

**VANCOMYCIN INDUCED RED MAN SYNDROME IN ELDERLY MAN: A CASE REPORT**Sai Charitha Sreeram<sup>1\*</sup>, V. Bhavya<sup>1</sup>, P. Lakshmi<sup>2</sup> and D. Ranganayakulu<sup>3</sup><sup>1</sup>Student, Department of Pharmacy practice, Sri Padmavathi School Of Pharmacy, Tiruchanoor, Tirupathi, Andhra Pradesh, India.<sup>2</sup>Associate professor, Department of Pharmacy practice, Sri Padmavathi School Of Pharmacy, Tiruchanoor, Tirupathi, Andhra Pradesh, India.<sup>3</sup>Principal, Sri Padmavathi School Of Pharmacy, Tiruchanoor, Tirupathi, Andhra Pradesh, India.**\*Corresponding Author: Sai Charitha Sreeram**

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**ABSTRACT**

Vancomycin is a glycopeptide antibiotic active against gram positive bacterial infections. It is commonly used to treat Methicillin Resistant Staphylococcus Aureus (MRSA) infections. Most important adverse reaction with vancomycin is hypersensitivity reaction. It is of two types, one is anaphylaxis and other Red Man syndrome (RMS). RMS is also known as "red neck syndrome. It is more common with rapid infusion of Vancomycin. RMS is usually presents with pruritus, erythematous rash commonly involving head, neck and upper part of body and less frequently with chest pain, hypotension and cardiovascular collapse. Discontinuation of antibiotic and treatment with antihistaminic can abort most of the reactions. Slow intravenous administration of vancomycin should minimize the risk of infusion-related adverse effects. This case concerns an elderly man who developed a 'Red Man Syndrome' reaction whilst on intravenous vancomycin therapy for Chronic rheumatic heart disease (CRHD).

**KEYWORDS:** Red man syndrome, Antihistamines, Chronic rheumatic heart disease, Antibiotic, Vancomycin and Anaphylaxis.

**INTRODUCTION**

Vancomycin was first found by Dr. E. C. Kornfield from soil and is naturally produced by *Amiclotopsis Orientalis*.<sup>[1]</sup> Vancomycin is a glycopeptide antibiotic originally derived from *Streptomyces (Norcadia) orientalis*, is being widely used for severe Gram-positive bacterial infections. It is an alternative drug for serious staphylococcal and streptococcal infections, including endocarditis, when allergy precludes the use of penicillins and cephalosporins.<sup>[2]</sup> It acts by inhibiting cell wall synthesis in Gram positive organisms.<sup>[1]</sup>

Major indications for the use of Vancomycin include infections caused by Methicillin Resistant Staphylococcus Aureus (MRSA) and Multidrug Resistant Staphylococcus Epidermis (MRSE), treatment of pseudomembranous colitis and endocarditis.<sup>[3]</sup> The incidence of red man syndrome varies between 3.7% and 47% in infected patients.<sup>[4]</sup> The most common vancomycin adverse effects are unrelated to serum drug concentration and include fever, chills, and phlebitis.<sup>[2]</sup>

Vancomycin can cause two types of hypersensitivity reaction: the red man syndrome and anaphylaxis. Red Man Syndrome (RMS) is thought to be an infusion-related reaction consisting of pruritus, an erythematous rash involving the face, neck and upper torso.<sup>[4]</sup> Agitation, dizziness, headache, chills, fever and perioral paresthesia are also described. In severe cases patients may also complain of chest pain and dyspnoea.<sup>[5]</sup> It appears to be due to vancomycin-induced histamine release without involvement of preformed antibodies.<sup>[4]</sup>

Discontinuation of the vancomycin infusion and administration of diphenhydramine can abort most of the reactions. Slow intravenous administration of vancomycin should minimize the risk of infusion-related adverse effects.<sup>[6]</sup>

**CASE REPORT**

A 38-years-old man, he was brought to the hospital with chief complaints of fever, breathlessness and pain during defecation associated with bleeding since 15 days which is gradually progressing. His history of present illness states that fever was intermittent, high grade associated

with chills and rigors, evening rise of temperature. Breathlessness which is insidious in onset, grade II type not associated with cough, hemoptysis, chest pain, palpitation, bowel and bladder disturbances. Past history reveals that the patient had Mitral valve regurgitation since 7 years and is on treatment with ACITROM 2mg H/S. He also had a history of Pulmonary tuberculosis 1 year back and used Anti tubercular drugs for 3 months & then discontinued.

At the time of admission, he was conscious and coherent. Laboratory data included Routine haemogram revealed haemoglobin 6.3 gm%, platelets 0.63 lakhs/cumm, packed cell volume 32%, total leukocyte count 3,600 cells/mm<sup>3</sup>, urinalysis, liver and renal functions, with normal triglyceride, cholesterol, and uric acid levels. Serum creatinine 0.8mg/dl, serum electrolytes - sodium 128mmol/l; potassium 3.2mmol/l; chloride 98mmol/l. Complete hemogram revealed Pancytopenia and USG Abdomen reveals gross splenomegaly. Antibiogram reveals isolation of *Streptococcus pneumoniae*. From the above laboratory examinations, physical examination and past history, the patient was diagnosed as Chronic Rheumatic Heart Disease with Mitral Valve Regurgitation and was on treatment with IV Fluids, Tab. Folvite (folic acid)5mg PO OD, Tab. Paracetamol 500mg PO TID, Tab. VIT-C PO OD, Tab. Metronidazole 400mg PO BD, Tab. IFA 200mg PO OD, Inj. Augmentin 1.2g IV BD, Inj. Vancomycin 1g in 100ml NS IV BD, Tab. Pantop 40mg PO OD and Tab. Acitrom (Acenocoumarol) 2mg H/S. Diagnosis of Red Man Syndrome due to Vancomycin fast infusion was made and then Tab. CETRIZINE 10mg PO BD was initiated, after that vancomycin was infused slowly for one hour. And the patient was discharged after 10 days.

