Skin reactions probably attributed to the use of phenytoin and vancomycin

Reações cutâneas provavelmente atribuídas ao uso de fenitoína e vancomicina

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CASE REPORT

ABSTRACT

Cutaneous reactions are the most common adverse events attributed to medications. Stevens-Johnson syndrome or erythema multiforme is a severe and acute reaction determined by medications, especially aspirin, phenytoin, and vancomycin. The authors report the case of a 36-year-old woman who developed Stevens-Johnson syndrome and three cases of patients who developed skin rash after receiving phenytoin and vancomycin.

Descriptors: Chemical reactions; Hypersensitivity; Pharmaceutical preparations/adverse effects; Skin diseases; Phenytoin/adverse effects; Vancomycin/adverse effects; Case reports

RESUMO

Reações cutâneas são as reações adversas mais comuns atribuídas a medicamentos. A síndrome de Stevens-Johnson ou eritema multiforme é uma reação grave e aguda determinada por medicamentos, especialmente aspirina, fenitoína e vancomicina. Relata-se o caso de uma mulher de 36 anos que desenvolveu a síndrome de Stevens-Johnson e três casos de pacientes que desenvolveram rash cutâneo após o recebimento de fenitoína e vancomicina.

Descritores: Reações químicas; Hipersensibilidade; Preparações farmacêuticas/efeitos adversos; Dermatopatias; Fenitoína/efeitos adversos; Vancomicina/efeitos adversos; Relatos de casos

INTRODUCTION

Adverse reactions to drugs are relevant complications of drug treatment¹. It is estimated that 5 to 15% of patients treated with some form of medication develop adverse reactions, and 2 to 3% of these reactions are cutaneous².

Skin reactions associated with the use of medications, usually observed as morbiliform or maculopapulous exanthema, frequently comprise the initial form of presentation of more severe reactions, such as Stevens-Johnson syndrome and toxic epidermal necrolysis³.

The incidence of Stevens-Johnson is estimated as approximately one to three cases per million inhabitants a year⁴. Stevens-Johnson syndrome or erythema multiforme is an acute and severe adverse skin reaction that occurs within one or two weeks after beginning drug treatment. Stevens-Johnson is a complex immune disorder involving the skin and mucous membrane and is associated with a high rate of morbidity and mortality. The mechanism by which the syndrome is manifested is not yet clear, and once set off, the reaction progresses rapidly and the patient’s skin resembles a burn, which leads the patient to be treated as a major burn victim⁵.

Several antiepileptic drugs, including phenytoin, have been associated with the development of Stevens-Johnson syndrome⁶.

Drug treatment with vancomycin, an antibacterial medication of the tricyclic glycopeptide class, is also related to the development of systemic and cutaneous reactions, including Stevens-Johnson syndrome⁷.

In this article, we present case reports of four patients who developed skin rashes after the use of vancomycin associated with phenytoin, and in one case, the patient developed Stevens-Johnson syndrome.

CASE REPORT

First case

A 36-year-old female patient was admitted to the hospital with a diagnosis of head and spinal trauma, after a road accident. The patient presented with difficult to treat aspiration pneumonia and remained in the neurology ICU for 70 days. She was treated with vancomycin: 1 g
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On the 23rd day of vancomycin and phenytoin treatment, the patient developed diffuse polymorphic erythema with mouth lesions and typical palm-plantar lesions characteristic of Stevens-Johnson syndrome, with rostro-caudal progression of the clinical picture. The medical treatment consisted in discontinuation of vancomycin and phenytoin, since they are the most likely drugs to have caused the onset of the reaction, and as a precaution, dipyrone was substituted by paracetamol. The patient was treated with teicoplanin and later, linezolid replaced vancomycin. After the tenth day from onset of the reaction, phenobarbital was discontinued.

The reaction persisted for approximately 60 days with periods of improvement and relapse, and the patient was treated with hydroxyzine: 30 mg q6 hours, hydrocortisone: 100 mg q6 hours with gradual tapering of the dose, topical treatment of the lesions, and immunoglobulin.

