Platelet Antibodies in Children With Sepsis

Uğur DİLMEN
Şinasi ÖZSOYLU

SEPSİSLİ ÇOCUKLARDA TROMBOSİT ANTİKORLARI

Department of Pediatrics, Hematology Section, Faculty of Medicine, Hacettepe University, Ankara, TURKEY

Geliş Tarihi: 8 Ocak 1988

SUMMARY

Platelet specific antibodies were determined in the sera of 35 children with gram negative sepsis by using opsonophagocytic test. The ages of the patients rcnged between 2 days and I 7 years and serum was obtained from them in early phase of sepsis before antibiotics and/or blood administariton.

The sera of ¡3 healthy children and 19 patients with idiopathic thrombocytopenic purpura (1TP) served as negative and positive controls of the test. It did not show the presence of antiplatelet antibodies in all II chddren of sepnts with thromboytopema. Although the results of opsonophagocytic test were compatible with platelet antibodies in 17 of 24 children with sepsis, thrombocytopenia was not shown in any of them.

The test which was carried out also in 10 patients with acuteiymphoblastic leukemia (ALL) in 6 cases of Fanconi and 5 cases of acquired aplastic anemia (AAA) as a control for thrombocytopenia, did not indicate the presence of platelet antibodies in them.

Key Word*: Thrombocytopenia, platelet antibodies, sepsis

T J Restaren Med Sel V.6, N.3, 1988. 445-447

ÖZET

Otuz beş sepsisli çocukta opsurıofagositik test ile trombosit antikorları araştırılmıştır. Çocukların yaşlan 2 gün ile l 7 yd arasında değişmekte idi. Trombosit antikorları hastalığın erken devresinde antibiotik ve kan verilmeden bakılmıştı. Onüç sağlıklı çocuk ile 19 idiopatik troınbositopenic purpuralı hasta serumu negatif ▷e pozi'if kontrol olarak çalışıldı. Trombositopenili 10 akut lenfoblastik lösemili, 6 Fanconi ve 5 akiz aplastik anemili hiçbir çocukta trombosit antikorları gösterilemedi.

Sepsisli ve trombositopenili 11 çocuktan hiç birisindede trombosit antikorluı gösterilemedi. Sepsisli troınbositopenisiz 24 hastadan 17'sinde trombosit antikorları işaret edildi. Remisyondaki ITP vakalarında da opsonofagositik testle antikor gösterilmiş olması dikkate getirildi.

Anahtar Kelimeler: Troralıositopeni, tromhosıı antikorları, sepsis.

T Kİ Tıp BM Ara* Dergisi C.6. S.6, 1988, 445-447

INTRODUCTION

The presence of antiplatelet antibodies in patients with ITP was strongly suggested by Dr.Harrington et al in 1951. (1) Antiplatelet antibodies were shown by one of us (S.Ö) in every case of childhood ITP (2) which was not found markedly changed during remission (3).

The presence of antiplatelet antibodies by platelet associated immunglobulin (PAIgG) assay was also shown in patients with sepsis (4-6). Since the production of antiplatelet IgG is not expected to occur in few days of septicamia, we evaluated the presence of antiplatelet antibodies in serum of children with sepsis, with appropriate controls.

MATERIALS AND METHODS

Platelet specific IgG antibodies were determined in 35 children with sepsis in 10 patients with ALL, in 6 cases of Fanconi and 5 cases of AAA by using opsonophagocytic test as described previously (2). Thirteen healthy children and 19 patients with ITP served as negative and positive controls of the test. The ages of the patients of proven gram negative sepsis

