Case Report

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Drug-Associated Thrombocytopenia as a Rare and Devastating Side Effect of Octreotide in a Cirrhotic Patients: A Case Report and Current Literature Review

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Abstract

Variceal bleeding is one of the most serious outcomes encountered in portal hypertension. It represents one of the leading causes of death in cirrhotic patients. Octreotide infusion is the mainstay of treatment in variceal bleeding. It shows its effects by lowering portal venous pressure. Here, we present a patient with variceal bleeding who experienced sudden thrombocytopenia after octreotide infusion. Cessation of the octreotide therapy has resulted in a quick recovery of the platelet counts. Naranjo adverse drug reaction probability scale has revealed a probable relationship with 6 points. The case is reported in discussion with the existing 4 cases in the literature.

Keywords: Octreotide, thrombocytopenia, esophageal varices, liver cirrhosis

Introduction

Variceal bleeding is one of the most detrimental complications of portal hypertension. Variceal bleeding is associated with a 30-day mortality rate reaching 20 percent (1). Treatment consists of supportive management (i.e. saline, blood products), proton pump inhibitors and somatostatin analogs, namely octreotide. Somatostatin and octreotide help achieve hemostasis and prevent re-bleeding but neither have clearly shown benefit on mortality (2,3). Somatostatin and octreotide are generally well tolerated with minimal side effects. Although they have several common side effects, namely gallbladder stone and hyperglycemia, thrombocytopenia is not frequently encountered with only a few case reports in the literature.

Case Reports

A 76-year-old male patient with prior medical history of cirrhosis due to hepatitis C virus infection, familial Mediterranean fever, chronic obstructive pulmonary disease, hypertension and prostate adenocarcinoma was admitted to our hospital with recent onset melena. He had child-pugh class B cirrhosis with prior episode of variceal bleeding. Initial vital signs on admission were blood pressure of 100/60 mmHg, heart rate of 125 bpm, respiratory rate of 20 breaths/minute and oxygen saturation of 97 percent on ambient air. His physical examination was non-revealing apart from mild ascites. Laboratory findings on admission were hemoglobin level of 4.5 g/dL, platelet level of $156x10^3$/μL, and INR of 1.5. He received 1.5 liter of saline, 3 units of packed red blood cells, IV pantoprazole 80 mg bolus followed by 8 mg per hour and IV octreotide 50 μg bolus IV injection followed by continuous infusion at a rate of 50 μg per hour. Upper gastrointestinal endoscopy revealed non-bleeding esophageal varices and they were treated with band ligation with no treatment-related complication. Shortly after the initiation of octreotide treatment, platelet counts showed a fall trend with level of $108x10^3$/μL on the first day, $84x10^3$/μL on the second day and finally $63x10^3$/μL on the third day (Figure 1). The patient was consulted to the hematology department with laboratory tests, including a peripheral blood smear and coagulation panel which did not reveal any abnormalities. There

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were no possible medicines likely to contribute to new onset thrombocytopenia. Octreotide was discontinued on the third day with possible diagnosis of drug-induced thrombocytopenia. Following cessation of the drug, platelet counts dramatically improved, reaching 84x10^3/μL on the first day of the withdrawal, 109x10^3/μL on the second day and finally 146x10^3/μL on the third day. Written consent was obtained prior to discharge in order to write this study.

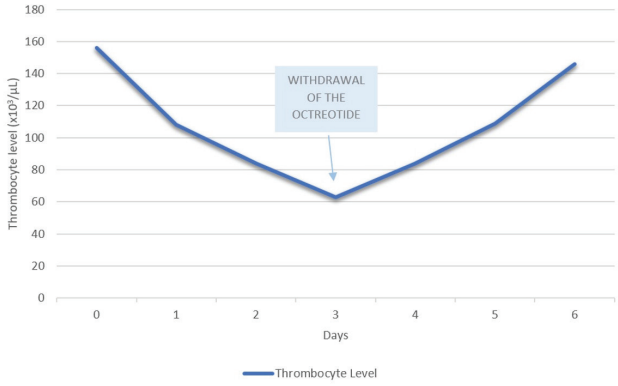

Figure 1. The course of platelet counts over time

Discussion

Thrombocytopenia related to octreotide infusion is an extremely rare and presumably overlooked adverse effect. Several case reports have been published with different characteristics were shown in Table 1 (4-7). While these studies show differences in time to nadir and recovery time of thrombocytes, they all report abrupt drop of thrombocytes shortly after introduction of octreotide and prompt initiation of recovery with the removal of octreotide, both consistent with our case. The mechanism of thrombocytopenia due to octreotide is mainly immunologic (8). Drug-induced thrombocytopenia refers to accelerated platelet wasting by antibodies that bind to glycoproteins on platelet cell membranes (9). Taking into consideration the fact that cirrhotic patients usually tend to become thrombocytopenic, any further insult leading to bleeding diathesis may lead to deleterious consequences. Naranjo adverse drug reaction probability score is a tool to assess whether a reaction is linked to the exposed drug (10). Scores are reported as ≤0 (i.e. doubtful), 1-4 (i.e. possible), 5-8 (i.e. probable) and ≥9 (i.e. definite). We calculated the score as 6, which reveals a probable link between octreotide and thrombocytopenia Appendix 1. Physicians must keep in mind that fall of thrombocyte levels shortly after octreotide infusion may be due to drug-induced thrombocytopenia and may require prompt withdrawal of drug.

Table 1. Case reports accessed via PubMed database. Note that platelet levels decrease more than 50% in 3 cases and 49% in 1 case

Author	Year	Number Of patients	Indication for octreotide therapy	Platelet level on admission (per mm^3)	Octreotide therapy duration (days)	Nadir platelet level (per mm^3)	Days to nadir	Days to platelet Recovery (after cessation of octreotide)
Hanna WT. et al (4)	1990	1	Enterocutaneous fistula	204.000	10	56.000	10	9
Demirkan K. et al (5)	2000	1	HCV induced cirrhosis	122.000	6	62.000	2	5
Chisholm S. et al (6)	2009	1	Alcohol-induced cirrhosis	144.000	3	28.000	5	N/A
Rashidi A. et al (7)	2011	1	Alcohol-induced cirrhosis	155.000	3	50.000	3	2

N/A: Not available, HCV: Hepatitis C virus

Authorship Contributions

Concept: S.E.A., A.T.G., Design: S.E.A., A.T.G., O.K., Data Collection or Processing: S.E.A., A.T.G., Analysis or Interpretation: S.E.A., A.T.G., O.K., Literature Search: S.E.A., A.T.G., Writing: S.E.A., A.T.G., O.K.

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Appendix 1. Naranjo adverse drug reaction probability scale result of the patient					
	Question	**Yes**	**No**	**Do not know**	**Score**
1.	Are there previous conclusive reports on this reaction?	+1	0	0	+1
2.	Did the adverse event appear after the suspected drug was administered?	+2	-1	0	+2
3.	Did the adverse reaction improve when the drug was discontinued or a specific antagonist was administered?	+1	0	0	+1
4.	Did the adverse event reappear when the drug was re administered?	+2	-1	0	0
5.	Are there alternative causes (other than the drug) that could on their own have caused the reaction?	-1	+2	0	+2
6.	Did the reaction reappear when a placebo was given?	-1	+1	0	0
7.	Was the drug detected in blood (or other fluids) in concentrations known to be toxic?	+1	0	0	0
8.	Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	+1	0	0	0
9.	Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	+1	0	0	0
10.	Was the adverse event confirmed by any objective evidence?	+1	0	0	0
TOTAL SCORE					+6

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