

Case report-Olgu sunumu

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Spironolactone induced thrombocytopenia in a patient with liver cirrhosis

Karaciğer sirozlu hastada sprinolaktona bağlı trombositopeni

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Abstract

Although it is rare, drug-induced thrombocytopenia is important since it may cause fatal results like bleeding. Mostly spironolactone is used for ascites palliation in the cirrhotic patients. Thrombocytopenia has been reported with thiazide group of diuretics. But thrombocytopenia caused by spironolactone is rarely seen. We presented our patient with ascites diagnosed as liver cirrhosis that developed severe thrombocytopenia after receiving two weeks of spironolactone treatment.

Keyword: Liver cirrhosis, spironolactone, thrombocytopenia

Özet

İlaça bağlı trombositopenide nadir olmasına rağmen, kanama gibi ölümcül sonuçlara neden olabileceği için önemlidir. Karaciğer sirozu olan hastalarda asite yönelik diüretik tedavisinde, çoğu zaman sprinolakton kullanılmaktadır. Tiazid grubu diüretiklerde trombositopeni rapor edilmiştir. Ancak Spironolaktona bağlı trombositopeni oldukça nadir görülmektedir. Karaciğer siroz tanısı konulan asitli hastamızda sprinolakton tedavisi başladıktan yaklaşık iki hafta sonra şiddetli trombositopeni gelişmesi üzerine sunduk.

Anahtar sözcükler: Karaciğer sirozu, spironolakton, trombositopeni

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Introduction

Many drugs may cause thrombocytopenia by various immunological mechanisms. Diuretics constitute the basis of treatment in ascites patients with cirrhosis. Spironolactone which is an aldosterone antagonist retaining potassium and excreting sodium in the distal convoluted renal tubules is frequently prescribed in cirrhotic patients with ascites [1]. Recognized side effects of spironolactone are gynecomastia and hyperkalemia. But thrombocytopenia caused by spironolactone has rarely been reported [2-4].

Case report

A 64-year old male was hospitalized due to abdominal pain and distension. Physical examination revealed that body temperature was 36,8°C, blood pressure was 110/80 mmHg, pulse rate was 100/min rhythmic, there was ascites in the abdomen, breath sounds decreased at the lung bases bilaterally and dullness during abdominal percussion were determined. Laboratory test results were as follows: hemoglobin: 15.1g/dL, white blood count: 7.98x10⁹/L, platelet count: 154x10⁹/L, prothrombin time: 14.7 seconds, AST: 66

IU/L, ALT: 43 IU/L, total/direct bilirubin: 2.1/0.6 mg/dL, lactic dehydrogenase: 212 IU/L, total protein: 7.2g/dL, albumin: 3 g/dL, HbsAg was (+), AntiHCV was (-), AntiHIV was (-) and HBV DNA was (-). Abdominal USG revealed that liver parenchymal structure was rough and granulated and the length of spleen was 13 cm. Paracentesis fluid was consistent with transudation. Furosemide, spironolactone and propranolol were initiated to the patient when he was discharged. The patient was hospitalized again after two weeks following discharge due to thrombocytopenia (Table 1). It was considered to be due to spironolactone from the history of the patient. Laboratory test results were as follows: hemoglobin: 15g/dL, white blood count: $7.5 \times 10^9/L$, platelet count: $3 \times 10^9/L$, prothrombin time: 16 seconds, AST: 64 IU/L, ALT: 40 IU/L, total/direct bilirubin: 3.2/0.8mg/dL, lactic dehydrogenase: 113 IU/L, total protein: 6.5g/dL, Alb: 2.4g/dL. Peripheral smear was consistent with thrombocytopenia and no other pathology was determined. Microbiological tests and cultures were normal. Ten units random and five units apheresis platelet suspensions were administered to the patient for thrombocytopenia. Following discontinuation of spironolactone among the drugs, platelet count increased rapidly and reached the plasma level of $160 \times 10^9/L$ after one week.

Table 1. Laboratory test results of the patient.

