

Suspected Case of Vancomycin Induced Thrombocytopenia (VIT)

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Abstract

Vancomycin is one of the most effective antimicrobials used for gram positive infections and has been used widely at our set up in emergency department. Association of Vancomycin with thrombocytopenia have not been encountered frequently. Herein we are presenting a case of 79-year-old lady who was operated for right hip replacement and during her clinical management required Vancomycin which led to thrombocytopenia and platelet count improved after drug discontinuation and a positive de challenge was observed. We concluded this causality as "Possible category" according to WHO-UMC causality categories.

Keywords: Vancomycin; Drug Induced Thrombocytopenia; Rare Adverse Drug Reaction; Post-Operative Patient; Vancomycin Induced Thrombocytopenia (VIT)

Introduction

Vancomycin, the class originator for glycopeptides is, a tricyclic antibiotic produced by *Streptococcus orientalis*. It possesses activity against the vast majority of gram-positive bacteria including MRSA, penicillin-resistant streptococci, and ampicillin-resistant enterococci [1]. Commonly associated side effects are attributed to its histamine producing potential leading to Vancomycin flush, reversible ototoxicity and in some cases renal involvement. Association of Vancomycin with thrombocytopenia have not been encountered frequently [2]. It is one of the most effective antimicrobials used for gram positive infections and has been used widely at our set up in emergency department. Vancomycin administration has been documented in scarce literature [3].

Herein we are presenting a case of 79-year-old lady who was operated for right hip replacement and during her clinical management required Vancomycin which led to thrombocytopenia and platelet count improved after stopping the drug.

Case Details

A 79-year-old female was brought to Emergency Department of our hospital with complains of breathlessness for 10 days. She had a history of trauma due to fall at home 10 days back and fractured her right hip for which replacement arthroplasty was done 5 days back in a private hospital. After that 2 pints of Packed Cell Volume (PCV) and BIPAP support was given. She suffered a post-operative respiratory failure, endotracheal tube was inserted and put on mechanical ventilation. One pint of Packed Cell Volume (PCV) was given and inotropic support started. She was stable, so extubated the day after and again reintubated next day. The patient was brought to the emergency at our hospital which is a tertiary care hospital for further medical care.

On examination she was conscious, and vitals were: Blood pressure - 130/80 mm Hg, Heart rate - 60/min, Temperature - within normal limits and RBS - 140 mg/dL. Echocardiography was suggestive of dilated left atrium and ventricle, inferior wall hypokinesia with apical aneurysm. Clinically she was diagnosed as having left ventricular failure complicated by anaemia and type 2 respiratory failure.

At the time of admission, she was already on intravenous Sulbactam + Cefoperazone [Zostum] (1.5 gm) BD and intravenous Metronidazole (500 mg) TDS. She was sent to an intensive care unit for further management. Relevant laboratory investigations are depicted in table 1.

No	Investigations	Day 1 (Vancomycin commenced)	Day 6 (Vancomycin stopped)	Day 10
1.	CBC			
	Hb (g/dl)	9.2	8.7	7.5
	WBC (kU/L)	17.16	17.13	19.15
	RBC (ml/cu mm)	3.35	3.25	2.85
	Hematocrit (%)	29.5	27.7	24.9
	Platelet count (x 10 ³ /mm ³)	278	90	163
2.	Arterial Blood Gases (ABG)			
	pH	7.48	7.45	7.03
	pCO ₂ (mm Hg)	41.1	26.3	89.6
	pO ₂ (mm Hg)	216	192	58
3.	Blood urea (mg/dL)	107	85.6	96.3

Table 1: Laboratory findings.

Considering her clinical course intravenous Linezolid (600 mg) BD started next day from her admission with a platelet count of 348 x 10³/mm³. Culture from endotracheal tube shown *E. coli* and *Acinetobacter* organisms and showing sensitivity to Aminoglycosides. After getting this reports, intravenous Vancomycin started on Day 9 of hospitalization, 1 gm stat followed by 1 gm BD. At that time platelet count shown 260 x 10³/mm³ which were within the normal range. Linezolid was withdrawn 2 days after starting of Vancomycin treatment and intravenous Meropenem 1 gm TDS was added and Vancomycin was continued. The next platelet count reading showed a decline to 216,128 and 99 x 10³/mm³ in the next subsequent days. Her urine routine examination report on day 5 of Vancomycin treatment showed presence of blood and many red cells, suggestive of haematuria. Vancomycin administration was terminated after clinical suspicion and platelet count was monitored on a daily basis. Subsequent improvement in platelet count was observed after 2 days of stopping the treatment which raised to 163 x 10³/mm³ after 5 days of stopping Vancomycin, and urine routine examination report on this day was showing no signs of haematuria.

Linezolid was given for 10 days and Vancomycin for 6 days. Subsequent decrease in platelet count and improvement in platelet count after stopping Vancomycin is shown in figure 1. On the basis of platelet count and urine examination report physician suspect Vancomycin induced thrombocytopenia (VIT) and reported to the nearest pharmacovigilance centre.

