

Pseudothrombocytopenia in Case of Acute Viral Hepatitis A

Akut Hepatit A Virüs Enfeksiyonu Olgusunda Psödötrombositopeni

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Keywords

Pseudothrombocytopenia, hepatitis A virus infection, glycoprotein, ethylenediaminetetraacetic acid

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Psödötrombositopeni, hepatit A virüs enfeksiyonu, glikoprotein, etilen diamin tetraasetik asit

Received/Geliş Tarihi : 08.01.2015

Accepted/Kabul Tarihi : 10.03.2015

doi:10.4274/meandros.2048

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Presented in: This study was presented in 37th National Hematology Congress and published as abstract in congress issue

Abstract

Pseudothrombocytopenia is a laboratory-based iatrogenic phenomenon. Pseudothrombocytopenia is not important in terms of bleeding and does not require transfusion of thrombocytopenia. If not identified at the early stages, pseudothrombocytopenia can lead to patients undergoing unnecessary investigations and overtreatment. Here we present a childhood case of pseudothrombocytopenia caused by hepatitis A virus (HAV) infection. A 9-year-old male was referred to our department for thrombocytopenia (thrombocyte count $70 \times 10^9/L$). The liver was palpable 3-4 cm below the costal margin. Leukocyte count was $6.52 \times 10^9/L$, hemoglobin 14.7 g/L, hematocrit 46.6%, thrombocyte count $58 \times 10^9/L$. Aspartate transaminase 79.8 U/L, alanine transaminase 116.9 U/L, gamma-glutamyl transferase 156 U/L, alkaline phosphatase 1114 U/L, total bilirubin 0.98 mg/dL, and direct bilirubin 0.6 mg/dL. Other biochemistry values were normal. Anti HAV immunoglobulin M and immunoglobulin G were positive. The patient was diagnosed with hepatitis A. A peripheral smear revealed many thrombocyte clusters composed of 10-20 cells. HAV infection was thought to be the reason for pseudothrombocytopenia. The pseudocytopenia started to recover as the HAV infection got better and the thrombocyte count increased to over $150 \times 10^9/L$ at the end of a year. Peripheral smear evaluation is critical for accurate detection of thrombocytopenia and should be considered the initial step in cases with a familial or medical history of thrombocytopenia.

Öz

Psödötrombositopeni iyatrojenik bir laboratuvar fenomendir. Psödötrombositopeni kanama bakımından (riski) önemli değildir ve trombosit verilmesini gerektirmez. Bu fenomenin erken evrede tanınmaması, hastaların gereksiz tetkiklere ve gereksiz tedavilere maruz kalmasına neden olmaktadır. Biz burada, hepatit A virüs (HAV) enfeksiyonunun neden olduğu psödötrombositopenili bir çocuk olgusu sunuyoruz. Dokuz yaşındaki erkek hasta, trombositopeni (trombosit $70 \times 10^9/L$) nedeni ile bölümümüze yollandı. Karaciğer kot altında 3-4 cm ele geliyordu. Hastada, lökosit $6,52 \times 10^9/L$, hemoglobin 14,7 g/L, hematokrit %46,6, trombosit $58 \times 10^9/L$. Aspartat aminotransferaz 79,8 U/L, alanin aminotransferaz 116,9 U/L, gama-glutamil transferaz 156 U/L, alkalen fosfataz 1114 U/L, total bilirubin 0,98 mg/dL, direkt bilirubin 0,6 mg/dL ve diğer biyokimya değerleri normal idi. Anti HAV immünoglobulin M ve immünoglobulin G pozitif bulundu. Hepatit A kabul edilen hastanın periferik yaymasında çok sayıda 10-20'li trombosit kümeleri görüldü. Psödötrombositopeni nedeninin HAV enfeksiyonu olduğu düşünüldü. Nitekim HAV enfeksiyonu geriledikçe, psödötrombositopeni de düzelmeye başladı ve trombosit sayısı, bir yılın sonunda $150 \times 10^9/L$ 'nin üzerine çıktı. Tıbbi ve aile öyküsünde trombositopeni olan olgularda periferik yayma değerlendirilmesi çok önemlidir ve ilk adım olmalıdır.

Introduction

Hematology laboratories have got its share from the recently emerging developments in technology. Thus, electronic blood count devices have become frequently used equipment. The interpretation of findings of these devices which get much truer results in a shorter span of time compared to earlier devices may sometimes cause problems (1). Although thrombocytopenia does not occur actually, the number of thrombocyte may be low in counts. Unreal thrombocytopenia must be doubted for patients who have thrombocytopenia but not petechia and ecchymosis. Even if this case may take place in the presence of huge blood platelets and their satellitosis, the most frequently seen factor is aggregation of thrombocyte (pseudothrombocytopenia). The aggregation of thrombocyte in pseudothrombocytopenia comes into existence with anticoagulant-dependent thromboagglutinin. It is mostly seen when ethylenediaminetetraacetic acid (EDTA) is used as an anticoagulant. As aggregated thrombon are perceived as leucocyte in blood count devices because of their volume, the number of thrombocyte is low (2). Pseudothrombocytopenia is an iatrogenic laboratory phenomenon. It does not have a risk of haemorrhagia and necessitate thrombocyte to be supplied. However, that the case becomes unrecognizable ends up with unnecessary further examination and treatment of patients. Therefore, pseudothrombocytopenia is an important clinical problem. We aim at presenting a child case in which pseudothrombocytopenia develops as a result of hepatitis A virus (HAV) infection.

