Idiopathic thrombocytopenic purpura: A 15-year natural history study at the Children's Hospital Rijeka, Croatia

Roganović, Jelena; Letica-Crepulja, Marina

Source / Izvornik: **Pediatric blood & cancer, 2006, 47, 662 - 664**

Journal article, Published version
Rad u časopisu, Objavljena verzija rada (izdavačev PDF)

https://doi.org/10.1002/pbc.20995

Permanent link / Trajna poveznica: https://urn.nsk.hr/urn:nbn:hr:184:147044

Pediatr Blood Cancer 2006;47:662–664

Idiopathic Thrombocytopenic Purpura: A 15-year Natural History Study at the Children's Hospital Rijeka, Croatia

Jelena Roganovic, MD, PhD* and Marina Letica-Crepulja, MD

We review a 15-year experience with childhood idiopathic thrombocytopenic purpura (ITP) at a tertiary-care pediatric hospital in Croatia. Data confirm that ITP is typically a self-limited bleeding disorder that usually presents with mild symptoms in children between 1 and 10 years of age and affects both sexes equally. At presentation, more than half of the children had platelet counts of $<10 \times 10^9$/L. The absence of preceding viral infection and insidious onset of symptoms were significantly associated with development of chronic ITP. In our experience, observation without specific therapy seems to be the optimal approach to a child with ITP. Pediatr Blood Cancer 2006;47:662–664. © 2006 Wiley-Liss, Inc.

Key words: child; idiopathic thrombocytopenic purpura

INTRODUCTION

Idiopathic or immune thrombocytopenic purpura (ITP) is the most common acquired bleeding disorder of childhood, accompanied by many controversies in diagnosis and management [1,2]. In this study, retrospective data obtained from a pediatric referral center were analyzed to determine clinical characteristics, management practice, and outcome of children with ITP.

MATERIALS AND METHODS

We retrospectively reviewed hospital records of all patients ≤18 years of age with the discharge diagnosis of idiopathic or immune ITP treated at the University Children's Hospital Rijeka, Croatia, from January 1991 to December 2005. A total of 85 consecutive patients with the diagnosis of ITP were identified. Six patients were excluded due to thrombocytopenia from other causes (three neonatal alloimmune, two pseudothrombocytopenia, one systemic lupus erythematosus) and 79 medical records were available for further review. Information extracted from the medical record for each patient included the following: name, gender, date of birth, date of presentation, a history of antecedent infection or vaccination, initial platelet count and platelet counts done thereafter, bleeding manifestations, duration of symptoms, treatment, platelet response to therapy, complications of ITP, and final outcome.

Patients were classified by severity of bleeding manifestations in three groups: mild, moderate, and severe. Mild symptoms consisted of bruises and petechiae, without mucosal bleeding. Moderate symptoms were classified by mucosal bleeding (epistaxis, gum bleeding, oral blood blisters, menorrhagia, gastrointestinal, and urinary bleeding) that did not require medical intervention. Severe symptoms included mucosal bleeding that required immediate medical intervention and/or need for blood transfusions, suspected or documented intracranial hemorrhage, or life-threatening or fatal hemorrhage in any site. The children were followed as outpatients by the attending hematologist for a period of at least 6 months or until resolution of disease, defined as a platelet count greater than 150×10^9/L for at least 3 months without any treatment. Children with acute and chronic ITP were analyzed separately. Chronic ITP was arbitrarily defined as persistent thrombocytopenia for more than 6 months following initial diagnosis [3]. Subgroups of patients were characterized and compared using descriptive statistics. χ^2 test was used to assess significance; $P < 0.05$ was considered statistically significant.

RESULTS

Patient Characteristics

Seventy-nine children met the inclusion criteria. Because of the retrospective nature of the study, complete data were not available for each patient. Fifty-two percent (41 of 79) of children were male and 48% (38 of 79) were female. The mean age (SD) of presentation was 5.77 (4.45) years. The highest proportion (53 of 79.67%) of children was aged 1–10 years, followed by older children (age 10–18 years: 17 of 79.22%) and infants (0–1 year: 9 of 79.11%). The youngest patient was 1 month of age at presentation and the oldest was 16 years of age.