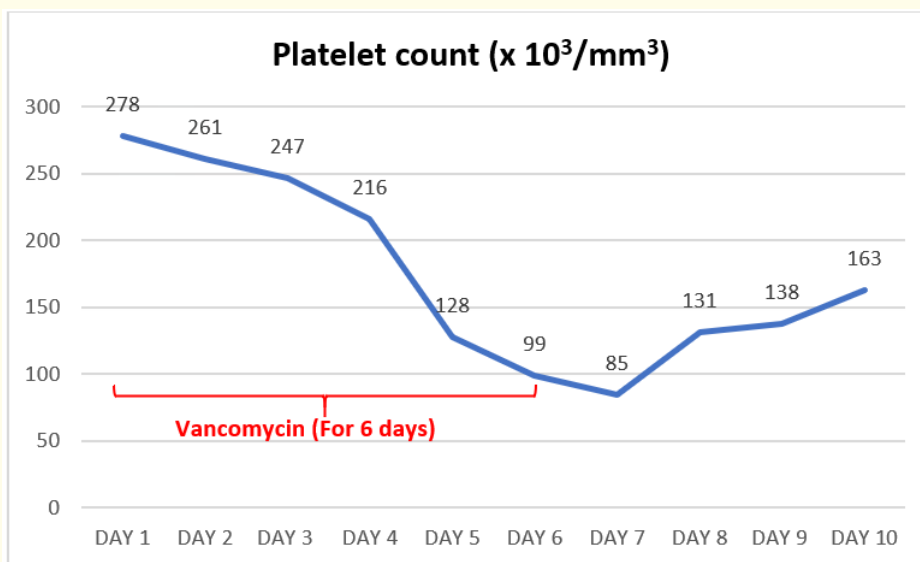


Figure 1: Graph depicting the progression of platelet count in vancomycin-induced thrombocytopenia (Day 1: Vancomycin commenced; Day 6: Vancomycin stopped).

Discussion

Thrombocytopenia defined as a platelet count $< 100 \times 10^3/\text{mm}^3$ or $> 50\%$ drop in the platelet count from baseline. Drug induced thrombocytopenia may be due to suppressive effects of drug on bone marrow or could be due to immune mediated lysis of platelets [4].

The adverse events on the blood elements are usually type 2 hypersensitivity reaction, which are also called cytolytic reaction with major targets being cells of the circulatory system. The drugs in question here combines with its antibodies (IgG) and these complexes adhere to the surface of blood cells which leads to activation of compliment which can destroy the cell membrane. These mechanisms have been cited for Methyldopa and Quinidine induced haemolytic anaemia and Rifampin induced thrombocytopenia [5]. Vancomycin being a glycopeptide might combined with platelet glycoprotein IIb/IIIa and disturbs the membrane integrity and causes platelet destruction. Thrombocytopenia with Vancomycin is reversible and completely resolved after drug discontinuation. It may cause symptoms related to thrombocytopenia like haemorrhages, ecchymoses, and haematuria [6]. Haematuria was also observed in our case and resolved after drug discontinuation. Findings in table 1. may not have a direct correlation with thrombocytopenia in our case but it has been kept to rule out other disease conditions which are responsible for fall in platelet count. Herein patient was diagnosed as having Acute kidney injury and some laboratory values pertaining to renal function were deranged pointing to known Adverse Drug Reaction to Vancomycin which is renal involvement.

Association of Vancomycin with thrombocytopenia remains unknown but physician should be watchful of bleeding complications which could be associated with Vancomycin and other antibiotics. There have been studies in literature that the fall in the platelet count might not be acute but occur over few days. In one report, a 51-year-old man was diagnosed with acute severe alcohol-induced pancreatitis complicated by development of a peripancreatic fluid collection, developed fever of unknown origin and was treated with intravenous Vancomycin and Piperacillin with Tazobactam. On day 6 of Vancomycin therapy his platelet count dropped to $46 \times 10^9/\text{L}$ ($237 \times 10^9/\text{L}$ on day 1 of treatment) and by day 8 of therapy platelets had fallen to a nadir of $9 \times 10^9/\text{L}$. A clinical diagnosis of VIT was made and the drug withdrawn. After 3 days a significant improvement in the platelet count was noted, rising to $56 \times 10^9/\text{L}$ [7]. In one recent report, a 3-month-old girl was given intravenous Vancomycin for purulent meningitis. Her platelet count decreased after a week. As with all allergic reactions the offending drug Vancomycin was stopped and patient was given steroids as per routine protocol. Patient's platelet count fell in the normal range in less than a week [2].

The diagnosis of drug induced thrombocytopenia is always to keep in mind when patient is receiving many drugs in an intensive care unit. In our case the patient was also given Linezolid. Although we could have attributed this fall in platelet count to Linezolid which is well known to cause this Adverse drug reaction (ADR) [8], but on the case details there was no significant decline in platelet count after Linezolid therapy and no significant rise after stopping the drug. With Vancomycin discontinuation, a positive de challenge was observed. The causality is labelled as possible since Linezolid and Sulbactam + Cefoperazone (Zostum) could also lead to such platelet fall but, in this case, the temporal relationship is missing.

Conclusion

Vancomycin induced thrombocytopenia is not an adverse effect we frequently attribute to this drug as we attribute to Linezolid, Rifampicin or Sulphonamides. Physician should always be watchful of fall in platelet count if a recent antimicrobial is added to patient's prescription, especially in intensive care unit where patient is frequently on broad spectrum antibiotics.

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Conflict of Interest

None declared.

Ethical Approval

Not required.

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