IJBC 2012;3: 119-123

Evaluating the Prognostic Significance of Bone Marrow Megakaryocyte Count in Patients with Idiopathic Thrombocytopenic Purpura

Eghbali A[1]*, Arzaninan M[2], Chehrei A[3] , Jadidi R[4], Sabbagh A[5]

1- Assistant professor, Pediatric Hematologist & Oncologist, Department of Pediatrics, Arak University of Medical Sciences, Arak, Iran

2- Assistant professor, Pediatric Hematologist and Oncologist, Shahid Beheshti University of Medical Sciences, Tehran, Iran

3- Assistant professor, Department of Pathology, Arak University of Medical Sciences, Arak, Iran

4- Assistant professor,PhD of Health management , Arak University of Medical Sciences, Arak, Iran

5- Assistant Pediatrics, Department of Pediatric, Arak University of Medical Sciences, Arak, Iran

***Corresponding Author:** Eghbali A, Email:aziz_eghbali@yahoo.com*

Submitted:25-08-2011, Accepted: 15-03-2012

Abstract

Background: Previous studies about the relationship between bone marrow megakaryocyte count and the chronicity of ITP has yielded paradoxical results. The aim of the present study was to investigate any relationship between the megakaryocyte count in the bone marrow and the chronicity of ITP.

Materials and Methods: This study was performed to compare the primary bone marrow aspiration megakaryocyte count, obtained early upon the diagnosis of ITP, between chronic ITP (case) and acute ITP (control) groups among patients aged less than 15 years old, at Mofid Hospital, Tehran and Amir-Kabir Hospital, Arak. Data collected was analyzed using SPSS version 18. The project was approved by local Ethics committee and written informed consent was obtained from all parents.

Results: Three hundred and seven patients with ITP including 212 patients with acute ITP (69.1 %) and 95 patients with chronic ITP (30.9 %) participated in the study. The bone marrow megakaryocyte count was increased in 263 patients (85.7 %), decreased in 7 patients (2.3 %), and normal in 37 patients (12.1%). Among 212 patients with acute ITP, the bone marrow megakaryocyte count was increased in 182 patients (85.8 %), decreased in 5 patients (2.4%), and normal in 25 patients (11.8 %). Among 95 patients with chronic ITP, the bone marrow megakaryocyte count was increased in 81 patients (85.3 %), decreased in 2 patients (2.1 %), and normal in 12 patients (12.6%). There was no statistically significant difference between two groups regarding the megakaryocyte count.

Conclusion: Based on our findings it seems that the variant of bone marrow megakaryocyte count is not related to the chronicity among patients with ITP.

Keywords: Bone marrow aspiration, children, immune thrombocytopenic purpura, megakaryocytic

Introduction

Immune thrombocytopenic purpura (ITP) is defined as isolated thrombocytopenia with normal bone marrow and the absence of other causes of thrombocytopenia [1]. ITP in pediatric patients manifests as isolated thrombocytopenia, petechiae, and purpura. ITP is one of the most common causes of thrombocytopenia in pediatric patients and one of the problems associated with ITP is its chronicity. The acute form of the disease is more common and happens in 70-80% of cases, and is cured in less than 6 months, while 20-30% of the cases convert to chronic form [1-5] .

Bone marrow aspiration in patients with ITP is carried out to determine the presence of megakaryocytes and refuting other causes for thrombocytopenia such as leukemia and aplastic anemia [6]. Although platelets disruption is the main cause of thrombocytopenia in patients with ITP, it has been demonstrated that disturbance in platelet production might also be involved in the disease process. Platelet production disturbance is either due to the direct impact of autoimmune antibody against megakaryocytes or the impairment of platelet coating antibodies due to bone marrow

macrophages [7].

Usually, in pediatric patients, both genders equally develop the acute form of the disease, whereas female patients, especially in older ages, are more likely to develop the chronic form of this disease. The onset of the disease among children is often sudden and acute while it normally has a gradual course of development among adults.

