

**Case report**

**Red man Syndrome: an unusual complication of vancomycin beads**

Juyal A<sup>1</sup>, Khurana G<sup>2</sup>, Maheshwari R<sup>3</sup>

**Abstract:**

Vancomycin is a bactericidal antibiotic. It is commonly used to treat Methicillin Resistant Staphylococcus Aureus (MRSA) infections. It is also used locally with Polymethyl methacrylate to treat chronic bone infections. Locally placed beads deliver high concentration of antibiotics locally with few adverse effects as compared to parenteral therapy. There are two complications mentioned on intravenous infusion of vancomycin namely anaphylactic reaction and red man syndrome; but there is no known literature on complications arising from vancomycin impregnated cement beads. We report a case of red man syndrome following usage of vancomycin impregnated cement beads which is not reported in any available orthopaedic literature.

**Keywords:** vancomycin beads; Red man syndrome

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**Introduction :**

Vancomycin can cause two types of hypersensitivity reaction – the red man syndrome and anaphylaxis. The red man syndrome (RMS) is the most common complication of vancomycin therapy<sup>1</sup>, with studies reporting an incidence of 3.7% to 47% in infected patients and up to 90% in healthy volunteers<sup>2</sup>. It is thought to be an infusion-related reaction consisting of pruritus, an erythematous rash involving the face, neck and upper torso. In milder form this reaction may be mistaken for an allergy, where patient commonly begins to experience itching and warmth over the head and chest, with or without the development of a rash and the condition may go unreported. Patients commonly complain of the sensations of burning and itching. Agitation, dizziness, headache, chills, fever and perioral paresthesia are also described<sup>3</sup>. In severe cases patients complain of chest pain and dyspnoea<sup>4</sup>.

Although the reaction is more likely to occur with rapid intravenous infusion of vancomycin, it may also occur when infusion is given at slower rate. If the symptoms consistent with this type of reaction occur, slowing the rate of infusion for at least over two hours and pre-treating with a histamine-1 antagonist prior to any subsequent doses of vancomycin is recommended<sup>4</sup>.

Vancomycin-impregnated polymethyl methacrylate

beads are commonly being used in orthopaedics for the treatment of Methicillin-Resistant S. Aureus osteomyelitis with efficacy reported<sup>5</sup>.

**Case report:**

A 48 years old male patient presented with one year old infected nonunion fracture tibia with plaster cast. Patient had no co-morbidities or any history of drug allergy. In the past patient had undergone multiple surgeries without any complications, but the infection persisted. So, another debridement was planned under spinal anaesthesia. After debridement and excision of the dead and infected tissue, vancomycin impregnated bone cement beads were placed in the bone defect after sensitivity test of vancomycin. Operative and immediate post operative periods were uneventful. Three hours post surgery, patient first complained of throat pain and respiratory distress. Few minutes after onset of symptoms, blood pressure and pulse were unrecordable and patient went into cardiac arrest. Redness was noted all over the face, trunk and upper limbs. Cardio pulmonary resuscitation was started immediately with chest compressions and simultaneously patient was intubated and Injection Adrenaline, Atropine, Hydrocortisone, Dopamine infusion and Chlorpheniramine (due to unavailability of Inj. Hydroxyzine) were given following which the patient revived. However, after about 15 minutes patient again went in hypotension

1. Anil Juyal, Professor, Department of Orthopaedics

2. Gurjeet Khuran, Professor & Head, Anaesthesiology

3. Rajesh Maheshwari, Professor & Head, Department of Orthopaedics

HIHT University, Swami Rama Nagar, Doiwala, Dehradun (Uttarakhand), India

**Corresponds to:** Dr. Anil Juyal, Professor, Department of Orthopaedics, HIHT University, Swami Rama Nagar, Doiwala, Dehradun (Uttarakhand), India. Email: [draniljuyal.hiht@gmail.com](mailto:draniljuyal.hiht@gmail.com)

and cutaneous symptoms (redness of skin) worsened. By that time we suspected him to be case of RMS due to vancomycin. Patient was immediately shifted to operating room and vancomycin beads were removed along with wound lavage with normal saline. On removal of Vancomycin beads, the cutaneous symptoms gradually disappeared within one hour along with gradual improvement of vitals.

#### Discussion:

In 1970s, Buchholz first started using antibiotic impregnated bone cement to treat infected arthroplasties<sup>6</sup>. Hence forth, antibiotic impregnated beads were developed to treat local infections of bone and soft tissue which is being continued to this day by many orthopaedic surgeons. The advantage of these antibiotic beads is that they deliver a high concentration of antibiotics locally while avoiding high systemic concentrations, thus avoiding adverse effects that are often associated with parenteral antibacterial therapy. In addition, methylmethacrylate bone cement does not significantly affect the immune response of the body.

Hypersensitivity reactions to vancomycin occur via two different mechanisms. While both reactions involve mast cell activation, vancomycin-induced anaphylactic reactions are mediated by immunoglobulin (Ig) E, while anaphylactic reactions (i.e., RMS) are not<sup>7</sup>. RMS occurs due to histamine release from mast cells and basophils located in the skin, lung, gastrointestinal tract, myocardium, and vascular system<sup>8</sup>.

Antibiotics such as ciprofloxacin, amphotericin B,

rifampicin and teicoplanin can potentially cause red man syndrome<sup>9</sup>. Red man syndrome is aggravated in patients receiving vancomycin with opioid analgesics or muscle relaxants<sup>4</sup>. The adverse effect of red man syndrome can be relieved by antihistamines. Prophylactic dose of hydroxyzine can significantly reduce the chances of red man syndrome.

Okuno et.al<sup>10</sup> in an anaesthetic journal, reported development of RMS in an elderly lady induced by Vancomycin-infusion along with vancomycin impregnated Polymethyl methacrylate beads after 11 days of insertion, which resolved after the removal of the beads.

Eventhough red mans syndrome is associated with rapid IV infusion of vancomycin but as seen in the above scenario, placement of vancomycin impregnated beads locally can also give rise to red man syndrome. Although the treatment protocol remains the same, but the management has to be aggressive and may require removal of the vancomycin impregnated beads along with antihistaminics in order to relieve the symptoms and save the life of the patient.

#### Key Message:

Vancomycin beads are commonly being used by orthopaedicians to treat Methicillin Resistant Staphylococcus Aureus (MRSA) infections. However, it should be kept in mind that in spite of a normal sensitivity test; locally placed vancomycin beads sometimes induce the red man syndrome, which may be life threatening to the patient.

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