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Case Report

A rare case of Colistin induced maculopapular rash

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Abstract

Approximately 2–3% of hospitalized patients are known to experience an adverse drug reaction (ADR). Dermatologic ADRs account for 10–30% of ADRs, and are commonly reported to be associated with antibiotic use. The classes of antibiotics most commonly reported to cause cutaneous reactions are the penicillins, cephalosporins, and fluoroquinolones. Polymyxin E is known to cause such reactions, but rarely. Here, we report a case of a colistin- induced maculopapular rash in an 84-year-old male. To the best of our knowledge, this is the first case of colistin-induced maculopapular rash to be reported in India.

Key words: Maculopapular rash; etiology; colistin.

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Introduction

There has been a resurgence in Colistin usage, despite its severe adverse effects such as nephrotoxicity and neurotoxicity, because of the rise of multiple drug resistant (MDR) Gram-negative pathogens such as *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Klebsiella pneumoniae*. However, it rarely causes itching or skin rashes. Colistin is a polymixin antibiotic produced by strains belonging to *Bacillus polymyxa* var. *colistinus*. It is a combination of two cyclic polypeptides namely, colistin A and B, which acts on the cell membrane by binding to the lipopolysaccharides and phospholipids of Gram-negative bacteria [1,2]. We report a case of maculopapular rash which developed in an 84-year-old male patient who had been administered colistin due to *Acinetobacter baumannii* cellulitis. To our knowledge this is the first reported case of colistin-induced maculopapular rash in India.

Case Report

An 84-year old male patient came to a hospital in India with complaints of swelling and pain in the right limb since three days. The swelling of the foot was rapidly progressive to the region below the knee and was associated with throbbing pain. The patient had been previously admitted to the hospital with similar complaints about two years previously. The patient did not have any history of hypertension or diabetes.

On local examination, diffuse edema of the pitting type and local rise in temperature were observed, along with multiple blebs which were filled with discharges over the lower third of the leg. The patient was admitted immediately.

Debridement was done on the day of admission. As a pre-operative medication, the patient was administered piperacillin and tazobactam, paracetamol, and pantoprazole intravenously. Postoperatively, piperacillin and tazobactam were continued. As the patient had a fever spike of 100 degrees Fahrenheit, piperacillin and tazobactam were stopped and antibiotic therapy continued with injection of colistin. According to the pus culture and antibiotic susceptibility report, the Gram-negative bacterium *Acinetobacter baumannii,* was isolated and showed resistance towards piperacillin and tazobactam; it d was sensitive to minocycline with minimum inhibitory concentration (MIC) less than 1, and to tigecycline and colistin with MIC less than 0.5.

After adjustment of the antibiotic, the patient's body temperature dropped to normal, but he developed a maculopapular itchy rash on the chest after 5 days of colistin administration and. He was given a stat dose of pheniramine to give symptomatic relief from the rash. Colistin was stopped and there was complete recovery from the rash within 24 hours, confirming that the rash was colistin induced. The patient had no previous history of such allergies.

As the patient's infection had been reduced, he was prescribed topical clindamycin to complete the treatment.

The laboratory examinations revealed the following results: Hb: 11.0 g/dL, PCV: 33.7%, RBC count: 3.81cells/µL; urea: 60mg/dL, Na: 130 mEq/L, K: 5.7 mEq/L. Based on these results he was prescribed trypsin and chymotrypsin, multivitamin, and calcium polystyrene sulfonate. The patient's K levels returned to normal after 3 days and the calcium polystyrene sulfonate was stopped. At that time, the patient felt better and was discharged on his own request.

Discussion

In the case described here, the patient was on multiple doses of colistin (polymixin E) intravenously for five days. The subsequent laboratory findings were unable to identify the exact etiology of the maculopapular rash in this patient with cellulites. There was no evidence, also not in the literature, that the other drugs that the patient received, would cause a maculopapular rash. Drug induced reactions are difficult to diagnose and require keen clinical observation [3]. However, when the colistin was stopped, the rash subsided, strongly suggested that the rash could be attributed to colistin.

Typically, a maculopapular rash is presented as a pattern of macules and papules. A macule is a small, flat, red area of discoloration, and a papule is a small, red, raised lesion. As a result, a maculopapular rash appears as red bumps against a red background. These rashes usually last for 2-21 days, depending on the etiology [4].

A range of adverse reactions have been reported to be linked to colistin use, from gastric irritation, urticaria, hyperpigmentation, neurological paralysis and anaphylaxis to in some cases hospitalization or even death. The incidence of skin allergic reaction due to colistin usage has been reported to be ~2% among patients who received single or multiple doses [5.6].

Colistin causes disruption of cells by competitive displacement of divalent cations (Ca^{and2} and Mg^{and2}) in the phospholipids of the cell membrane, leading to the leakage of cellular components. The leaked cellular components or the active forms of colistin may result in itching or rash; however the exact mechanism of colistin causing rash is unknown [5,7].

In addition, age, gender, hepatic function, renal function, concomitant drug use and/or intercurrent diseases may play a role as predisposing factors in inducing the rash, by altering various pharmacokinetic and pharmacodynamic properties of colistin [8]. In this case age, gender and extent of infection might have been predisposing factors.

The causality assessment of the adverse drug reaction (ADR) was carried out using the Naranjo Scale, a method for estimating the probability of adverse drug reactions [9]. The assessment revealed the ADR to be 'probably' associated with colistin.

Conclusion

The use of colistin has been augmented over the years and continues to increase. Colistin induced dermatological adverse drug reactions and colistin resistance due to inappropriate drug use is increasing drastically and is turning into a major concern in the clinical field [10]. Colistin should only be used when there is an absolute indication or when the benefits greatly outweigh the risks.

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