Kidney Res Clin Pract 34 (2015) 57–59

Kidney Research and Clinical Practice

journal homepage: http://www.krcp-ksn.com
Contents lists available at ScienceDirect

Case Report

Immunoglobulin E-mediated hypersensitivity reaction after intraperitoneal administration of vancomycin

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Article history:
Received 23 June 2014
Received in revised form
26 August 2014
Accepted 12 September 2014
Available online 5 December 2014

Keywords:
Hypersensitivity
Intraperitoneal administration
Peritoneal dialysis
Vancomycin

Abstract

Intraperitoneal (IP) vancomycin is widely used to treat Gram-positive peritonitis associated with peritoneal dialysis. There have been two cases of red man syndrome (RMS), a vancomycin-specific nonimmunologic reaction, associated with IP vancomycin. However, immune-mediated hypersensitivity reaction to IP vancomycin has not yet been reported. A 49 year old woman on continuous ambulatory peritoneal dialysis developed her first peritonitis episode. The patient was treated with IP vancomycin once/wk for 4 weeks. She experienced mild itching and flushing throughout her body for 1 day after the second treatment. Whenever vancomycin was administered, generalized urticaria and a prickling sensation developed, and the intensity increased gradually; however, these symptoms improved after vancomycin was discontinued. An allergic skin test was performed 6 weeks after the previous urticarial episode, and an intradermal skin test revealed a positive response to vancomycin. To our knowledge, this is the first case report of immunoglobulin E-mediated hypersensitivity reaction to IP vancomycin administration.

Introduction

Vancomycin is a commonly used tricyclic glycopeptide antibiotic for the broad range of Gram-positive bacteria. Increased vancomycin use has frequently been demonstrated to produce various adverse drug reactions. The most common toxicity associated with vancomycin is red man syndrome (RMS). Other adverse effects reported include anaphylaxis [1], vasculitis, ototoxicity, fixed drug eruptions, fever, phlebitis, nephrotoxicity, interstitial nephritis, agranulocytosis, thrombocytopenia, linear immunoglobulin (Ig)A bullous dermatosis, toxic epidermal necrolysis, and more rarely Stevens–Johnson [2], or drug rash with eosinophilia and systemic symptoms syndrome.

Intraperitoneal (IP) vancomycin is widely used to treat Gram-positive peritonitis associated with peritoneal dialysis. Vancomycin-related adverse reactions are usually associated with intravenous administration or, less frequently, with oral administration [3,4]. There have been few reports regarding adverse reactions to vancomycin after IP administration, except for two cases of RMS [5,6]. However, to our knowledge, this report is the first to describe a case of IgE-mediated hypersensitivity reaction after IP administration of vancomycin.

Case report

A 49 year old, 53 kg woman on continuous ambulatory peritoneal dialysis since August 2011 developed her first

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http://dx.doi.org/10.1016/j.krcp.2014.09.005

episode of peritonitis in February 2014. She had hypertension and hypothyroidism, with no recent changes in medication. She did not have any allergic disease or previous episodes of hypersensitivity reaction.

The patient visited our hospital because she experienced cloudy effluent for 1 day. She did not have abdominal pain or fever, and physical examination showed no abdominal tenderness. Turbid dialysis effluent was observed, and white blood cell (WBC) count of the effluent was 2,300/mm^3, of which 85% was comprised of polymorphonuclear leukocytes (PMNL). Empirical antibiotic therapy with IP tobramycin and cefazolin was started at our outpatient clinic.

On her second visit the next week, effluent culture revealed *Micrococcus luteus* (Gram-positive aerobic cocci that are commonly found in the environment and can be opportunistic pathogens in immunocompromised patients). Her antibiotic regimen was changed to 2 g of IP vancomycin/wk. Two grams of vancomycin was mixed with 2 L of 1.5% dialysate and instilled into the peritoneal cavity within 15 minutes. Vancomycin was administrated once/wk for 3 weeks during her first peritonitis episode.

A few hours after the second administration of vancomycin, the patient experienced flushing and pruritus throughout her body, which lasted for a few days. Following the third administration, the patient experienced a prickling sensation, pruritus, and a flushing sensation approximately 20 minutes after completion of the instillation. A skin rash, which lasted for 1 week, occurred in the cervicofacial area, extended over the trunk, and into her upper extremities and upper leg area. WBC count of the effluent decreased to 50/mm^3 with no PMNL after the first vancomycin administration, and a zero cell count was recorded after the third administration, which is also when the follow-up effluent culture yielded no growth of any microorganism.

The patient developed a second episode of peritonitis 25 days after the last vancomycin administration. As with the previous episode, she had turbid effluent with no subjective symptoms, and WBC count of the effluent was 1,800/mm^3 with 83% PMNL. We started IP vancomycin and tobramycin at our outpatient clinic. Ten minutes after vancomycin administration, she developed a severe prickling sensation, pruritus, generalized urticarial rash, and throat tightness (Fig. 1). Intramuscular epinephrine with intravenous antihistamine and dexamethasone were applied once because of the possibility of anaphylaxis, and the patient was admitted. Her vital signs were as follows: blood pressure, 130/80 mmHg; pulse rate, 95 beats/min; body temperature, 37°C; and respiratory rate, 20 breaths/min. There was no wheezing during physical examination. Laboratory tests results were as follows: WBC, 6,500/mm^3; hemoglobin, 10.2 g/dL; platelet, 176,000/mm^3; blood urea nitrogen, 41.31 mg/dL; creatinine, 6.71 mg/dL; eosinophil count, 480/mm^3 (reference 50–500/mm^3), and total IgE 3,240 IU/L (reference 0–100 IU/L). WBC count of the effluent was 50/mm^3 with no PMNL.

