

Vancomycin-Induced Thrombocytopenia: A case report

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Vancomycin has been implicated as a cause of thrombocytopenia since 1990. In a recent report of The New England Journal of Medicine, the BloodCenter of Wisconsin has identified Vancomycin-Dependent, Platelet-Derived antibodies to detect Vancomycin induced thrombocytopenia. In this case report, a 65-year old male was treated with Vancomycin for osteomyelitis. On the 10th day of treatment, he had a fever and developed a rash. Angiopathic petechiae were most pronounced on his back and arms. His platelet count dropped from $189 \times 10^3/\text{mm}^3$ to $1 \times 10^3/\text{mm}^3$ in 48 hours. This case report supports the use of drug-dependent antibody assays to identify and confirm the cause of thrombocytopenia in patients who show a precipitous drop in platelet levels while receiving vancomycin.

Vancomycin is an antibiotic frequently used in the treatment of MRSA (Methacillin resistant *Staphylococcus aureus*). In podiatry, Vancomycin is the most commonly used IV antibiotic for the treatment of MRSA soft tissue infections and MRSA osteomyelitis. The most recent studies have suggested a 10 to 20-fold increase in the use of Vancomycin in the past 25 years. [1, 2] There are a number of drugs that can cause thrombocytopenia. [3] Very often, patients who are on prolonged IV antibiotic treatment are also placed on Heparin to prevent DVT and pulmonary embolism. Heparin, or Lovanox, has been implicated in causing thrombocytopenia in such cases. [4] In this setting, thrombocytopenia is characterized by an acute drop in the platelet count. In the combined use of Vancomycin and Heparin, it is often difficult to determine whether the thrombocytopenia is caused by Vancomycin-induced immune antibodies or a Heparin-induced response.

In a recent study of *The New England Journal of Medicine*, Drygalski, et al, have correlated IgG and IgM antibody levels in thrombocytopenia caused by an immune response to intravenous Vancomycin. More importantly, there now appears to be a valuable test available that can detect Vancomycin-Dependent, Platelet-Reactive Antibodies in patients who develop thrombocytopenia while on Vancomycin. [5] This case report describes the clinical presentation and treatment course of a patient who developed thrombocytopenia while on Vancomycin.

Case Report

A 65-year old diabetic male was treated with Vancomycin for osteomyelitis of the foot. He underwent surgery for osteomyelitis of the foot on February 19th, 2007. He was placed on Vancomycin on February 21st, 2007 after sensitivity reports revealed organisms susceptibility to Vancomycin. The patient had a history of diabetes mellitus, gout, chronic kidney disease, congestive heart failure, hypertension and hypercholesterolemia.

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FIGURE 1 Acute thrombocytopenic purpura was seen on the patient's back and arms. Microangiopathic petechiae were evident with purpura and ecchymosis of the flexor region of both arms.

His medication list was extensive. The patient was on Coreg 25mg, Lasix 40mg, Digitek 0.125mg, Avandia 4mg, Lisinopril 5mg, Glyburide 5mg, KCl 20 meq, Allopurinol 300mg, Welchol 650mg, Zetia 10mg, Indomethacin 25mg prn for gout, Prevacid 30mg, Aspirin 81mg, Quinine 325mg prn for leg cramps, Viagra 100mg, Calcium 600mg and Glucosamine/Chondritin 500/400.