The prognosis of this disease is often uncertain and unpredictable as there are no criteria for predicting the chronicity of the disease. Several studies have shown old age, female sex, and the insidious onset of the disease as the main factors identifying the course of ITP [5].

Several studies have been performed regarding the significance of the bone marrow megakaryocyte count in predicting the chronicity of ITP, with controversial results [8-15].

Immune disruption is not the only thrombocytopenic mechanism in ITP, and the disruption in the quality of bone marrow megakaryocytes is one of the potential causes of thrombocytopenia in this disease, especially in its chronic form [16-18].

Ren et al. observed that the higher bone marrow megakaryocyte count decreased the possibility of the ITP to become chronic [8], whereas Uçar, et al. did not find a significant relationship between the chronicity of ITP and bone marrow megakaryocyte count [16]. In another descriptive study Alavi et al. found no significant difference between the bone marrow megakaryocyte count among acute and chronic patients [19].

The present study was conducted to examine the relationship between megakaryocyte count in bone marrow and the chronicity of ITP.

Materials and Methods

This study was performed among ITP patients aged less than 15 years-old referred to Mofid Hospital, Tehran, Iran and Amirkabir Hospital, Arak, Iran during 2009-2010 period. ITP was considered as isolated thrombocytopenia for which drug-induced, infectious, collagen vascular, and congenital causes have been ruled out. We discussed with the parents their children's problem and the necessity of bone marrow aspiration to determine the next steps of treatment. We then obtained written informed consent from all parents. The project was approved by the local ethics committee of medical college of Arak.

The case group included children aged less than 15 years old, with chronic ITP for which other causes of thrombocytopenia had been excluded and the control group, consisted of patients with acute ITP in whom thrombocytopenia had been cured in a period of less than six months. Both groups were selected through convenient sampling. The sample size was calculated with a power of 80%, control to case ratio of 2, odds ratio of 2.8 and the exposure in the control group of 75%. Based of these parameters we estimated to need 89 patients for the case group and 178 patients for the control group.

Bone marrow slides for patients with acute and chronic ITP were examined and the mean number of megakaryocytes in bone marrow was counted with 10x magnification and recorded. Since the number of patients with acute ITP was far more than those with chronic ITP, selecting a control group was rather easy. The data were collected using a datasheet and was analyzed by SPSS

Table 1: Demographic variables of ITP patients participating in the study

	n	Mean age ± SD	Gender	
Acute ITP	212	4.03±0.14	Female	102
			Male	110
Chronic ITP	95	5.17±0.7	Female	53
			Male	42
All patients	307	4.3±0.36	Female	155
			Male	152

software for windows version 18. Chi-square test was run to compare the two groups. .

Bone marrow megakaryocytic count was performed with a microscope lens adjusted at 10x. At this magnification if there were more than 5 megakaryocytes, it was considered increased; within the range of 3-5 was considered normal; and finally less than 3 was considered decreased.

Results

Three hundred and seven patients including 212 acute ITP (69.1 %) and 95 chronic ITP (30.9 %) patients participated in our study. Overall, there were 152 males (49.5%) and 155 females (50.5%). The mean age was 4.3±0.36 years and patients ranged from two months to 14 years old. According to table 1, the mean age in the control group with acute ITP was 4.03±0.14, while it was 5.17±0.7 in the case group with chronic ITP, which shows a significant difference between the two groups (P=0.04).

Among all patients, the bone marrow megakaryocyte count was increased in 263 patients (85.7%), was normal in 37 patients (12.1%), and decreased in 7 patients (2.3%).

In the acute ITP group (n=212), the bone marrow megakaryocyte count was increased in 182 patients (85.8%), was normal in 25 patients (11.8%), and decreased in 5 patients (2.4%). In the same way, in the chronic ITP group (n=95) megakaryocyte count was increased in 81 patients (85.3%), normal in 12 patients (12.6%), and decreased in 2 patients (2.1%). The difference was not statistically significant (P=0.97).

