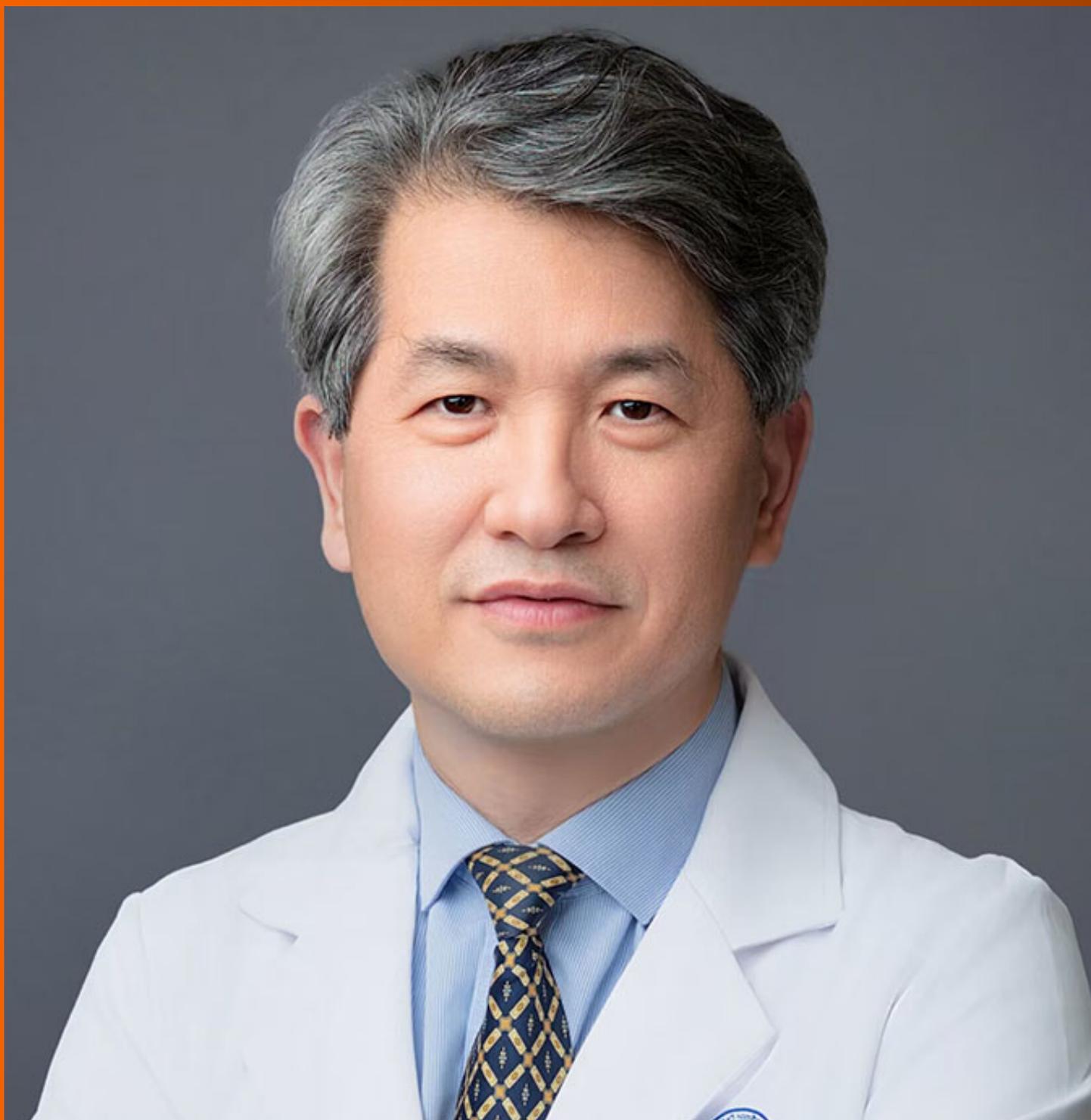


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## Vancomycin flushing syndrome in orthopaedic practice: A case report

Fawaz M Al-Anii, Mir Sadat-Ali, Khalid Waleed Al-Tabash, Ahmad I AIMulhim, Sulaiman A AIMousa, Abdulaziz M AlHawas

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### Abstract

#### BACKGROUND

Vancomycin flushing syndrome (VFS), also known as red man syndrome, is an allergic reaction to vancomycin. It typically presents as a rash on the face, neck, and upper torso after intravenous administration of vancomycin. VFS is blamed on rapid intravenous infusion of vancomycin during management and rarely happens after local use. A review of the literature showed that in the last 23 years, 4 such cases have been reported. Here, we add another case of VFS developed after slow local absorption of vancomycin in cement beads.