	First hospitalization	Second hospitalization	Spironolactone 8.day after discontinuation	Normal range
White blood counts ($\times 10^9/L$)	7.98	7.5	6.32	4-11
Hemoglobin (g/dL)	15.1	15	13,4	14-18
Platelets ($\times 10^9/L$)	154	3	160	150-400
Aspartate aminotransferase (IU/L)	66	64	53	5-40
Alanine aminotransferase (IU/L)	41	33	20	5-54
Gamma-glutamyl transpeptidase (IU/L)	22	27	25	7-50
Alkaline phosphatase (IU/L)	54	55	57	38-126
Lactic dehydrogenase (IU/L)	143	128	193	98-192
Prothrombin time (seconds)	14.7	16	16	10.7-13

Discussion

There are many reasons causing thrombocytopenia. These occur as a result of decrease of its production in bone marrow, increase of its destruction in the spleen and platelet destruction. Thrombocytopenia is defined to be a lower platelet count in the blood compared to the normal range (approximately $150 \times 10^9/L$) [2]. Drug-induced thrombocytopenia is not common. Frequency of thrombocytopenia is highly variable among the drugs. Incidence of drug-induced thrombocytopenia could not be determined exactly. Estimated minimum incidence of thrombocytopenia was determined to be approximately 10 cases per 100000 population in the studies performed. But this rate is higher among hospitalized patients and in elderly patients [5].

Drug-induced thrombocytopenia occurs usually due to heparin. Some drugs (chemotherapeutics and valproic acid) cause thrombocytopenia with dose-dependent myelosuppression mechanism. Unexpected thrombocytopenia occurs usually due to drug-induced immunological mechanisms. Drug-induced antibodies cause platelet destruction by strictly binding to the epitopes on the platelet surface glycoproteins [5, 6].

According to the information adapted by George et al. [7]

1. Recovery of thrombocytopenia permanently following discontinuation of the drug that is considered to be responsible for thrombocytopenia
2. The drug that is considered to be responsible for thrombocytopenia should be the single drug used since the beginning of thrombocytopenia or in case of multiple drug use; the platelet count should increase after discontinuing the suspicious drug while at the same time the patient continues to administer the other drugs.
3. Exclusion of the other causes of thrombocytopenia.
4. Recurrence of thrombocytopenia after initiation of the drug again.

According to the information adapted by George et al. [6], our case was also appropriate for items 1, 2 and 3. It was considered that thrombocytopenia developed due to spironolactone probably. In addition, presence of severe thrombocytopenia seen in the adults increases the possibility of drug-induced thrombocytopenia [5].

Thrombocytopenia generally occurs approximately 5-7 days after drug use. Furosemide, thiazide and bumetanide are diuretics that can cause thrombocytopenia [2, 4]. Spironolactone induced severe thrombocytopenia ($<20 \times 10^9/L$) is rarely seen. Fatal intrapulmonary and intracranial bleedings due to severe thrombocytopenia may occur [2, 4]. Since platelet count decreased to the level of $3 \times 10^9/L$ in our patient due to spironolactone, ten units random and five units apheresis platelet suspensions were administered to the patient.

Aggressive thrombocyte transfusion should be given to the patients with severe thrombocytopenia in order to prevent potential fatal complications. Corticosteroid is frequently administered but it has no benefit in drug-induced thrombocytopenia. Although corticosteroids are not effective, they are still recommended for use in patients with severe symptoms due to drug-induced thrombocytopenia. Intravenous immunoglobulin and plasma exchange can be performed but their benefit is indefinite [4, 5].

In conclusion, severe drug-induced thrombocytopenia developed in our patient with liver cirrhosis approximately 2 weeks after administration of spironolactone for ascites. Platelet count began to increase after discontinuation of the drug and reached normal levels approximately 2 weeks in the patient. Platelet counts should be carefully monitored in the patients with liver cirrhosis and receiving spironolactone treatment. It should be kept in mind that spironolactone may be one of the causes of thrombocytopenia and platelet counts should be carefully monitored during the treatment.

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