Case Report

VANCOMYCIN ASSOCIATED PALMO-PLANTAR ERYTHEMA IN A HEMODIALYSIS PATIENT

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A 65-year-old woman with end-stage renal disease (ESRD) on maintenance hemodialysis was admitted for fever and chills for 3 days accompanied by forearm arterio-venous graft (AVG) swelling. Hematogram revealed marked leukocytosis (25800/µL) and blood culture reported methicillin-resistant Staphylococcus aureus (MRSA). Vancomycin (1 gram every 4 days) was used for AVG MRSA infection. Skin itching over palmar and plantar areas developed after a 2-week course of vancomycin. Palmar and plantar erythema occurred one day later and progressed to scaling lesions during the next 3 days. These desquamative lesions gradually improved after topical steroid use and vancomycin was withdrawn. We reported a vancomycin-induced palmo-plantar erythema in a patient with maintenance hemodialysis. This report suggests vancomycin should be prescribed to dialysis patients with more caution. (Acta Nephrologica 2009; 23: 43-46)

Key Words: palmo-plantar erythema, palmo-plantar erythrodysesthesia, acral erythema syndrome, vancomycin, end-stage renal disease

INTRODUCTION

Palmo-plantar erythema (PPE) or palmo-plantar erythrodysesthesia or acral erythema syndrome is a common skin manifestation of adverse drug reactions (ADRs) of oncological patients. It describes a specific type of skin lesion mostly induced by some chemotherapeutic agents such as 5-fluorouracil (5FU), doxorubicin, and cytosine arabinoside. It may occur in as many as 40% of treated patients.1

ADRs often manifest with dermatologic presentations. The overall incidence of serious ADRs was 6.7% of hospitalized patients.2 End-stage renal disease patients are susceptible to ADRs for their loss of an important organ for drugs/toxin excretion, pro-inflammatory status, polypharmacy (drug-drug interactions), drug-dialysis interaction, malnutrition, and altered immune or hormonal status.3

Vancomycin is one of the most frequently prescribed antibiotics in ESRD patients for catheter-related infections. ADRs caused by vancomycin administration are common in ESRD patients. Common ADRs of vancomycin include dermatological (Redman syndrome [RMS]), gastrointestinal (nausea and vomiting) and nephrotoxicity in chronic kidney disease patients.4

No case of PPE induced by vancomycin has been reported to date. Here, we describe a hemodialysis patient developing PPE after brief administration of intravenous vancomycin.

CASE REPORT

A 65-year-old woman was a patient with end-stage renal disease undergoing maintenance hemodialysis for 4 years. She was admitted for fever and chills for 3 days accompanied by left forearm arterio-venous graft (AVG) swelling.

On admission, the body temperature was 37°C, pulse rate was 83 beats per minute and respiratory rate was 18 per minute. The blood pressure was 153/88 mmHg. She appeared ill. The physical examination revealed mild basal crackles over the bilateral lung fields. The heart sounds were regular without murmur. The abdomen was soft and flat without tender point or shifting dullness. AVG swelling and erythema were noticed.

The initial lab findings showed marked leukocytosis

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with left shift (white blood counts: 25800/µL, segment 89.5% band: 0%) and a hematocrit of 29.4%. The serum albumin level was 2.8g/dl, blood urea nitrogen was 36 mg/dl, creatinine was 6.9 mg/dl, sodium was 140.3meq/L and potassium was 3.78meq/L.

Blood culture reported methicillin-resistant MRSA and AVG infection was impressed. Vancomycin (Sterile Vancomycin Hydrochloride, USP from Amycolatopsis orientalis; Hospira Inc.; dosage: 1 gram intravenous infusion every 4 days,) was used according to bacteriologic sensitivity tests. After a 2-week course of vancomycin, the patient complained of pruritus on her groin, palms and soles region and then an infiltrated swelling erythema gradually developed on her palm and soles in the following days [fig. 1, 2]. After consultation with a dermatologist regarding a vancomycin associated palmo-plantar erythema, vancomycin was discontinued and shifted to teicoplanin. Topical steroids were applied for these skin lesions. The erythematous and desquamative lesions gradually improved after 1 week.

Fig. 1. Painful, symmetrical, and edematous erythema of bilateral palms with prominent scaling and membranous desquamation

Fig. 2. Symmetric desquamation of bilateral dorsal hands, most obvious over the digits
DISCUSSION

The pharmacokinetics of vancomycin may partly explain partly the susceptibility of ESRD patients to ADRs. The hypoalbuminemia is a frequent finding in ESRD patients and this contributes to a decreased vancomycin binding capacity from a normal 30-55% to an average of 18% in ESRD patients. Besides, the elimination half-life prolongs to 7.5 days in contrast to the normal 4 to 6 hours. Dermatopathies induced by vancomycin include RMS, bullous pemphigoid, delayed cutaneous hypersensitivity, erythema multiforme, linear IgA dermatosis, pruritus, and rash. Vancomycin can also cause severe adverse effects including hypotension and cardiac arrest, which have been associated with rapid intravenous administration. Cardiac arrest has been reported in two patients receiving intravenous vancomycin and is more likely to occur with rapid administration. Myocardial release of histamine may be involved in some cardiovascular events associated with anaphylactoid reactions. Histamine causes both RMS and hemodynamic instability. For these reasons and because reactions seemed to improve after administering antihistamines, epinephrine and hydrocortisone, recommendations for managing these cases have included administering fluids, antihistamines, or corticosteroids. Patients with a history of RMS should receive pretreatment with antihistamines and an extended infusion time.