Daily administration of IP tobramycin (40 mg) was maintained, and antihistamine with topical steroid cream was applied. During her stay at the hospital, her symptoms gradually improved and subsequent effluent cell count remained zero. She was discharged after 3 days with no skin rash or pruritus. Effluent culture yielded no growth at the time of discharge, so the patient was discharged with IP cefazolin with oral ciprofloxacin. Five days after she visited our hospital, WBC count of the effluent was 25/mm^3 with no PMNL, and culture obtained upon admission yielded *Micrococcus luteus*.

Figure 1. Pruritic diffuse erythematous patches on the thigh.

Oral linezolid was prescribed because there was possible a cross-reactivity with teicoplanin [7]. Six weeks after the previous urticarial episode, we performed an allergic skin test with vancomycin. A skin prick test yielded negative results. Subsequently, intradermal skin tests with 1:100,000 and 1:10,000 dilutions were performed. Vancomycin began to elicit a response at a dilution of 1:10,000 (5 μ/mL), with a wheal diameter of 5 mm × 10 mm. A negative control test using saline showed no response.

Discussion

Vancomycin can cause several types of hypersensitivity reactions, such as the anaphylactoid reaction known as RMS, IgE-mediated immediate hypersensitivity reaction, and, less frequently, delayed hypersensitivity reactions. To date, the most common toxicity with vancomycin is RMS, which is caused by vancomycin-induced nonimmunologic degranulation of mast cells and basophils, resulting in the release of histamine, independent of preformed IgE or complement [8]. RMS typically presents with pruritus and erythematous rash that affects the face, neck, and upper torso. In many patients, RMS presents as mild, transient pruritus at the end of the infusion that subsequently vanishes [8].

Vancomycin-induced IgE-mediated immediate hypersensitivity reactions are rare but do occur, and re-administration of vancomycin can cause bronchospasm or cardiovascular collapse in affected patients [1]. In this case, the patient is presumed to have type I IgE-mediated hypersensitivity reaction to vancomycin. Her

history revealed a gradual increase in intensity and duration of symptoms, which suggests immune-mediated sensitization. The distribution of skin lesions was generalized rather than confined to the upper torso, which persisted over several days. The patient experienced throat tightness that may be associated with laryngeal edema caused by type I hypersensitivity reaction. More importantly, the positive result in the intradermal skin test using vancomycin reflects a strong possibility of IgE-mediated hypersensitivity reaction in our patient. Skin tests with drugs help to determine the cause and mechanism of drug hypersensitivity reactions. In type I IgE-mediated allergic drug reactions, skin prick and intradermal tests may provide rapid and supportive evidence for diagnosis or exclusion of IgE-mediated reactions [9]. Unfortunately, vancomycin-specific IgE or vancomycin-induced basophil activation test were not performed in this case, because they were not available in our hospital. It is our limitation that such tests were not performed to demonstrate more evidence of IgE-mediated mechanism in drug hypersensitivity.

Linezolid and teicoplanin are alternative drugs that can be used if a patient experiences vancomycin-induced anaphylaxis. IP daptomycin might also be an alternative for treating Gram-positive peritonitis in vancomycin-intolerant patients [10]. However, allergic cross-reactivity between vancomycin and teicoplanin has been reported [7]. In this case, linezolid was used because of the patient's susceptibility to *M. luteus* and the possibility of cross-reactivity with teicoplanin. Vancomycin desensitization is a possible strategy to safely induce drug tolerance and limit the possibility of a type I hypersensitivity reaction [11].

Drug hypersensitivity reactions can be developed via multiple administration routes, but one via the IP route is extremely rare. There was only one previous case report of a hypersensitivity reaction to IP administration of a chemotherapeutic agent (carboplatin) [12], but there have been no previous reports regarding IP administration of antibiotics. Various antibiotics are used intraperitoneally to treat dialysis-associated peritonitis, including vancomycin. IP vancomycin has been known to be associated with chemical peritonitis [13], eosinophilic peritonitis [14], and RMS [5,6]; however, there have been no previous reports on immune-mediated hypersensitivity reactions.

Systemic absorption of vancomycin is evident even after IP administration, thus making it natural for hypersensitivity reactions to occur. However, in contrast to the case with intravenous administration, early elevations of vancomycin concentration in serum are avoided when the drug is given intraperitoneally, and overall absorption rate is slower. These high concentrations are thought to elicit more frequent histamine-mediated reactions during intravenous vancomycin therapy [15].

To our knowledge, this is the first case of IgE-mediated hypersensitivity reaction induced by IP vancomycin. Clinicians should keep in mind that hypersensitivity reactions may occur even when vancomycin is administered intraperitoneally.

Conflict of interest

The authors report no conflicts of interest.

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