With regard to the relationship between the chronicity of the disease and patient's gender, in the acute ITP group, 110 patients (51.9%) were male and 102 patients (48.1%) were female and in the chronic ITP group, 42 patients were male (44.2%) and the remaining 53 patients were female (55.8%). In our study there was not a significant difference between the two groups (P=0.22) considering the gender (Table 2).

The mean platelet count upon diagnosis, among all patients, in the pretreatment period was 20000±1000 with the range of 2000-76000, while it was 163000±11000 with the range of 14000-1118000 three days in the post treatment period.

The mean platelet count upon diagnosis and in the pretreatment period was 19000±1000 in the acute ITP group and 21000±2000 in the chronic ITP group, while three days after treatment these values were 161000±13000 and 166000±20000 in acute and chronic ITP groups respectively which did not show a significant difference between the two groups (P=0.6).

According to our data, there was not a significant correlation between the platelets count before treatment and three days after treatment (P=0.45). Moreover, although there was not a significant correlation between the platelet count after treatment and the age of patients, a significant correlation was observed between the platelet count before or after treatment and the age of patients (P<0.001).

Regarding the relationship between the platelet count before treatment and the bone marrow megakaryocyte count, the mean platelet count was, 20000±1000 in increased bone marrow megakaryocyte count group , 21000±5000 in

Table 2: The relationship between the chronicity of ITP and the number of bone marrow megakaryocytes.

Megakaryocyte count / Chronicity	Number of megakaryocytes			Total
	Increased	Normal	Decreased	
Acute	182 85.8%	25 11.8%	5 2.4%	212 100.0%
Chronic	81 85.3%	12 12.6%	2 2.1%	95 100.0%
Total	263 85.7%	37 12.1%	7 2.3%	307 100.0%

normal bone marrow megakaryocyte count group , and 15000±4000 in decreased bone marrow megakaryocyte count group, which did not show a significant difference (P=0.34).

In addition, with regard to the relationship between the platelet count three days after treatment and the bone marrow megakaryocyte count in groups with increased, normal, and decreased megakaryocyte count the mean platelet count was, 165000±12000, 155000±34000, and 106000±23000 respectively, which did not present a significant difference (P=0.24).

Discussion

In the present study, among 307 patients, 212 patients had acute ITP and 95 patients had chronic ITP. This proportion was similar to other studies. In our study the mean age was higher in the chronic group compared to the acute group which was also in agreement with other studies [1-5].

The comparison of megakaryocyte count in the bone marrow of patients with acute ITP and the patients with chronic ITP did not indicate a significant difference. This is in line with the findings of Uçar et al., Alavi et al., and Jubelirer et al. [16, 18, 19], but it is in contrast with the findings of Ren et al. [8]. The number of patients in the present study and Ren et al. study was almost the same, but the sample size in Uçar et al. study was small and was not highly reliable. These differences highlight the need for further research with a higher number of participants. In our study, the platelets count before treatment and three days after treatment did not show a significant correlation. Moreover, although there was not a statistically significant correlation between age and the platelet count after treatment, there was a significant correlation between age and the platelets count before treatment.

We encountered some constrains during the present study namely missing some patients in the follow up period due parent's poor cooperation.

Conclusion

Based on our findings it seems that the variant of bone marrow megakaryocyte count is not related to the chronicity among patients with ITP.

Acknowledgments

The authors would like to thank the staff at oncology departments of Amir Kabir Hospital, Arak, and Mofid Hospital, Tehran.