RMS also named red-man syndrome is the most widely known skin manifestation of vancomycin use. The reaction may occur within a few minutes of starting the infusion or near its completion, and skin rash subsides several hours after completing an intravenous infusion. It is suggested vancomycin be administered slowly (over one hour) to avoid RMS and blood pressure monitoring should be undertaken during IV infusion. However, slow infusion does not preclude the risk of red-man syndrome. The dermatological presentation of red-man syndrome is characterized by flushing, erythema, and pruritus, usually affecting the upper body, neck, and face more than the lower body that occurs during faster rates of vancomycin administration. Skin lesions subside within minutes or hours without dermatological sequelae.

Two case reports in the literatures described for generalized exfoliative dermatitis (GED) of vancomycin in hemodialysis patients. The first reported vancomycin associated with generalized exfoliative dermatitis in a 51-year-old man with end-stage renal disease. The patient received 1 gram every of vancomycin five days for treating pericarditis caused by Staphylococcus aureus. Thirty-one days after vancomycin administration, a rash developed which desquamated 10 days later. Because of high vancomycin serum levels related to the renal failure, the rash persisted for 5 weeks after vancomycin was discontinued. The second case described erythema multiforme progressing to exfoliative dermatitis in a 29-year-old woman with end-stage renal disease receiving intra-arterial vancomycin 1500mg/2L overnight for a catheter infection per 3 weeks plus rifampicin 300mg oral twice a day for the first 2 weeks. Erythema multiforme developed 2 days after the secondary dose of vancomycin and progressed to exfoliative dermatitis. Her condition improved over the next three weeks, and she recovered completely.

As described above, PPE is a common dermatopathy in patients receiving chemotherapy. Its initial manifestation is dysesthesia or tingling of the palms and soles. It is followed in a few days by painful, symmetrical, edematous erythema which is most obvious over the distal pads of the digits. Skin lesions may spread to the dorsal hands and feet, and can be accompanied by a bulliform eruption of the scalp, neck, trunk and extremities. Several days later, the erythema may deepen into dusky color; turns into areas of pallor, blisters, desquamations, and re-epithelialize. The desquamation is the most prominent part of the syndrome. Blisters developing over pressure areas of hands and feet are variants. The patient usually recovers without complication, although full thickness ischemic necrosis rarely occurs in the blistering areas. The histopathology is nonspecific, with necrotic keratinocytes and vacuolar changes along the basal cell layer.

In contrast to upper-body skin distribution and rapid-on rapid-off nature of RMS and generalized skin involvement of GED, no case of PPE (presented with localized exfoliative dermatitis) has been reported in the literature in hemodialysis patients following administration of vancomycin. Besides, the National Reporting System of Adverse Drug Reactions in Taiwan data base revealed vancomycin to be the third most reported drug causing ADRs. Most ADRs are dermatological and include: RMS, erythema multiforme, allergy, itching, injection site swelling, mucosal ulcer, eye lid swelling, and bulla formation. Similarly, no PPE has been reported to the data base.

The pathogenesis of PPE has not been properly clarified till now. Some hypotheses have been addressed in the literatures. Some suggested PPE to be a direct toxic effect of the chemotherapeutic agents on the skin. Sweat glands are richly distributed on the palms and soles and may concentrate the therapeutic drugs. Others pointed out the high turnover rate of epidermal basal cells in the palms and soles makes them susceptible to
cytotoxic drugs. They also documented higher thymidine phosphorylase and dihydropyrimidine dehydrogenase activities in the palms. These enzymes may convert capecitabine (a pro-drug of 5FU) to 5FU in the palms and local toxicity was displayed.28

However, in our case, the skin lesion developed after short-term administration of vancomycin. Possible idiosyncratic mechanism should be expected in hemodialysis patients who developed PPE with vancomycin.

The causal-resultant relationship between vancomycin and PPE was supported with a reasonable time relation, and MRSA bacteremia was unlikely to be the cause of PPE. Besides, no other confounding medication was used before she developed PPE. In addition, PPE followed a clinically reasonable improvement after vancomycin was withdrawn. However, definite evidence by rechallenging vancomycin was not available for this patient. Thus, the strength of evidence was probable or likely.27

Most PPE patients require only local supportive care including cold compresses and elevation. Cooling the hands during treatment may reduce the severity of the reaction by reducing drug accumulation. Modification of the dose schedule can be beneficial.

CONCLUSION

Acral erythema, palmo-plantar erythema and palmo-plantar erythrodyssesthesia syndrome are used interchangeably to describe this special skin manifestation mostly caused by chemotherapeutic agents. To the best of our knowledge, vancomycin induced generalized exfoliative dermatitis has only been reported in two case reports and no localized form (PPE) has been reported till now. The three exfoliative patients either localized or generalized were all anephric. This was not regarded as coincident but the clinicians should be cautious when prescribing vancomycin especially in ESRD patients.

REFERENCE