#### CASE SUMMARY

A 44-year-old male with a known case of hypertension, no history of allergies to medications, and a history of chronic osteomyelitis of the right tibia with discharging sinus over the anterolateral aspect of the leg. The pus culture grew *Staphylococcus aureus*, which was sensitive to clindamycin and vancomycin. The patient underwent irrigation and debridement with the placement of vancomycin cement beads made from 4 g of vancomycin powder and 40 g of polymethyl methacrylate. Three hours postoperatively, the patient developed a pruritic, erythematous, macular rash predominantly on his face, neck, chest, and lower extremities and to a lesser extent his upper extremities. A diagnosis of VFS was made and was successfully treated with cetirizine (10 mg, oral) and methylprednisolone sodium succinate (125 mg, intravenous). The patient continued to have itching with a facial rash for 12 h with gradual improvement. A decision was made to not remove the beads as the patient continued to improve. Gradually, the rash disappeared after 96 h with no further sequela.

#### CONCLUSION

VFS can occur not only after rapid intravenous injection of vancomycin but also

with local release, as in our case. As orthopaedic surgeons routinely use vancomycin with polymethyl methacrylate in chronic osteomyelitis and revision arthroplasty, they should be aware of such a complication occurring.

**Key Words:** Vancomycin; Anaphylactic reactions; Red man syndrome; Vancomycin flushing syndrome; Case report

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**Core Tip:** Vancomycin-related allergic skin reactions are not uncommon and are typically reported to occur after rapid intravenous infusion. However, this complication can also occur when vancomycin is implanted for slow release. Since orthopaedic surgeons routinely use vancomycin with polymethyl methacrylate, they should be aware of this complication occurring despite its rarity.

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## INTRODUCTION

Vancomycin inhibits cell wall synthesis of bacteria, making it a potent bactericidal against the majority of Gram-positive cocci[1]. Even though it has its own complications of resistance and other allergic reactions, it is still in use. One of the serious complications of using vancomycin is vancomycin flushing syndrome (VFS), also known as Red man syndrome (RMS), which is an anaphylactoid reaction. It presents as a pruritic, erythematous rash on the face, neck, and upper torso, hypotension, angioedema, and cardiac arrest[2-5]. The initial reports of this complication were reported due to rapid infusion of vancomycin at 1000 mg over 1 h[6]. Later reports did suggest it can happen even after slow infusion as well[7].

Vancomycin is routinely used in orthopaedic practice preoperatively as a prophylactic antibiotic and postoperatively to treat bone and joint infections[8,9]. Serious allergic reactions like VFS can occur. VFS developed in our patient with chronic osteomyelitis after the insertion of vancomycin-impregnated beads. A review of the literature on VFS in orthopaedic patients showed that 4 cases of VFS occurring after local implantation have been reported in the last 23 years (Table 1)[10-13].

## CASE PRESENTATION

### Chief complaints

A 44-year-old male presented with chronic osteomyelitis of the right tibia. The patient presented to the orthopaedic clinic due to right leg pain and swelling, the inability to bear weight, and multiple attacks of subjective fever. The right leg pain suddenly progressed over the prior 3 mo, without a history of recent trauma. The pain increased at night and later became constant even during rest. The pain was located mainly on the proximal right tibia with radiation to the right knee and middle third of the right leg. The patient also experienced multiple attacks of fever and night sweats.

### History of present illness

The patient had an open fracture 22 years ago with an infection and was diagnosed with chronic osteomyelitis with a discharging sinus. The sinus had closed, but the pain continued. He was treated with evacuation of the abscess and courses of antibiotics.

### History of past illness

The patient had a history of hypertension.

### Personal and family history

No personal or family history relevant to the presentation. No history of allergy to medications was reported.

