Reactive thrombocytosis in pediatric infectious diseases

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In this prospective study 659 children, aged 16 months to 12.5 years, with infections were evaluated to determine the incidence and duration of secondary thrombocytosis associated with infections. While thrombocytosis was detected in 81 (12.29%) cases and it was seen more in males thrombocytopenia was detected in 39 (5.92 %) cases. The statistical comparison of mean thrombocyte, leukocyte, absolute neutrophil count of the group with thrombocytosis and its control group was important (p<0.001). The statistical difference of these values between the groups with infections but without thrombocytosis and control group was also significant (p<0.001). Children with thrombocytosis associated with infections had significantly higher values of mean thrombocyte, leukocyte, absolute neutrophil count than children with infections but without thrombocytosis. Thrombocytosis lasted 3-28 days (mean 7 days). No complication related to thrombocytosis was detected in any of the patients and no therapy was employed. [Turk J Med Res 1996; 14(3): 102-105]

Keywords: Thrombocytosis, Infections

Thrombocytosis associated with infections is not rare and is most frequently seen in very young infants (1). With the widespread use of electronic blood cell counters, instances of elevated platelet counts are being encountered more often in pediatric practice (2,3).

The number of circulating platelets in normal persons is maintained within a range (150.000-450.000) (4). The factors regulating the platelet count are poorly understood. Two thirds to three quarters of all platelets are in the peripheral circulation, but in dynamic equilibrium with a pool of platelets within the spleen (5). Platelet count in excess of 450.000/mm^3 may be accounted as thrombocytosis (1). Thrombocytosis may be the result of a primary hematological disease (e.g., such as myeloproliferative disorders) or secondary to a coexisting physiologic or pathologic process, in which case it is termed reactive. Primary thrombocytosis is a disease of adult life and is extremely rare in children. Secondary thrombocytosis is due to either splenectomy with resulting transfer of the splenic pool into the peripheral circulation or increased production due to stimuli such as inflammation, iron deficiency anemia or hemorrhage (3,5). This type of thrombocytosis usually is asymptomatic and disappears following therapy or remission of the primary disorder. A specific treatment such as anticoagulant therapy is not required and it does not cause any complication (3,6).

We planned this study to determine the incidence, influencing factors and duration of thrombocytosis in pediatric patients applied to our clinic with infectious diseases.

MATERIALS AND METHODS

This prospective study included 659 children applied to Pediatrics Clinic School of Medicine of Atatürk University between January 1992 and February 1993 as inpatients and outpatients with infectious diseases. Thrombocytosis associated with infections caused except by acute or chronic infection was not included in the study. The control groups consisted of 406 children aged 0.5-6 years and 262 children aged 6-12 years. Complete blood counts, including platelet counts were performed on EDTA-anticoagulated venous blood using the Cell-Dyn 1500 Automated Hematology Analyzer. Platelet counts more than 450.000/mm^3 were accepted as thrombocytosis Cases with thrombocytosis were followed up and the duration of thrombocytosis was observed.

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Results were evaluated in mean values, ranges and percentages. Univariate analyzes were performed with the Student t test. Categorical data were analyzed with unpaired Student's t test. Probabilities <0.05 were considered significant. Data tested for the difference between two proportions.

RESULTS

Thrombocytosis associated with infections was found in 81 (12.89%) of 659 cases applied to our clinic and treated as inpatients or outpatients with bacterial infectious diseases. The mean platelet count was 588±165/mm^3. Thrombocytosis incidence was found as 12.29% in our study. Mean age was 16±14 months (Range: 16 months to 12,5 years) in the patiens with trombocytosis and was 76 ± 6 months in cases without thrombocytosis. Of 81 cases, 34 (41.98 %) were females, 47 (58.02%) were males. The distribution of cases with trombocytosis according to the infections were shown in Table 1. Distribution of the cases according to platelet counts was shown in Table 2. Statistical comparisions were performed on children with upper respiratory tract infection, lower respiratory tract infection and otitis media since case number of the other groups were insufficient for statistical evaluation. Infectious thrombocytosis was more common in the group with upper respiratory tract infection than those in children with otitis media and the difference was statistically significant (p<0.05). The difference was not significant in the other evaluated groups.