References

1. Glanz J, France E, Xu S, Hayes T, Hambidge S. Population-based, multisite cohort study of the predictors of chronic idiopathic thrombocytopenic purpura in children. Pediatrics 2008; 121(3): 506-12.
2. Zeller B, Rujon fie J. Childhood ITP in the Nordic countries epidemiology and predictors of chronic disease. Acta paediatrica 2005; 94(2): 178-84.
3. Pratt EL, Tarantino MD, Wagner D, Hirsch Pescovitz O, Bowyer S, Shapiro AD. Prevalence of elevated anti thyroid antibodies and antinuclear antibodies in children with ITP. Am J Hematol 2005; 79(3): 175-9.
4. Kalpatthi R, Bussel JB. Diagnosis, pathophysiology and management of children with refractory immune thrombocytopenic purpura. Curr Opin Pediatric 2008; 20(1): 8-16.
5. Lanzkowsky PH. Manual of pediatrics Hematolgy

Table 3: The relationship between the chronicity of ITP and the patients' gender

Chronicity \ Sex	Sex		Total
	Male	Female	
acute	110 51.9%	102 48.1%	212 100.0%
chronic	42 44.2%	53 55.8%	95 100.0%
Total	152 49.5%	155 50.5%	307 100.0%

and Oncology. 4th ed. Burlington: Elsveire Academic Press; 2005. p. 250-63.
6. Halperin DS, Doyle JJ. Is bone marrow examination justified in idiopathic thrombocytopenic purpura? Am J Dis Child. 1988; 142(5):508-11.
7. DIGGS LW, HEWLETT JS. A study of the bone marrow from 36 patients with idiopathic hemorrhagic, thrombopenic purpura. Blood. 1948;3(10):1090-104.
8. Ren DQ, Gao H, Li ZC. Prognostic significance of peripheral blood cell and bone marrow megakaryocyte counts in patients with idiopathic thrombocytopenic purpura .journal of experimental hematology .2003 Apr;11(2):199-201 .
9. Ballem PJ, Segal GM, Stratton JR, Gernsheimer T, Adamson JW, Slichter SJ. Mechanisms of thrombocytopenia in chronic autoimmune thrombocytopenic purpura: evidence of both impaired platelet production and increased platelet clearance. J Clin Invest 1987; 80: 33 -40.
10. Siegel RS, Rae JR, Barth S. Platelet survival and turnover: important factors in predicting response to splenectomy in immune thrombocytopenic purpura. Am J Hematol 1989; 30: 206-12.
11. McMillan R, Luiken GA, Levy R, Yelensky R, Longmire RL. Antibody against megakaryocytes in idiopathic thrombocytopenic purpura. JAMA 1978; 239: 2460-62.
12. Isaka Y, Kambayashi J, Kimura K. Platelet production, clearance and distribution in patients with idiopathic thrombocytopenic purpura. Thromb Res 1990; 60: 121-31.
13. Podalak-Dawidziak M. Megakaryocyte progenitors in immune thrombocytopenic purpura. Thromb Research 1991; 62: 93-6.
14. Suvajdzic N, Rolovic Z, Elezovic I, Colovic M. Megakaryocytopoiesis in refractory chronic immune thrombocytopenia. Hematol Cell Ther 1999;41: 163-8.
15. Abgrall JF, Berthoy C, Sensebe L, Le Niger C, Escoffie M. Decreased in vitro megakaryocyte colony formation in chronic idiopathic thrombocytopenic purpura. Br J Haematol 1993; 85: 803 –4.
16. Uçar C, Oren H, Irken G, Ateş H, Atabay B, Türker M, et al. Investigation of megakaryocyte apoptosis in children with acute and chronic ITP. Eur J Haematol. 2003; 70(6): 347-52
17. Shi XD, Hu T, Feng YL, Liu R, Li JH, Chen J, Wang TY .A study on micromegakaryocyte in children with idiopathic thrombocytopenic purpura. Chinese journal of pediatrics. 2004, 42(3):192-5.
18. Jubelirer SJ, Harpold R. The role of the bone marrow examination in the diagnosis of immune thrombocytopenic purpura: case series and literature review. Clin Appl Thromb Hemost. 2002 , 8(1):73-6.
19. Alavi S, Malek F, Eghbali A, Arzanian M.T. The status of Immune Thrombocytopenic Purpura and relevant factors in patients in Mofid Children Hospital from 2003 to 2008, Iranian blood journal 2009 6(3): 165-73