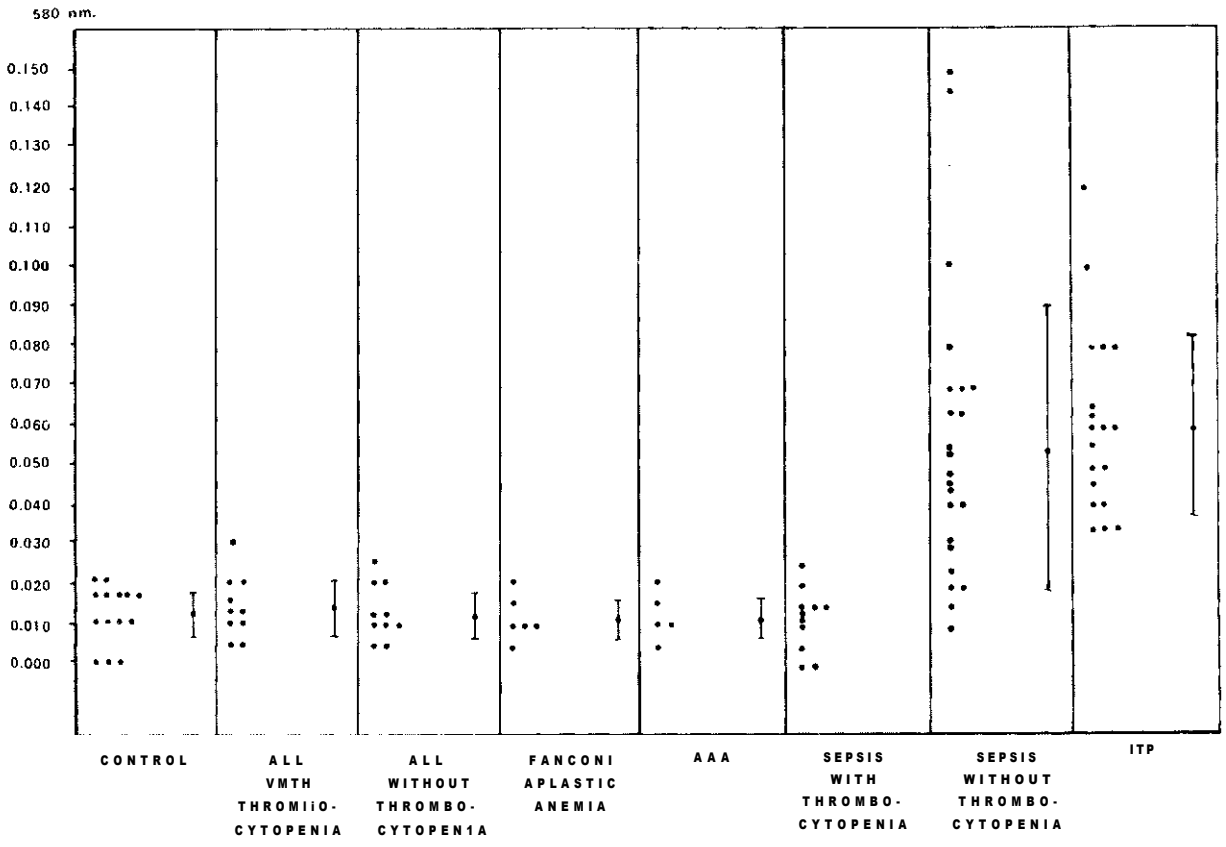
ranged between 2 days and 17 years (less then 1 months in 12 babies) 11 had thrombocytopenia (<100.000/>il); 11 of them were females and 24 were males. Blood culture results revealed E.Coli (14 cases), pseudomonas (11 cases), S.typhi (4 cases), klebsiella (3 cases), s.typhimurium (2 cases) and A.aerogenes (1 case). Disseminated intravascular coagulation (DIC) was most likely ruled out by normal prothrombin time (PT) (7) and partial thromboplastin time (PTT) (8). The ages of the patients with A L L ranged between 1,5 and 17 years; 4 were girls and 6 boys. The ages of the patients with Fanconi and acquired aplastic anemia (A A A) ranged 7 to 12 years (3 girls and 3 boys) and 4 to 16 years (4 boys and a girl) respectively. The ages of healthly controls and ITP cases ranged 3 and 12 years (7 and 12 of them were boys respectively). In all cases blood for platelet antibody determination was obtained prior to antibiotic administration and blood transfusion when the last was required.

The diagnosis of ITP was based on platelet counts of less than 50.000/ul, with an excessive or normal number of megakaryocytes in the bone marrow. No underlying disease was shown by lupus erythematosus preparation (performed 3 times), throat culture. Cooms test, fluorescent antinuclear antibody determinations. In no patient was there a history of drug-induced etiology and none of them had received platelet or blood transfusions prior to the study. The diagnosis of leukemia and aplastic anemia was verified by bone marrow examinations.

FINDINGS

NBT reduction read at 580 ***mn*** optical density ranged between zero and 0.020 (X= 0.01***2s*** 0.006; S.D) in healthly controls and 0.035 and 0.120 (X--0.06+ 0.023) in ITP cases. It ranged between 0.005 and 0.030 (X 0.013 • 0.007); 0.005-0.02 (X= 0.011 > 0.005) and 0.010-0.020 in leukemia, Fanconi and A A A cases respectively.

The optical density changes in all sepsis cases ranged between 0.010 and 0.150(X= 0.055t0.036) being elevated (>0.035) in 17 of 24 (70.8%) children (9 girls and 15 boys) with sepsis without thrombocytopenia. However, it was found not elevated in all 11 children of sepsis with thrombocytopenia (2 girls and 9 boys) (X=0.012±0.002; ranged 0 and 0.025) Fig:l).



DISCUSSION

Thrombocytopenia due to DIG are well known hematologic complications of gram negative septicemia (9,10). Another coagulopathy related to infection has been observed, without classic manifestations of DIG, with only reduced vitamin K-dependent coagulation factors. (11). The most recent work of Dr. Corrigan (12) strongly suggestes that this coagulation defect is related t o an anticoagulant directed to vitamin K dependent coagulation factors. PT and PTT would be found prolonged in both above conditions. Since these tests were within normal limits, the above both causes of coagulopathy due to septicemia, not be considered in our patients with sepsis. These findings were most likely due to our selection of very early sepsis cases who did not require antibiotic prior to the study.

