. History of fever is present in about 66% of children. In pathogenesis of primary ITP, initially thrombocytes studded with viral antigen are produced by bone marrow. Antibodies are produced against these viral antigens which show cross reactivity with antigens on the surface platelets and ultimate result is platelet destruction[10]. Antibodies of IgG nature are coating platelets and finally blood gets rid of these immunoglobulin G coated thrombocytes through macrophages present in the spleen, liver and bone marrow. These phagocytic macrophages are possessing Fc receptors for IgG[11].

Diagnosis of ITP is usually based upon history, physical examination, complete blood counts and peripheral blood smear findings. Other etiologies of thrombocytopenia when excluded are helpful in final diagnosis of a case of ITP. HIV, HCV and H. Pylori Infections must also be included in the list of disorders to be excluded first before declaring a final diagnosis of ITP. Autoimmune disorders like rheumatoid arthritis and systemic lupus erythematosus (SLE), malignant hematological disorders such as leukemias, lymphoproliferative conditions and myeloproliferative diseases, drugs like alcohol, heparin and quinidine are other etiologies of

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thrombocytopenia and must also be excluded before concluding a final diagnosis[12,13].

Few specialized and related tests were recommended by international working group (IWG) for suspected ITP cases. These tests detect human immunodeficiency virus, hepatitis C virus and antigen of helicobacter pylori. Direct antiglobulin test (DAT) and indirect antiglobulin test (IAGT) were also recommended[14]. Bone marrow study is not recommended by IWG in pediatrics ITP cases which are managed through observation and by parenteral immunoglobulins[15]. But at the same time pediatric hematologists generally suggest bone marrow aspiration to exclude leukemia before starting treatment with steroids[16]. Children who are positive for antinuclear antibodies are at high risk of entering into chronicity and may show refractory response to treatment[17].

MATERIALS AND METHODS

The site selected for this study was clinical laboratory of pediatric department at Mayo hospital, Lahore, and duration of study was from February 2009 to January 2013. Six hundred seventy-eight (678), bone marrow aspirations / biopsies were performed for the diagnosis of underlying hematological disorder. Fifty-eight children who were suffering from ITP were included in this study. All patients were less than fifteen years of age. Every child was advised to get a report of complete blood counts along with peripheral blood smear findings. Marrow aspiration and ultrasonography was carried out in all children. A proforma was designed to collect all required data. Hematology analyzer KX21was used for complete blood counts. Giemsa stain was used to stain slides of peripheral blood smear. Bone marrow aspiration was mandatory in all cases. Tibia was the preferred site for aspiration in children below two years, whereas posterior superior iliac spine or iliac crest was preferred for children above two years of age.

RESULTS

In this retrospective study children age ranged from 11 months to 13 years. Male compared to female ratio was 1.6:1.0. Among male children average age was 6.9 years and in female children it was 7.3 years. In our study cohort 23(39.6%) children were in age range of 11 months to 5 years, 27(46.6%) children ages ranged from 05 to 10 years and 8(13.8%) children were in range of 10 to 13.5 years (Table I).

In these selected children of ITP, extent of thrombocytopenia was variable. It was severe thrombocytopenia in 30(51.7%), moderate in 20 (34.5%) and mild in 8(13.8%) children (Table II). Children suffering from immune thrombocytopenia with counts less than 20,000 /c.mm, are at a high risk of intracranial hemorrhage.

In this study most commonly presenting clinical complaint was appearance of bruises and petechiae on different parts of body. Bleeding from other sites like nose bleed, gum bleed, skin hemorrhagic spots, blood in stool and vomiting of blood were less frequently complained. Two children complained of bleeding from ear. Organomegaly was a rare finding on physical examination as well as on ultrasonography (Table III).

