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Case Study

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CARVEDILOL INDUCED THROMBOCYTOPENIA

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ABSTRACT

Drug induced thrombocytopenia is suspected in patients with unexplained causes of acute thrombocytopenia, but documenting that a drug is the cause of thrombocytopenia can be challenging. Here we report a case of Carvedilol induced thrombocytopenia.

KEYWORDS: Drug induced thrombocytopenia, Carvedilol.

INTRODUCTION

Thrombocytopenia is often encountered in clinical practice. However, drug as a possible inciting cause for thrombocytopenia is often overlooked. Most Beta antagonist can cause thrombocytopenia, but the incidence is very low. We report a case of Carvedilol induced thrombocytopenia.

CASE REPORT

76 year old lady, a known patient of type 2 diabetes mellitus, systemic hypertension, hypothyroidism, and old cerebrovascular accident, presented with complaints of breathlessness since 1 week prior to admission. There was no history of fever, cough, sore throat and myalgia. She was admitted with a clinical diagnosis of severe anaemia with congestive cardiac failure and acute pulmonary oedema.

Routine laboratory investigations revealed severe anaemia (Hb-3.80g/dl), transaminitis (SGOT-2096, SGPT-605) with elevated bilirubin, CRP (46.6) and prolonged aPTT and INR (40.8 & 2.22) Occult blood was not detected in stool initially, and however it turned out to be positive on repeat analysis. Statins and antiplatelet were withheld in view of congestive hepatopathy and severe anaemia. Patient received packed cell transfusion. Patient's haemoglobin level rose to > 9 gm/dl and it remained stable thereafter. (Table-1). She was initiated on antibiotics (Ceftriaxone, Doxycycline), Oral hypoglycemic agents (Tab. Metformin), Insulin, furosemide infusion, betablockers (Tab. Carvedilol), angiotensin receptor blockers (Tab. Losartan) and nebulisations. However, she was noted to have progressive thrombocytopenia since 3rd day of hospitalization. (Table1) She was screened for Dengue which was negative. She underwent Contrast enhanced computed tomography of abdomen, which did not reveal any chronic liver parenchymal disease. Transaminitis gradually started resolving and normalized by 8th day (Table-1). In view of thrombocytopenia, Ceftriaxone, Doxycycline and Furosemide were withheld on day 5.Neverthless patient continued to have worsening of thromobocytopenia. At this point, though rare, the treating team considered the possibility of Carvedilol being the inciting agent. After stopping Carvedilol, platelet counts started rising within 24 to 48 hours and it became 1.12lakh by the 8th hospital day (Table-1). She came for follow up after 14 days and her platelet counts were 3.73 lakh.

TABLE – 1.

PARAMETERS	DAY1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 7	DAY 8
Haemoglobin g/dl	3.80	5.3	9.4	9.2	9.9	9.2	-	9.6
Total Leukocyte count in mm^3	8300	9100	9200			9000		
RBC	2.33	-	-	-	-	-	-	-
Platelets (Lakh/mm$^{3)}$	3.57lakh		1.23	0.94	0.82	0.69	0.82	1.12
CRP	46.6					14.1		
SGOT/SGPT (IU/L)	2096/ 605	2286/729	691/ 571	262/ 469		102/ 298		26/55

Serum Creatinine (mg/dl)	0.69	0.62	0.55		0.65		0.55	

DISCUSSION

In hospitalized patients, thrombocytopenia is often due to easily recognized clinical circumstances, such as the increased platelet destruction from sepsis, disseminated intravascular coagulation (DIC), dilutional effect of large volume transfusions or crystalloid infusion, mechanical destruction related to cardiopulmonary bypass or ventricular assist device, decreased bone marrow production from chemotherapy administration or platelet sequestration such as hypersplenism in those with portal hypertension.[1] When the aetiology of an acutely declining platelet count is not evident, medications must be considered as a potential culprit.[2]

Drug induced hematologic disorders are generally considered rare adverse effects. Various drugs cause thrombocytopenia. Drugs which commonly cause thrombocytopenia include heparin/low molecular weight heparin, glycoprotein IIb/IIIa inhibitors, vancomycin, linezolid, beta-blockers, beta lactam antibiotics, quinine, and antiepileptic drugs etc.[3]

Thrombocytopenia or thrombocytopenic purpura is listed as a possible adverse effect by the manufactures of atenolol, bisoprolol, carvedilol, labetalol, metoprolol, propranolol and nadolol.[4,5] Carvedilol associated thrombocytopenia is noted to be as low as <1-3%.[6]

Carvedilol is a nonselective β-adrenergic blocking agent with α1-blocking activity. It works by causing vasodilation and has negative chronotrophic effects on the heart and decrease blood pressure. Plasma concentrations achieved are proportional to the oral dose administered.[7]

The 3 proposed mechanisms by which beta blockers reduce platelet aggregation are by interacting with platelet cell membrane, by blocking beta 2 receptors on platelets and by decreasing plasma catecholamine levels.[8, 9, 10]

It is rapidly and extensively absorbed following oral administration, with absolute bioavailability of approximately 25% to 35% due to a significant degree of first-pass metabolism. The elimination half-life of carvedilol generally ranges from 7 to 10 hours. In this case thrombocytopenia improved within 24 hours after stopping Carvedilol.

CONCLUSION

The severity of drug induced thrombocytopenia can range from mildest of cell line reductions to life threatening reactions leading to increased morbidity and mortality. Thus clinicians should be aware of the agents known to cause thrombocytopenia. Like many adverse drug reactions, a definitive diagnosis of drug induced thrombocytopenia can be obtained only after discontinuation of offending agent and subsequent resolution of the adverse drug reaction. Thus if drug induced thrombocytopenia is expected, prompt discontinuation of the possible offending agent is crucial.

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