### Physical examination

On inspection, there was swelling of the right leg and skin redness on the anterior aspect of the proximal third of the right leg. We observed a skin scar with thin scar tissue over the tibia directly. There was no underlying soft tissue on the anterior aspect of the proximal right tibia with massive swelling and tenderness around this area. The patient had an intact neurovascular examination.

**Table 1** Review of literature of vancomycin flushing syndrome after local implantation of vancomycin

Ref.	Vancomycin used	Outcome
Hinarejos <i>et al</i> [10], 2015	Bone cement	Recovered
Juyal <i>et al</i> [12], 2015	Bone cement beads	Recovered
Chen <i>et al</i> [11], 2018	Cement spacer	Recovered
Harper and Incavo[13], 2019	Cement spacer	Recovered
Present case, 2023	Bone cement beads	Recovered

### Laboratory examinations

Laboratory findings included slightly increased leukocytes ( $12.3 \times 10^9/L$ ; normal range:  $4.5-11.0 \times 10^9/L$ ), haematocrit (40.2%; normal range: 41%-50%), platelets (522,000 mL; normal range: 150,000 to 450,000 mL), elevated erythrocyte sedimentation rate (95 mm/h, normal range: < 20 mm/h), and high C-reactive protein (133 mg/L; normal range: 0-10 mg/L). The patient had a discharging sinus on the anterior proximal third of the right leg in the centre of the previous scar. Culture from the sinus grew *Staphylococcus aureus*.

### Imaging examinations

Anteroposterior and lateral X-ray views showed multiple opacities, and magnetic resonance imaging showed a collection with high signal intensity in the proximal right tibia. The radiological studies revealed an intramedullary collection of the proximal right tibia with the impression of subacute osteomyelitis with multiple Brodie's abscesses of the proximal right tibia (Figure 1).

## FINAL DIAGNOSIS

Chronic osteomyelitis of the right tibia.

## TREATMENT

The patient underwent irrigation and debridement with the placement of vancomycin cement beads made from 4 g of vancomycin powder and 40 g of cement (1 g of vancomycin for each 10 g of cement) attached to size 1 proline and was placed intramedullary in the cavity through the two bone windows on the proximal and mid right tibia. Three hours postoperatively, the patient developed a pruritic, erythematous, macular rash predominantly on his face, neck, chest, and lower extremities and to a lesser extent his upper extremities. There were no signs of vital instability observed at the time (maximum area of skin rash was the infected, right lower limb and the patient's face and chest) (Figure 2). The patient started to become agitated due to itchiness. However, he remained clearly conscious, and the fine oxygen saturation was 98% in room air. The patient remained stable.

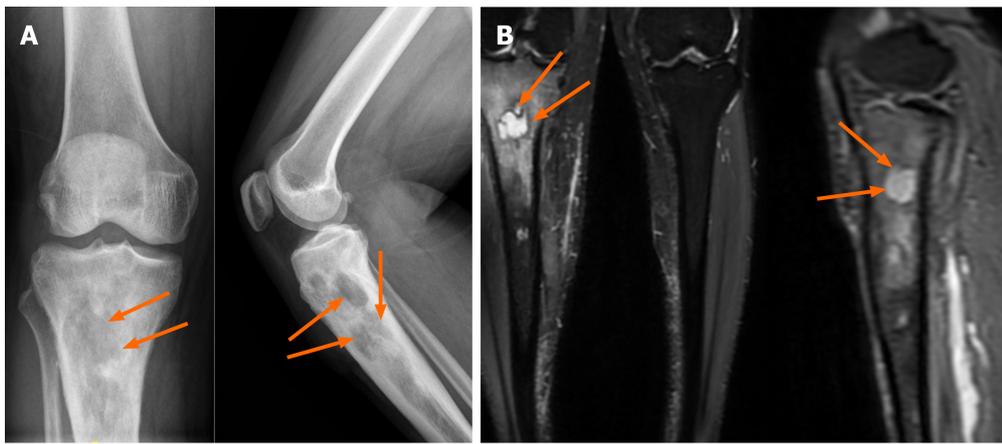
Urgent consultation of the on-call medical and infectious disease teams was completed; they examined the patient and recommended starting the patient immediately on cetirizine (10 mg, oral) and methylprednisolone sodium succinate (125 mg, intravenously). The patient continued to experience itching with a facial rash for 12 h with gradual improvement after therapy. He remained on close observation with close monitoring of respiration and other vital signs. The orthopaedic team made the decision to remove the antibiotics beads only if the patient hemodynamically deteriorated. The patient showed marked improvement 18 h after starting the medications; gradually, the rash started to decrease until it completely disappeared after around 96 h with no further sequela.