A history of antecedent viral infection within 3 weeks prior to the diagnosis of ITP occurred in 57% of children. Although there was a tendency toward more cases diagnosed in spring and a nadir in autumn, no significant seasonal occurrence was observed over a 15-year study period ($P = 0.206$). No post-vaccination case was noted.

Department of Pediatrics, Division of Hematology and Oncology, University Children's Hospital Rijeka, Rijeka, Croatia

*Correspondence to: Jelena Roganovic, Department of Pediatrics, Division of Hematology and Oncology, Istarska 43, HR-51000 Rijeka, Croatia. E-mail: jelena.roganovic@ri.htnet.hr

Received 27 June 2006; Accepted 27 June 2006

DOI 10.1002/pbc.20995

The mean initial platelet count was 20.07×10^9/L, ranging from 0 to 107×10^9/L. Most cases (44 of 79.56%) presented with a very low platelet count $<10 \times 10^9$/L, but clinically significant bleeding was infrequent. Fifty-nine percent of all patients presented with mild bleeding signs, 31% with moderate, and 10% with severe. Ninety-one percent of all children had cutaneous manifestations at presentation, 34% oral bleeding, 13% epistaxis, 4% gastrointestinal bleeding, 4% microhematuria, 4% conjuntival hemorrhage, and 4% menorrhagia. The most feared complication of ITP, intracranial hemorrhage, occurred in one patient (1%) with refractory chronic ITP 11 years from diagnosis. The same female suffered from intraperitoneal hemorrhage from a ruptured corpus luteum.

Acute Versus Chronic ITP

Fifty-three of 72 patients (74%) completely resolved their disease within 6 months and met the criteria for acute ITP. The other 19 patients (26%) had persistent thrombocytopenia for more than 6 months following presentation and were thus defined as chronic ITP. Table I shows patients characteristics for acute and chronic ITP.

Children with chronic ITP presented at older age than children with acute ITP. The mean age (SD) at presentation for acute patients was 5.02 (3.65) years and 7.05 (5.13) years for chronic patients without significant difference between the groups. The male/female ratio of children with acute and chronic ITP was not statistically significant. Sudden onset of the disease was associated with acute ITP, while chronic ITP was significantly more frequent in children with gradual onset ($P < 0.001$). A history of preceding viral infection, subsequently resolved, was significantly more common in acute than in chronic ITP ($P < 0.001$). The incidence did not appear to have a significant seasonal fluctuation in both groups ($P = 0.787$). There was no difference in the severity of bleeding symptoms in acute and chronic ITP, with the majority of cases presenting with mild bleeding ($P = 0.873$).

The mean presenting platelet count (SD) for chronic ITP was higher 30.66×10^9/L (31.18) than that for acute ITP (16.11×10^9/L) (19.56). However, there was no significant difference between acute and chronic cases ($P = 0.07$).

TABLE I. Patient Characteristics in Acute and Chronic ITP

	Acute ITP	Chronic ITP
Age		
<1 year	6/53 (11%)	2/19 (11%)
1–10 year	40/53 (76%)	10/19 (52%)
>10 year	7/53 (13%)	7/19 (37%)
Gender		
Male	32/53 (60%)	8/19 (42%)
Female	21/53 (40%)	11/19 (58%)
Onset of symptoms		
Sudden	48/51 (94%)	4/19 (21%)
Insidious	3/51 (6%)	15/19 (79%)
Viral infection		
Yes	35/48 (73%)	3/19 (16%)
No	13/48 (27%)	16/19 (84%)
Seasonal occurrence	No	No
Bleeding manifestations		
Mild	29/51 (57%)	12/19 (63%)
Moderate	17/51 (33%)	5/19 (27%)
Severe	5/51 (10%)	2/19 (10%)
Platelet counts at diagnosis		
$<10 \times 10^9$/L	28/50 (56%)	9/19 (47%)
$10–20 \times 10^9$/L	8/50 (16%)	0/19 (0%)
$>20 \times 10^9$/L	14/50 (28%)	10/19 (53%)

