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DELAYED HYPERSENSITIVITY REACTION SECONDARY TO INTRAPERITONEAL VANCOMYCIN ADMINISTRATION.

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ABSTRACT

Vancomycin has been a drug of choice for infections with a broad range of Gram-positive bacteria. Intraperitoneal (IP) Vancomycin is used to treat methicillin-resistant staphylococcal peritonitis, administered intermittently at 3 to 5 days intervals with trough level monitoring. Numerous adverse drug reactions (ADRs) have been reported with intravenous usage; however, the ADRs are not well known in intraperitoneal administration. We report a case of a delayed hypersensitivity reaction following intraperitoneal vancomycin administration. To date, this is the second case with a similar incidence.

Keywords: Intraperitoneal, Hypersensitivity, Peritonitis, Vancomycin.

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ABSTRACT

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Keywords: Adverse drug reactions, Delayed hypersensitivity, Intraperitoneal, Peritonitis, Vancomycin.

INTRODUCTION

Vancomycin is a drug of choice for Gram-positive bacterial infections, especially the *methicillin-resistant Staphylococcus aureus* (MRSA), *Corynebacterium jeikeium*, resistant strains *Streptococcus pneumoniae*, pseudomembranous colitis and enterococcus.[1] It is an alternative to penicillins and cephalosporins allergies. Intraperitoneal (IP) Vancomycin is used in MRSA peritonitis for a three-week duration, administered at 3 to 5 days intervals with through level monitoring.[2]

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Numerous Vancomycin adverse drug reactions (ADRs) have been reported, especially with intravenous administration. Pruritus, erythematous and vasculitic lesions, fixed drug eruptions, Red Man syndrome (RMS), and immediate or delayed hypersensitivity are the commonest cutaneous manifestations.[3] Systemically, fever, nephrotoxicity, and haematological abnormalities were described. Rarely, Stevens-Johnson Syndrome (SJS)[4] or drug rash with eosinophilia and systemic symptoms (DRESS) syndrome have been reported. Two cases of RMS[5,6] involving Ig E-mediated response, and a case of DRESS have been reported.[1] This is the second case of a delayed hypersensitivity reaction following

intraperitoneal Vancomycin.

CASE REPORT

We present a 48-year-old man with End-Stage Kidney Disease (ESKD) secondary to diabetes. His peritoneal dialysis (PD) catheter was inserted and commenced on self-care, Continuous Ambulatory Peritoneal Dialysis (CAPD). He presented with turbid effluent and abdominal discomfort and no diarrhea or fever. He was treated as having PD-associated peritonitis; cell count was 200/mm^3 with 90% neutrophil. Empirically IP Ceftazidime and Cloxacillin were given.

After three days, staphylococcus *capitis* with sensitivity to vancomycin culture was obtained. We escalated to IP Vancomycin with a loading dose of 1.75g (30 mg/kg) and continued intermittent dose based on drug level. The infection responded significantly; zero cell count and clear fluid were obtained subsequently. His treatment was planned for a three-week duration. On average, he received a dose of 1g of Vancomycin each time, mixed with 2 liters of 1.5% PD dialysate at night exchanges. He had received up to seven doses of the antibiotic. There was no flushing, pruritus, or tingling sensation throughout the administration. The repeated culture came back as no growth.

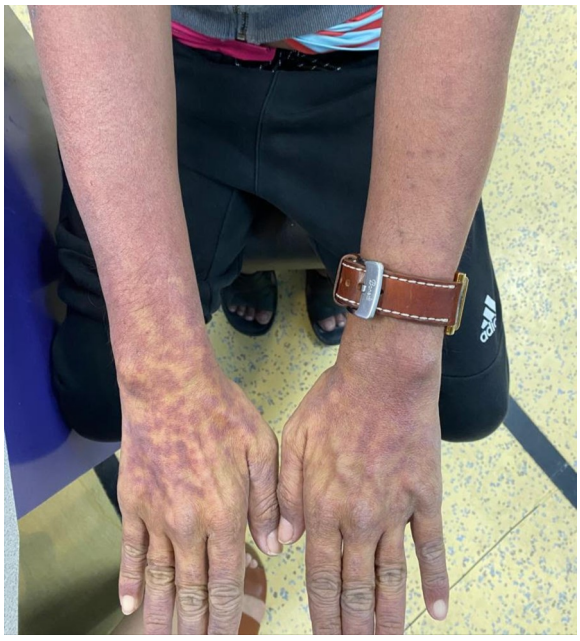

Figure 1: Erythematous petechiae that coalesce into macules seen over the upper right upper limb .

However, two weeks after completion of treatment, he complained of a five-day duration of generalised rashes associated with itchiness. It started from the wrists area extending to the upper and lower limbs, abdomen, and trunk (Figure 1). The scalp, face, and mucosal membrane were spared. There was no history of previous drug allergy, eczema, asthma, or atopy. He was afebrile, not in respiratory distress, with an absence of bronchospasm. No oral ulcers, lymphadenopathies, hepatomegaly, or splenomegaly were noted. Erythematous petechiae that coalesce into macules over upper and lower limbs, scattered over the lower back and abdomen were seen. There were a few areas of hyperpigmentation over the lower back.