## OUTCOME AND FOLLOW-UP

The beads were removed 4 mo postoperatively. The patient also received progressive irrigation and debridement with bone graft to the distal metaphyseal bone defect (window). The patient completed the antibiotics course according to the infectious disease team's recommendation (2 wk parenteral and 10 wk oral).

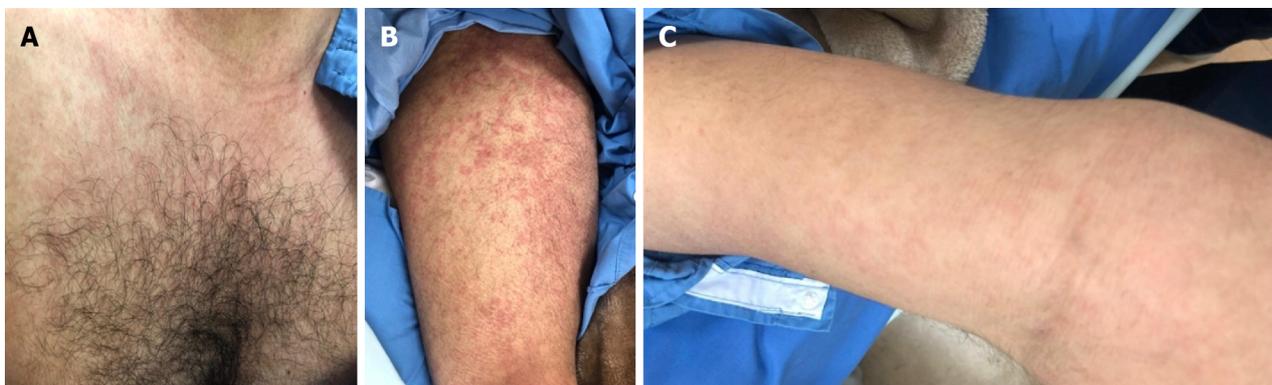
## DISCUSSION

Our patient who developed VFS due to vancomycin exposure during after a prolonged release was contrary to the initial reports of rapid infusion being the cause of VFS. Only 4 other orthopaedic cases in the last two decades have been reported where the complication occurred due to the slow release of vancomycin. It is believed that the side effects are



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**Figure 1 Imaging examinations.** A: An X-ray showed changes of chronic osteomyelitis in the right upper tibia; B: Magnetic resonance imaging showed changes of chronic osteomyelitis with abscess formation in the right upper tibia. The arrows indicate cavitation and changes due to chronic osteomyelitis.



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**Figure 2 Allergic reactions due to vancomycin.** A: Chest; B: Legs; C: Forearm.

due to impurities. However, even after increasing the purity, the side effects still occur. At present, it is recommended that vancomycin should be infused at a rate no faster than 1 g/h or 10 mg/min[13,14].

There are two issues that need to be addressed. Vancomycin induces allergic reactions due to its activation of mast cells, which release histamine independent of preformed immunoglobulin E or complement. The side effects range from pruritis to angioedema to cardiac arrest. It is prudent that antihistamines are started at the same time as vancomycin to avoid the reactions.

Secondly, the term “RMS” needs to be retired from the medical language as this term has racial implications relating to native American nations. Because reactions to vancomycin are not known to be race dependent and occur in children and women, RMS is a misnomer. Hence the term VFS should be used.

## CONCLUSION

In conclusion, VFS can occur either through rapid infusion or slow release of vancomycin, as in our patient. Since vancomycin-impregnated cement beads and spacers are routinely used in orthopaedic service, orthopaedic surgeons and trainees should be aware of such complications and should be ready to recognize and treat them early.

## FOOTNOTES

**Author contributions:** Al-Anii FM, Sadat-Ali M, Al-Tabash KW, AIMulhim AI, AIMousa SA, and AlHawas AM participated in the study of the case, review of the literature, and the writing of the manuscript.

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