After remission of the Stevens-Johnson syndrome, the patient was submitted to surgery for placement of a halo device to stabilize the cervical cranium and was released from the hospital.

Second case
A 53-year-old male patient was admitted to the hospital with diagnosis of complete occlusion of a carotid aneurism. On the 12th day of phenytoin treatment with 100 mg q8 hours and the second day of vancomycin treatment with 1 g q12 hours, he developed a skin rash attributed to the use of phenytoin, which was therefore discontinued and substituted by phenobarbital 100 mg q12 hours.

On the 17th day of vancomycin use, the patient developed generalized polymorphic erythema probably triggered by the use of vancomycin, which was discontinued and replaced by teicoplanin. The reaction, which persisted for 16 days, was treated with hydroxyzine 30 mg q8 hours and topical treatment.

Third case
A 53-year-old male patient with history of alcohol abuse was admitted to the hospital for treatment of liver failure and stroke. The patient’s neurological picture worsened during hospital stay with multiple organ and system failure, which progressed to death. The patient had used phenytoin 100 mg q8 hours during 10 days, and the medication had been substituted by phenobarbital 100 mg once a day. After the sixth day of phenobarbital and second day of vancomycin 1 g q12 hours, the patient developed a skin rash and lesions predominantly in the head, neck, and upper chest regions. Ten days after the onset of the rash and 12 days of vancomycin use, the patient’s pharmacodermia worsened; vancomycin was discontinued and hydroxyzine 10 mg q6 hours was introduced along with topical treatment of the lesions.

On the 19th day of skin rash, the patient’s pharmacodermia worsened and medical treatment consisted of discontinuation of the phenobarbital and replacement by carbamazepine 200 mg q8 hours. Five days later, the clinical spin picture improved.

Fourth case
This was a 63-year-old male patient with a history of diplopia and palpebral ptosis on the left, which began after myocardial bypass surgery. With a diagnosis of hypophyseal tumor, the patient was admitted to the hospital for neurosurgery for the transphenoidal removal of the tumor. The patient had used phenytoin 100 mg q8 hours during 16 days and on the third day after phenytoin discontinuation, the patient initiated treatment with vancomycin 1 g q12 hours for 27 days. On the 15th day of vancomycin treatment, the patient experienced vasculitis, and on the 27th day, he developed a skin rash. Vancomycin was discontinued and the patient was treated with hydroxyzine 10 mg q6 hours and topical lotion, with improvement of the skin rash 15 days after onset of the reaction.

DISCUSSION
Due to potential severity of Stevens-Johnson syndrome, the early detection and immediate discontinuation of the drugs suspected to have caused a reaction are vital for reducing morbidity associated with the syndrome.

Severe skin reactions resulting from the use of vancomycin are rare. Occurrence of the red man syndrome was reported after intravenous administration of vancomycin in 3 to 11% of patients. Other adverse reactions include nephrotoxicity (5%), skin eruptions (2 to 5%), neutropenia (2%), and rarely, Stevens-Johnson syndrome.

Some authors described an increased risk of developing Stevens-Johnson syndrome when phenytoin is associated with radiation therapy, while others reported possible increased risk when phenytoin is associated to corticosteroids.

Although there are cases in the literature of skin reactions during treatment with phenytoin and vancomycin used in monotherapy or in association with other medications or therapies, as in the case of...
phenytoin, there are no reports on the development of Stevens-Johnson when phenytoin and vancomycin are used in association with the drug therapy.

All cases reported occurred in neurological patients hospitalized in Neurology Intensive Care Units who had received, concomitantly or not, drug treatment with vancomycin and phenytoin. Because both medications cause skin adverse reactions, such as Stevens-Johnson, we suspect that the association of phenytoin and vancomycin may increase the appearance of skin reactions and the risk for Stevens-Johnson syndrome.

REFERENCES