Of 81 cases, 44 were followed up and recovery time of thrombocytosis asociated with infections was 3 to 28 days, with the mean value of 7 days, and thrombocytosis disappeared following therapy or remission of the primary disorder. Platelet count did not influence the recovery time (p>0.05), and there were no thrombotic complications in any of these patients. Leukocyte and absolute neutrophil count were also elevated as thrombocytes. Leukocyte count was less than 10.000/mm^3 in 30 cases (37.1 %) and it was more than 10.000/mm^3 in 51 cases (62.9 %) and mean leukocyte count was 14.8 ± 0.8 x 10^3/mm^3. Mean age, platelet, leukocyte and absolute neutrophil counts of the cases were shown in Table 3. Children with thrombocytosis associated with infections were younger than children without thrombocytosis (p<0.001). Mean ages of the children in the control groups were similar with earlier study groups. Thrombocytosis was not detected in the control groups. The results and the statistical evaluations were given in Table 4 and 5. The statistical difference of these values between the group with infections but without thrombocytosis and its control group was also significant (p<0.001). Children with thrombocytosis associated with infections had significantly higher values of mean thrombocyte, leukocyte, absolute neutrophil counts than children with infections but without thrombocytosis. Thrombocytopenia was observed in 38 (5.92%) cases and mean thrombocyte count was 97±68/mm^3 in these patients.

Table 1. Distribution of the cases with thrombocytosis according to infections.

Diseases	No of patients with thrombocytosis	%
Upper respiratory tract infection	27*	33.3
Lower respiratory tract infection	25	30.8
Otitis media	15*	18.5
Central nervous system infection	4	4.9
Bacterial gastroenteritis	3	3.7
Others	7	8-8
Total	81	100
Males	47	58.02
Females	34	41.98

"Statistical comparison: p < 0.05

Table **2.** Distribution of the cases according to platelet counts.

Platelet count (x. 10^3/mm^3)	No of patients	%
450 - 550	28	34.57
551- 650	26	32.10
651- 750	18	22.22
751-+	9	11.11
Total •	81	100.0

DISCUSSION

Until recent years, platelets were enumerated by directed visual counting of a diluted blood specimen in a hemocytometer chamber with phase contrast microscope. Platelet counts were not usually included in the routine complete blood cell count. Recently, the use of

Table 3. Mean age, leucocyte and absolute neutrophil count of the cases with thrombocytosis and without thrombocytosis.

	Without Thrombocytosis	With Thrombocytosis	Importance p
Age (months)	76 ± 6	16±6	<0.001
Platelet count	336+ 117	588± 165	<0.001
(x10³/mm³)	(172-446)	(450-348)	
Leukocyte count	9.7 ± 0.4	14.8 ±0.8	<0.001
(xI0³/mm³)			
Absolute neutrophil count	5.2 ± 0.4	7.9 ± 0.8	<0.001
(x I0³/mm³)			

Table 4.The statistical comparisons of the platelet, leucocyte and absolute neutrophil counts of the cases with thrombocytosis and control group.

	With thrombocytosis n=81	Control group n=406	
Platelet count	588+165	318±107	<0.001
(x IO^mm³)	(450-848)	(211-426)	
Leukocyte count	14.8±0.8	8.4+4.6	<0.001
(x IO^mm³)			
Absoiute neutrophil count	7.9±0.8	4.3±2.3	<0.001
(x 10³/mm³)			

Table 5. The statistical comparations of the platelet, leucocyte and absolute neutrophil counts of the cases without thrombocytosis and its control group.

	Without thrombocytosis n=578	Control group n=262	P
Platelet count	336± 117	276+121	<0.001
(xIO^mm³)	(172-446)	(155-397)	
Leukocyte count	9.7± 0.4	8.1 ± 4.2	<0.001
(xIO^mm³)			
Absolute neutrophil count (x 10³/mm³)	5.2± 0.4	4.2 ± 2.1	<0.001

electronic blood cell counters has provided an accurate platelet count as part of regular complete blood cell count. Until recent years thrombocytosis in pediatric patients was infrequently reported because, unlike thrombocytopenia, it is not usually associated with signs or symptoms that prompt the physician to order a platelet count. Now the accurate platelet counts are part of the routine complete blood cell count and thrombocytosis is being encountered much more frequently (2). Addiego et al reported that they have encountered within less than one year ten children with thrombocytosis and only one of them was related to infectious disease and thrombocytosis had continued four weeks (7).