He did not take any Glucosamine or Chondritin while in hospital. Vancomycin peaks and troughs were run on two separate days. Peaks were 28.5 and 36.6 mcg/m and troughs were 17.3 and 13.4 mcg/ml. His infection cleared after surgery; however, on the 10th day of treatment, he began to lose his appetite and had spiking fevers. His fever peaked to 102.5 Fahrenheit with ensuing petechial rash of his back and arms. (Fig. 1). His platelets showed a precipitous drop from $189 \times 10^3/\text{mm}^3$ to $1 \times 10^3/\text{mm}^3$ in 48 hours. The Lovanox and Vancomycin were immediately stopped. Blood Testing was performed including PF4 Elisa test, IgG and IgM assays and detection of Vancomycin-Dependent, Platelet-Reactive Antibodies. This last test required 5mL of serum plasma from the patient. There is only one lab in the country that can test for this antibody at this writing. The plasma was sent to the BloodCenter of Wisconsin. He was given 10 units of platelets without response. After the second day, the patient's platelets only increased to $3 \times 10^3/\text{mm}^3$. He also developed a nose-bleed, which was stopped by local packing. He was then given IV dexamethasone, Immunoglobulins and Epopen. After the fourth day, his platelets increased to $15 \times 10^3/\text{mm}^3$. By week's end, the patient's platelet count was over $100 \times 10^3/\text{mm}^3$.

Laboratory Assay

The Laboratory tested for both IgG and IgM in the patient's serum with and without Vancomycin present. (Table 1) The BloodCenter of Wisconsin certified a positive reaction detected in the patient's serum by flow cytometry in the presence of Vancomycin. These results indicated the presence of Vancomycin-dependent, platelet-reactive antibodies. This supports a diagnosis of vancomycin-induced, immune thrombocytopenia.

Patient's serum with Vancomycin	Patient's serum without Vancomycin
IgG - Positive	IgG - Negative
IgM - Negative	IgM - Negative

Table 1 Although there is a negative IgM assay in the presence of Vancomycin, a positive IgG assay by flow cytometry indicates the presence of vancomycin-dependent, platelet-reactive antibodies supporting the diagnosis of immune thrombocytopenia.

At this writing, the test is not cleared or approved by the FDA. The Laboratory claims the FDA has determined that such clearance or approval is not necessary. The test has been validated in house and is used for clinical purposes. It should not be regarded as investigational or for research. The laboratory is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as qualified to perform high complexity clinical laboratory testing. [8]

Discussion

Normal platelet counts range from $150 \times 10^3/\text{mm}^3$ to $450 \times 10^3/\text{mm}^3$. [7] Vancomycin-induced thrombocytopenia has rarely been reported in the literature. This appears to be the first report of Vancomycin-induced thrombocytopenia in the podiatry literature. The mechanism of drug-induced thrombocytopenia is one of *immunological platelet destruction*. The drug will bind to the fragment antigen binding (FAB) portion of an antibody. The antibodies will then attach to the drug-platelet complex and cause platelet destruction through complement activation. [5,6,7]. In Vancomycin-induced thrombocytopenia, the immunologic response is through hapten formation.

There is now compelling evidence that patients who develop Vancomycin-induced thrombocytopenia have Vancomycin-dependent antibodies. [5,6]

As late as 2003, Vancomycin-induced thrombocytopenia was confirmed by rechallenge of the medication or when heparin-induced thrombocytopenia was ruled out. [4,5,6]. Heparin induced thrombocytopenia is associated with a strongly positive human platelet factor 4 (PF4). This can be tested by ELISA and often returns to normal after the Heparin is stopped. [5] Many times, Vancomycin and Heparin are given concurrently in cardiac patients or patients who may require prolonged bed rest. In this case report, both Lovanox and Vancomycin is discontinued. Platelets were initially transfused during the acute phase in an attempt to increase platelet levels. This did not seem to cause any rise in platelet levels. Drygalski, et al, reported similar results in 11 of 14 patients who received platelet transfusions. [5] It could be theorized that circulating antibodies will continue to assert a platelet destructive affect making platelet transfusions ineffective in the acute phase of thrombocytopenia. Antibodies can also persist for many months after exposure to Vancomycin. [5]. Once the Vancomycin is stopped, in most circumstances, the platelet levels will normalize within 7 days. [6].

This case confirms similar results reported by *The New England Journal of Medicine*. We also conclude the use of drug-dependent antibody assays to identify and confirm the cause of thrombocytopenia in patients who show a precipitous drop in platelet levels while receiving Vancomycin.

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