Treatment and Outcome

Therapy was given to 18 of 78 (23%) patients. In 60 patients (77%), observation alone was the only clinical option. Corticosteroid therapy was preferred pharmacotherapy. Steroids (typically oral prednisone) were used in all 18 patients, and in 8 (44%) of these cases combined steroid and intravenous immunoglobulin (IVIG) therapy was administered. In three cases, multiple treatments were administered to the same patient. No patient was treated only with IVIG. Anti-D immunoglobulin was not utilized in this study. The overall response rate was 88% (15 of 17), 12% (2 of 17) of children did not respond to multiple combined treatment; one patient was lost from follow-up. There was no significant difference between treatment responses of patients treated with steroids alone versus combined steroids/IVIG ($P = 0.31$). One patient underwent laparoscopic splenectomy (a female with chronic refractory ITP and two episodes of life-threatening bleeding), without response.

Complete follow-up data on duration of ITP are available for 72 of 79 cases (91%) (Fig. 1). Three months after the diagnosis, the platelet count had stabilized in 43 of 72 cases (60%). By 6 months after diagnosis, 53 children (74%) achieved remission. From 19 children classified as chronic ITP, 7 (37%) resolved their disease; only 12 children had persistent thrombocytopenia during the follow-up period. The overall complete response rate of 72 patients in the study was 83%.

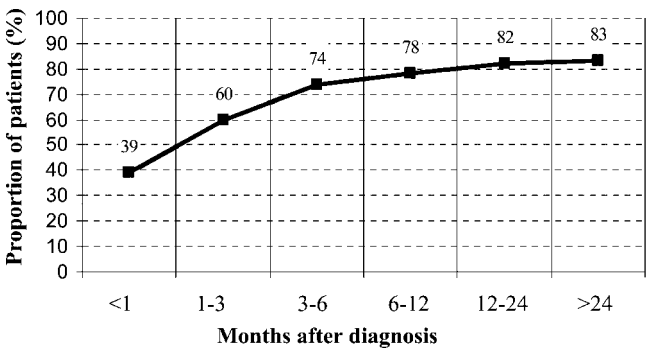

Fig. 1. Outcome of children with ITP. The curve shows the cumulative percentage of patients who achieved complete remission.

DISCUSSION

ITP is a heterogeneous bleeding disorder with a diverse natural history [4]. Treatment differs worldwide in terms of when to treat, what treatment to use and the need for hospitalization [5,6]. We therefore found it of interest to investigate presenting features, clinical course, management, and outcome of children with ITP in Croatia. The patient sample in our series is small, but this is a reasonably complete and unselected cohort. However, several factors may limit the validity of these observations. Data were collected from a 15-year period and from different pediatricians and thus may be somewhat heterogeneous. Outpatients were not included in the study and mild acute ITP cases could be underestimated. Follow-up data were not obtained for all patients; thus, chronic cases could be over-represented or develop secondary ITP.

The study confirmed well-known demographic data showing that most children remit rapidly [7]. Cut-off point of 6 months does not accurately define chronic ITP, as significant proportion of children resolve later in the course of the disease [8,9]. The patients who develop chronic ITP tended to present at older age and with higher initial platelet count. We have confirmed the significance of preceding viral infection and onset of disease [10,11] as prognostic factors to predict outcome of childhood ITP. The absence of prior infection and insidious onset of symptoms were significantly associated with the development of chronic disease.

Observation without platelet-enhancing therapies is well-established approach for children with newly diagnosed ITP at our institution. Although the observational strategy is becoming more and more popular [1], management with watchful waiting is rather the exception than a rule [12,13], and analysis of actual practice suggests that most children with ITP are treated with medication [14–18]. Only less than one fourth of patients were treated in our study, and the outcome regarding remission of thrombocytopenia was similar to that reported elsewhere for treated cases. This consistent ''watch and wait'' strategy is not likely to be due to a different phenotype of ITP in our patients. In Croatia, the tradition of medical decision-making is based on professional paternalism, and patients/parents are seldom active members of the healthcare team decision. In conclusion, our study could serve as a basis to establish national guidelines for investigation and management of childhood ITP. The study emphasizes the unique value of large prospective intercontinental studies.