Heath and Pearson found that thrombocytosis associated with infections (more than 500.000/mm³) occurred in 13% of children who had complete blood cell counts during ambulatory clinic or emergency department visits at their hospital and they were more likely to have clinical diagnosis of infection as otitis media, upper respiratory tract infection and bronchitis and it recovered within 3-6 weeks (8). Felici et al reported thrombocytosis as 12% and infections had the first place (9). Yohannan et al found thrombocytosis in infectious diseases at a rate of 30.6% with a mean platelet count of 628±149 in children (10). We also determined the incidence of thrombocytosis 12.29 % with a mean count of 588±165 and it was consistent with literature.

While Yohannan et al found thrombocytosis more in females, in our study males with infectious thrombocytosis were more than the females (10).

Children with thrombocytosis associated with infections were younger than children without thrombocytosis and this result was similar to the other studies (1-3). The mean age of our cases was 16 months and thrombocytosis was seen more frequently in male. Addiego et al reported the mean age as 12 months and it was seen in males as a rate of 60% (7). Yohannan et al reported that thrombocytosis associated with infections was significantly common causes of thrombocytosis in children under 5 years of age (10).

When we investigated the relationship between the localization of infection and thrombocytosis, we could not find any correlation. Chan et al and Heath et al found the central nervous system infections were the most encountered infection causing thrombocytosis 0,2).

Recently, several groups have demonstrated that interleukin-6 stimulates thrombopoesis in vitro and in vivo (11). Thrombocytosis seen in infections and certain inflamatory states may be an acute phase reaction (3,5). Interleukins-1, 6 and 11 have been shown to be mediators of acute phase reaction (12,13). In our study, platelet counts of cases were 450-500.000/mm³ in 34.57% and more than 750.00/mm³ in 11.1%. Heath

et al reported this as 12.9% in the cases with platelet counts more than 500.000/mm^3* , and as 2% in the cases with platelet counts more than 700.000/mm^3 (2).

There are many different studies about the recovery time of thrombocytosis associated with infections. Thomas et al considered the elevation of thrombocyte count in a group of patients with meningitis of *H. influenzae* after the 4th day as a recovery phenomena (14). Heath et al reported the recovery time of thrombocytosis for outpatients as 3-6 weeks. According to literature it is known that there is no relation between the platelet count and recovery time (2).

In our study, children with thrombocytosis associated with infections had significantly higher mean thrombocyte, leukocyte, absolute neutrophil count than ($p<0.001$). The statistical difference of these values between the group with infections but without thrombocytosis and control group was also significant ($p<0.001$). Children with thrombocytosis associated with infections had significantly higher values of mean thrombocyte, leukocyte, absolute neutrophil counts than children with infections but without thrombocytosis. It was consistent with literature (2).

We encountered no complication in the follow-up of the cases with infectious thrombocytosis and the any type of therapy was not given. This condition was in consistence of literature (1-6,15).

As a consequence, we observed that thrombocytosis associated with infections is usually not symptomatic but not uncommon in childhood, this condition is an acute phase reactant and it recovers in average of seven days (3-28 days) with the treatment of infection, no complication is associated and specific treatment is not required.

Pediatrik enfeksiyöz hastalıklarda reaktif trombositoz

Bu çalışmada çocuklarda enfeksiyon hastalıklarına bağlı trombositoz insidansını ve süresini belirlemek amacıyla yaşlan 16 ay-12.5 yıl arasında değişen 659 çocuk prospektif olarak değerlendirildi. Olgulann 81 (%12.29)'inde trombositoz saptanırken, 39 olguda (%5.92) trombositopeni gözlendi. Trombositoz erkeklerde daha sıktı. Enfeksiyona bağlı trombositozu olan grubun ortalama trombosit, lökosit, ve mutlak nötrofil sayılan ile kontrol grubunun değerleri arasında anlamlı farklılık vardı (p<0.001). Bu değerler enfeksiyonu olup trombositozu olmayan grupta da kontrol grubundan belirgin olarak yüksekti (p<0.001). Yine enfeksiyona bağlı trombositozu olan grup enfeksiyonu olan fakat trombositozu olmayan grupla karşılaştınldığında ortalama trombosit, lökosit ve mutlak nötrofli sayılan istatistiksel olarak anlamlı şekilde yüksekti (p<0.001). Trombositozun 3-28 gün (ortalama 7 gün) sürdüğü saptandı. Hiç bir hastada trombositoza bağlı komplikasyon gözlenmedi ve herhangi bir tedavi uygulanmadı. fTurk J Med Res 1996; 14 (3): 102-105]

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