Although more children less than one month of age (5 of 12) had thrombocytopenia (41.66%) compared to older children (6 of 23; 26.1%) with sepsis it was not found significantly different. The type of bacteria in general, did not seem to be related to thrombocytopenia either.

It was surprise to us that with the exception of 7 cases, elevated serum opsonophagocyytic activity (> 0.035 m/u) was shown most of the 24 children with sepsis who had no thrombocytopenia; in contrast none of 11 children with thrombocytopenia; had elevated activity (X 0.012< 0.002).

Our findings once more indicate that opsonophagocytic activity is a reliable method in diagnosis of ITP in children since it was found elevated in all potieents with ITP but not other thrombocytopenic conditions such as sepsis, A A A , Fanconi aplastic anemia and leukemia cases. Platelet counts was less than $76x10^3$/ul (X=50X10^3/M1) in all A L L cases prior to treatment and following induction remission with vincristine sulfate and corticosteroid administration, were found more than $I60x10^3/_M1$ (X=$227x10^3$M), but no changes on serum opsonophagocytic activity (X=0.013±0.007 vs 0.012*0.006 respectively) was observed.

We don't have a good explanation for the elevation of serum opsonophagocytic activity in some sepsis cases. But opposite of the finding in cases of ITP elevated serum opsonophagocytic activity in sepsis cases did not correspond to the presence of thrombocytopenia. Therefore we believe that the pathogenesis of thrombocytopenia in sepsis is quite different than ITP and the specificty of PAIgG should be reevaluated at least in children with this contition. Since PAIgG increases in cases with elevated serum IgG (6, 13) one may postulated that increased PAIgG is not pathogenically related to thrombocytopenia but elevation of serum IgG level which would be expected in sepsis. If we would determine serum IgG level which would be expected in sepsis. If we would determine serum IgG levels in septicemia cases we might detect the difference between the patients with and without thrombocytopenia.

The elevation of PAIgG and platelet associated IgM have also been shown in some patients with leukemia, myelofibrosis, hepatitis and bone marrow hypoplasia (14). However, there was no changes from normal controls by opsonophagocytic test in some of above conditions.

KAYNAKLAR

1. Harrington WJ, Minnick V, Hollingswoth JW, Moore CV: Demonstration of thrombocytopenic factor in blood of patients with idiopathic thrombocytopenic purpura. J Lab Clin Med 38:1-10(1951).
2. öztürk M, özsoylu §, Laleli Y.: The specificity of antiplatelet antibodies in ITP. Turk J Pediatr. 24:75-81, 1982.
3. özsoylu §, Allahverdi H, Laleli Y, Pirnar A.: Platelet survival in childhood idiopathic thrombocytopenic purpura in remission. J Pediatr. 89:388-390, 1976.
4. Kelton JG, Neame PB, Geuldie J and Hirsh J.: Elevated platelet associated IgG in the thrombocytopenia of septicemia. N EnglJ Med. 300:760-764 1979.
5. Kekomaki R, Kekomaki M, Elfving J.: Platelet associated IgG in septicemia. N Engl J Med, 301:271-271, 1979.
6. Duedari N, George G, Cacitti A M, Sabatier C, Mannoni P, Papin M.: Platelet associated IgG in septicemia. N EnglJ Med. 301: 271-272, 1979.
7. Ouick AJ: Prothrombin in hemophilia and obstructive Jaundice. J Biol Chem, 109:73-74, 1935.
8. Rodman NF, Barrow EM, Iraham JB.: Diagnosis of control of hemoploid states with the partial thromboplastin time (PTT) test. Am J Clin Path 29:523-538, 1958.
9. Yoshikawa T, Tanaka KR, Guze LB.: Infection and disseminated intravascular coagulation. Medicine, 50: 237-258, 1971.
10. Corrigan JJ.: Bacterial infection and disseminated intravascular coagulation, in Eaker D. Waldstrom T (Eds): Natural Toxins. New York Pergamon Press. 1980, pp:147-154.
11. Goldenfarb PB, Zucker S, Corrigan JJ Jr et al: The coagulation mechanism in acute bacterial infection. Br J Haematol, 18:643-652, 1970.
12. Corrigan JJ Jr: Vitamin K-dependent coagulation factors in gram .negative septicemia. Am J Dis Child 138:240-242, 1984.
13. Nel K, Stevens K, Mouton A, Pretoius FJ: Platelet bound IgM in autoimmune thrombocytopenia to total platelet protein content, Brit J Haemat, 49:293-302, 1981.