Table I: Age and Sex Distribution (n=58)

Age	Male	Female	Total
11months- 60 months.	14	09	23(39.7%)
05 - 10 years	17	10	27(46.5%)
10 – 13.5 years	05	03	08(13.8%)
Total	**36**	**22**	**58 (100%)**

Table II: Platelet Counts Distribution

Platelet counts	n	%age
10-20 $x10^9$ / L	30	51.7
20-50$x10^9$ / L	20	34.5
50-199$x10^9$/L	08	13.0
Total	**58**	**100**

Table III: Presenting Clinical Features in ITP

Presenting features	Frequency	%age
Bruises	42	72.4
Petechiae	33	56.9
Nose bleed	25	43.1
Purpura	20	34.5
Fever	20	34.5
Gum bleed	18	31.0
Arthralgia	18	31.0
Hepatomegaly	15	25.9
Lymphadenopathy	15	25.9
Hepatosplenomegaly	12	20.7
Melena	09	15.5
Post traumatic bleed	08	13.8
Oral ulcers	06	10.3
Splenomegaly	05	8.6
Hematemesis	04	6.9
Bleeding from ear	02	3.4

DISCUSSION

Immune thrombocytopenia (ITP) is frequently diagnosed pediatric hemorrhagic disorder with variable clinical presentation. It is classified as an autoimmune hematological disorder with classical isolated thrombocytopenia. In this disease platelets are being destroyed by an immunogenic mechanism both in peripheral blood and bone marrow. Majority of ITP cases are seen between two to five years[18]. In pediatric patient immune thrombocytopenia is usually a self-limiting disorder having an acute onset. In about 80% of children, this disorder resolved without any specific therapeutic measures within six to twelve months[19]. Only few children of ITP present clinically with alarming hemorrhagic tendency that requires therapeutic support[20]. A case of acute ITP is declared as entering into chronic phase when its duration is more than six months without any known etiology and platelet count is less than $100x10^9$/ L persistently[21].

During this period six hundred and seventy eight (678), children were admitted in pediatric oncology ward with suspicion of hematological disease and bone marrow aspiration / biopsy was done all cases. After bone marrow study results, 236 children were finally diagnosed as cases of malignant hematological disorder. Benign blood disorder was confirmed in 442 children. Out of 442 children only 58 children were finally declared as suffering from ITP. Average age of pediatric patient in this small group was 7.1 years and gender wise male / female ratio came out as 1.6:1.0. Frequency of ITP among total bone marrow study cases was 8.55% and among benign hematological disorders it was 13.10%.

Two different studies conducted by Zahid et al[22]and Fazal et al[23] in Pakistan declared their results similar to this study. Three other studies carried out in India and Pakistan by Khan et al[25], Ali et al[24] and Majumdar et al[26]declared slightly higher values of immune thrombocytopenia cases than ours (Table IV).

Table IV: Frequency comparison of Bone Marrow based studies in ITP.

Reference of study	Total children	Benign Total disorders number	Total ITP patients	ITP frequency among Total	ITP frequency among Benign
Rahim F et al. 2005.	424	309	40	9.4%	12.9%
Khan A et al. 2008.	198	174	31	15.7%	17.8%
Zahid Gul et al. 2014.	249	190	19	7.6%	10.0%
Ali I et al.2015.	140	125	18	12.9%	14.4%
Majumdar et al. 2015.	150	86	25	16.0%	29.1%

CONCLUSION

Our study finally concluded that bone marrow aspiration / biopsy is a vital procedure to identify these variable etiologies. In resource poor setups like our own, bone marrow aspiration is a top priority procedure to confirm diagnosis of immune thrombocytopenia and at the same time to rule out any hematological malignancy involving marrow functional activity. It is also pointed out that bone marrow examination in immune thrombocytopenia is sometime unnecessarily advised than truly needed. Pediatricians argument in favor of their decision to go for bone marrow examination is that they intend to exclude leukemia before administration of steroids. So final conclusion after this study is that pediatric patients presenting with immune thrombocytopenia must be advised to get bone marrow aspiration examination prior to start of steroidal treatment. Bone marrow aspiration before start of treatment will also help to exclude any malignant hematological disorder affecting bone marrow functional activity.

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