REFERENCES

1. Kühne T. Idiopathic thrombocytopenic purpura of childhood: A problem-oriented review of the management. Transf Apher Sci 2003;28:243–248.
2. Medeiros D, Buchanan GR. Idiopathic thrombocytopenic purpura: Beyond consensus. Curr Opin Pediatr 2000;12:4–9.
3. Imbach P. Immune thrombocytopenic purpura. In: Lilleyman J, Hann I, Blanchette V, editors. Pediatric hematology. London: Churchill Livingstone; 2000. pp 437–453.
4. Kühne T, Buchanan GR, Zimmerman S, et al. A prospective comparative study of 2540 infants and children with newly diagnosed idiopathic thrombocytopenic purpura (ITP) from the Intercontinental Childhood ITP Study Group. J Pediatr 2003;143: 605–608.
5. British Committee for Standards in Haematology General Haematology Task Force. Guidelines for the investigation and management of idiopathic thrombocytopenic purpura in adults, children and in pregnancy. Br J Haematol 2003;120:574–596.
6. George JN, Woolf SH, Raskob GE, et al. Idiopathic thrombocytopenic purpura: A practice guideline developed by explicit methods for the American Society of Hematology. Blood 1996; 88:3–40.
7. Imbach P, Zimmerman S. Local and cultural aspects of childhood idiopathic thrombocytopenic purpura. J Pediatr Hematol Oncol 2003;25:S68–S73.
8. Jayabose S, Levendoglu-Tugal O, Ozkaynkak MF, et al. Long-term outcome of chronic idiopathic thrombocytopenic purpura in children. J Pediatr Hematol Oncol 2004;26:724–726.
9. Imbach P, Kühne T, Müller D, et al. Childhood ITP: 12 months follow-up data from the prospective Registry I of the Intercontinental Childhood ITP Study Group (ICIS). Pediatr Blood Cancer 2006;46:351–356.
10. Bruin M, Bierings M, Uiterwaal C, et al. Platelet count, previous infection and FCGR2B genotype predict development of chronic disease in newly diagnosed idiopathic thrombocytopenia in childhood: Results from a prospective study. Br J Haematol 2004;127:561–567.
11. Ahmed S, Siddiqui AK, Shahid RK, et al. Prognostic variables in newly diagnosed childhood immune thrombocytopenia. Am J Hematol 2004;77:358–362.
12. Dickerhoff R, Von Ruecker A. The clinical course of immune thrombocytopenic purpura in children who did not receive intravenous immunoglobulins or sustained prednisone treatment. J Pediatr 2000;137:629–632.
13. Bolton-Maggs PH, Dickerhoff R, Vora AJ. The nontreatment of childhood ITP (or ''the art of medicine consists of amusing the patient until nature cures the disease''). Semin Thromb Hemost 2001;27:269–275.
14. Bolton-Maggs PH, Moon I. Assessment of UK practice for management of acute childhood idiopathic thrombocytopenic purpura against published guidelines. Lancet 1997;350:620–623.
15. Sutor AH, Harms A, Kaufmehl K. Acute immune thrombocytopenia (ITP) in childhood: Retrospective and prospective study in Germany. Semin Thromb Hemost 2001;27:253–267.
16. Vesely SK, Buchanan GR, Adix L, et al. Self-reported initial management of childhood idiopathic thrombocytopenic purpura: Results of a survey of members of the American Society of Pediatric Hematology/Oncology, 2001. J Pediatr Hematol Oncol 2003;25:130–133.
17. Rosthřj S, Hedlund-Treutiger I, Rajantie J, et al. Duration and morbidity of newly diagnosed idiopathic thrombocytopenic purpura in children: A prospective Nordic study of an unselected cohort. J Pediatr 2003;143:302–307.
18. Marks MK, Vadamayalan B, Ekert H, et al. Intended management of children with idiopathic thrombocytopenic purpura: A national survey. J Paediatr Child Health 2005;41:52–55.