Case Report

Liver function disorder (hepatitis) and thrombocytopenia were detected in a 9-year-old boy in state hospital where he had gone due to stomachache and he was transferred into our department in order that thrombocytopenia's reason (thrombocyte $70 \times 10^9/L$) was searched. There were no epistaxis, melena, hematuria, ecchymosis and drug utilization in the patient and history of hemorrhagic diathesis in the family. In patient's examination, the liver was 3-4 cm under rib. There were not any symptoms (petechia, purpura and ecchymosis) connected to the haemorrhagia and lymphadenopathy in any parts of

his body. In the patient, leucocyte was $6.52 \times 10^9/L$, hemoglobin was 147 g/L, hematocrit was 46.6%, thrombocyte was $58 \times 10^9/L$, aspartate transaminase was 79.8 U/L, alanine transaminase was 116.9 U/L, gamma-glutamyl transferase was 156 U/L, alkaline phosphatase was 1114 U/L, total bilirubin was 0.98 mg/dL, direct bilirubin was 0.6 mg/dL and other biochemistry values were all normal. Anti-HAV immunoglobulin M and immunoglobulin G was positive. A lot of thrombocyte clumps in 10-20 were seen in peripheral smear of the patient regarded as an infection of hepatitis A (Figure 1). In the patient for whom pseudothrombocytopenia is considered, thrombocyte satellitosis and macrothrombocyte were not observed. In the venous blood taken into citrated tube, the number of thrombocyte was got as $101 \times 10^9/L$ by an automatic instrument. It was considered that HAV infection had caused pseudothrombocytopenia. Hence, pseudothrombocytopenia started to get better as HAV infection regressed and thrombocyte numbers have mounted over $150 \times 10^9/L$ after one year.

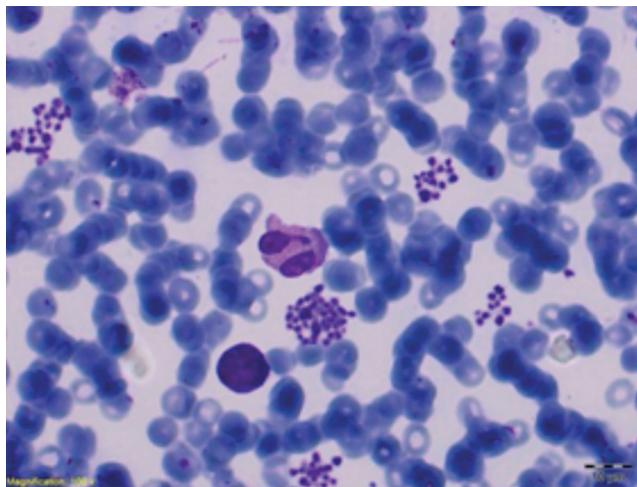


Figure 1. A lot of aggregated thrombon have been monitored in peripheral smear done from the blood in tubes with ethylenediaminetetraacetic acid

Discussion

Seventeen percent of patients evaluated because of thrombocytopenia were diagnosed of pseudothrombocytopenia in a study conducted by Cohen et al. (3). Holmes et al. (4) stated pseudothrombocytopenia as 0.1% in general population, but Bragagni et al. (5) stated it as 1.26% for hospitalized patients. This is seen at the rate of (1/1000) in healthy individuals depending upon

autoimmune, neoplastic, hepatic and cardiovascular diseases, infections, obstetric problems and drug use (2). The combined strength that low temperature and EDTA generate when they attach to calcium ions releases glycoprotein IIb epitope by affecting glycoprotein IIb/IIIa molecule which is normally hidden and occupies thrombocyte area. If autoantibody exists against this epitope in the individual, antibody causes thrombocytes to aggregate by attaching to them (2). The relation between viral infections and pseudothrombocytopenia depending on EDTA has been stated in few cases in literature. Tomonari et al. (6) reported a case of pseudothrombocytopenia depending on EDTA in the course of hepatitis A infection. In another study conducted on viral infections causing pseudothrombocytopenia, hepatitis A in 72.2% of cases, cytomegalovirus in 11.1% and influenza A H1N1 infection in 5.6% were detected (7). Although its exact incidence is not known in childhood, it is determined more rarely. Natural antibodies causing aggregation in thrombocytes connected with EDTA appear normally in people at the rate of 1/1000. They may be permanent for the life as well as they may appear due to infection and drug use and then disappear (1). Also, in our case, the antibody developing after infection lost its efficiency when thrombocytes were detected as normal about one year later. There are a few methods for the diagnosis of pseudothrombocytopenia. The most frequently used one is to detect the aggregation which is normally not supposed to exist in peripheral smear from the tube with EDTA taken for hemogram. In smears from heparin containing or citrated tubes, thromboagglutination may not be monitored. But, an aggregation may be monitored in smears done with other anticoagulants in small parts of cases, too. Pseudothrombocytopenia may be discovered at the rate of 20% in even counts repeated in a citrated tube (8). Similarly, thrombocyte count higher than the one with EDTA but lower than normal values was detected in the count repeated in the citrated tube in our case. In cases of thrombocytopenia without clinical findings, pseudothrombocytopenia must be excluded firstly. This prevents unnecessary examination and treatment procedures. The pathogenesis of pseudothrombocytopenia is not completely clear.

However, it may be seen during some clinic outlooks where viral infections are situated. In countries like ours where acute HAV infection is endemic, as in our case, pseudothrombocytopenia depending upon EDTA may be observed rarely in the course of acute HAV infection. Consequently, pseudothrombocytopenia should be taken into consideration for cases that do not have the symptom of thrombocytopenia but have low thrombocyte count. In cases with thrombocytopenia in medical and family history, consideration of peripheral smear is very important and should be the first step.

Ethics

Peer-review: Externally and internally peer-reviewed.

Informed Consent: Informed consent was obtained from patients' parents who participated in this case.

Financial Disclosure: The author declared that this study has received no financial support.

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