His eosinophil count was marginally elevated at 11% (0.58 x 10^9), and there was a mild elevation of ALT at 72 U/L. He was diagnosed as having a delayed hypersensitivity reaction to IP Vancomycin. He was started on intravenous hydrocortisone, Betnovate ointment (BVO) 1:2, and aqueous cream as an emollient. The skin lesions improved, and he was discharged with oral prednisolone for a week. Unfortunately, no skin biopsy was performed. After ten days, there was complete resolution of the skin lesion with residual hyperpigmentation seen. The patient was given a Drug Allergic Card to Vancomycin to prevent the recurrence of the incident. The ADR was reported to the National Centre for Adverse Drug Reactions Monitoring of Malaysia.

PATIENT'S PERSPECTIVE

The development of generalized rashes can be troublesome to the patient, especially as it disfigures his appearance. Being labelled al-

lergy to Vancomycin might challenge management if the patient is infected with another MRSA infection. He otherwise recovered well, and all skin lesions disappeared. However, he must be careful in receiving any antibiotics in the future to prevent similar incidents from happening.

DISCUSSION

Drug hypersensitivity reactions may develop via multiple administration routes (peroral, intravenous, intramuscular, subcutaneous) but they are extremely rare via intraperitoneal (IP).[7,8] There have been reports associating IP vancomycin with chemical and eosinophilic peritonitis.[4,9] The RMS and a case of Ig E mediated immune reaction[3] and another of DRESS[7] were described previously. An intraperitoneal administration of Vancomycin leads to systemic absorption thus, hypersensitivity reactions may occur.[3] Vancomycin-related allergic reactions were postulated to be caused by the non-immune mediated (RMS) and Ig E- mediated immediate hypersensitivity reaction (Type I). Rarely delayed (Type IV) hypersensitivity reactions have also been reported.[3]

We presumed that our patient developed type IV delayed hypersensitivity reaction to the vancomycin. This occurrence is an outcome of a T cell-mediated immune reaction with a gradual increment in symptoms, intensity, and duration. The generalized skin lesions occurred on day ten after completion of IP Vancomycin and lasted for approximately two weeks.

Unfortunately, we did not perform a skin prick test or skin biopsy as the patient refused, which is the best way of determining the cause and mechanism of drug hypersensitivity reactions. We also did not perform vancomycin-specific Ig E or vancomycin-induced basophil activation test as there was no suggestion of an Ig E-mediated hypersensitivity.

Management includes symptomatic treatment with antihistamines and steroids. Immediate withdrawal of the offending drug must be made if the patient develops the reaction while the drug is still being administered. Linezolid (MAO inhibitor) or other glycopeptide and lipopeptide antibiotics (teicoplanin, daptomycin) are alternative replacement antibiotics.[1] IP Daptomycin is also an option.[10] Desensitization of Vancomycin is a possible strategy to induce drug tolerance in type I hypersensitivity reaction safely. However, there is little literature on desensitization in type IV reactions.[11,12] This approach is contraindicated in severe or life-threatening delayed drug hypersensitivity reactions, such as Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN). One should always consider all forms of hypersensitivity reactions with the usage of vancomycin intraperitoneally.

CONCLUSION

Delayed hypersensitivity reaction after intraperitoneal Vancomycin administration is rare; however, the occurrence can be life-threatening if not detected and managed early.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1: M.-J. Hwang, J.-Y. Do, et al., "IgE-mediated hypersensitivity reaction after intraperitoneal administration of vancomycin,". Kidney Research and Clinical Practice 2015;34:57–59.

2: P. K. Li, C. C. Szeto, B. Piraino, et al., "ISPD peritonitis recommendations: 2016 update on prevention and treatment," Peritoneal Dialysis International 2016;36:481–508.

3: Kupstaite R, Baranauskaite A, et al. Severe

vancomycin-induced anaphylactic reaction. Medicina (Kaunas) 2010; 46:30–33.

4: D. I. Charney and S. F. Gouge, "Chemical peritonitis secondary to intraperitoneal vancomycin," American Journal of Kidney Diseases 1991;17:76–79, 1991.

5: Husserl F, Back S. Intraperitoneal vancomycin and the "red man" syndrome. Perit Dial Int. 1987; 7:262.

6: Bailie GR, Kowalsky SF et al. Red-neck syndrome associated with intraperitoneal Vancomycin. Clin Pharm. 1990; 9:671–672.

7: Teerath Kumar, Iris Teo, et al. Case Report Systemic Toxicity of Intraperitoneal Vancomycin. Hindawi Case Reports in Nephrology Volume 2016, Article ID 3968690.

8: Bosse D, Lemire C, Ruel J et al. Severe anaphylaxis caused by orally administered Vancomycin to a patient with Clostridium difficile infection. Infection. 2013; 41:579–582.

9: M. H. Rosner and B. Chhatkuli, "Vancomycin-related eosinophilic peritonitis," Peritoneal Dialysis International 2010;30:650–652.

10: Gilmore JF, Kim M, LaSalvia MT, Mahoney MV. Treatment of enterococcal peritonitis with intraperitoneal daptomycin in a vancomycin-allergic patient and a review of the literature. Perit Dial Int. 2013; 33:353–357.

11: S. Anne, E. Middleton Jr., and R. E. Reisman, "Vancomycin anaphylaxis and successful desensitization," Annals of Allergy 1994;73:402–404.

12: Legendre DP, Muzny CA, Marshall GD, Swiatlo E. Antibiotic hypersensitivity reactions and approaches to desensitization. Clinical Infectious Diseases. 2013; 58:1140–1148.