#### ADR ANALYSIS

The causality assessment of Red Man Syndrome with Vancomycin using Naranjo's causality assessment scale and WHO-Uppsala monitoring is indicated as probable association with Vancomycin. It showed that there is temporal relationship between drug and reaction is present.

#### DISCUSSION

Vancomycin in past has been known as "Mississippi mud" due to its association with many adverse drug reactions including hypersensitivity (anaphylaxis, Red Man syndrome), neutropenia. The impurities associated with Vancomycin were thought to be associated with the reactions. So the purifications of Vancomycin did result in decrease in reactions. But still today use of Vancomycin is associated with many adverse drug reactions. Adverse drug reactions to Vancomycin may range from mild pruritis and redness which may often go unnoticed to severe hypotension and cardio-vascular collapse.<sup>[3]</sup>

Vancomycin kills a variety of bacterial pathogens. Red man syndrome is a hypersensitive allergic reaction that happens because the antibiotic interferes with immune system cells. In the case of vancomycin and Redman syndrome, the symptoms can be mild and are not life-threatening. Certain components of the immune system are responsible for causing these symptoms. Cells called mast cells and basophils contain storage granules of a substance named histamine. Histamine is one of the signal molecules of the immune system, and plays a role in the development of inflammation. Abnormally high levels of histamine in the circulation then causes the symptoms associated with Redman syndrome. The rash and itchiness represent an unnecessary activation of the immune system.<sup>[2]</sup>

Most of the hospital protocols require vancomycin to be infused over 60 min, as a minimum. The anaphylactic reaction is mediated by IgE. Red man syndrome, an anaphylactoid reaction, is caused by the degranulation of mast cells and basophils, resulting in the release of histamine independent of preformed IgE or complement. The extent of histamine release is related partly to the amount and rate of the vancomycin infusion. Signs of red man syndrome would appear about 4–10 min after an infusion started or may begin soon after its completion.<sup>[6]</sup>

The 'Red Man Syndrome' seen in association with intravenous vancomycin administration is not a true allergic reaction. It appears to be due to vancomycin-induced histamine release without involvement of preformed antibodies.<sup>[4]</sup> Use of vancomycin may change the way blood cells are produced and low levels of platelets might result, or white blood cell counts could change. In rare cases, the drug can damage the kidneys or damage hearing. While it's good at eradicating certain infections, it can be hard on the body.<sup>[2]</sup>

The effects of red man syndrome can be relieved by antihistamines. Pretreatment with hydroxyzine can significantly reduce erythema and pruritus. Administration of diphenhydramine to patients before starting vancomycin infusion (1 g over 1 hour) can prevent the occurrence of red man syndrome with the first dose of vancomycin. Other studies have shown that combining an H1 receptor blocker with an H2 receptor blocker such as cimetidine may help to prevent or reduce the risk of red man syndrome.<sup>[6]</sup>

If RMS appears, vancomycin infusion should be stopped immediately. To abort most of the reactions, a dose of 50mg diphenhydramine hydrochloride is given intravenously or orally.<sup>[1]</sup> Hypotension will require intravenous fluids and, if severe, vasopressors may be needed. Hypotension can be troublesome if it occurs during anesthesia following the use of vancomycin for surgical prophylaxis. Therapy with a  $\beta$ -blocker before surgery has been found to be protective against hypotension caused by vancomycin infusion.<sup>[6]</sup>

Patient experienced itching and warmth over the neck, hands and chest, with the development of rash and then headache, chills & fever are also described on the 6th day after the vancomycin was administered. These signs of red man syndrome were appeared within 10 min after fast infusion of vancomycin intravenously. Then Vancomycin therapy was stopped immediately and regular antihistamines i.e., Tab. CETRIZINE 10mg orally twice daily was prescribed. The rash then cleared and did not return. Rechallenge with intravenous vancomycin was initiated but it was administered slowly for 1 hour in 100ml Normal saline. No other drug therapy was altered during this time, and no other potential allergens were indentified.

## CONCLUSION

Red Man Syndrome (RMS) was common in the past due to impurities in vancomycin preparation. This is the reason for the drug to be nicknamed as “Mississippi mud”. Each intravenous dose of vancomycin should be administered over at least a 60 min interval to minimize the infusion-related adverse effects. Longer infusion times should be used in patients receiving doses considerably larger than 1 g vancomycin.

RMS is infusion related reaction and is less common when low dose of vancomycin is given frequently. Rapid infusions should be avoided. When rapid infusion is mandatory, premedication with anti-histaminics should be used to decreases incidence of RMS. If reaction occurs, treatment with antihistaminic like diphenhydramine can treat most of reactions.

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