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Case Report

Neosensitization to Multiple Drugs Following Trimethoprim/Sulfamethoxazole-induced Drug Reaction with Eosinophilia and Systemic Symptoms syndrome

Fatma Zgolli[1,2]*, Ons Charfi[1,2], Imen Aouinti[1,2], Ghozlane Lakhoua[1,2], Sihem El Aidli[1,2], Riadh Daghfous[1,2] and Ahmed Zaiem[1,2]

[1]*National Center Chalbi Belkahia of Pharmacovigilance, Tunisia*

[2]*University of Tunis El Manar, Faculty of Medicine of Tunis, Tunisia*

***Corresponding Author:** Fatma Zgolli, National Center Chalbi Belkahia of Pharmacovigilance and University of Tunis El Manar, Faculty of Medicine, Tunisia.

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Abstract

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome is a rare and potentially life-threatening adverse drug-induced reaction. Its evolution is unpredictable. Exceptionally, Dress syndrome can induce multiple hypersensitivity reactions related to chemically unrelated drugs, without the reintroduction of the causative medication. This is neosensitization, distinct from cross reactions.

The present case report describes a female patient who experienced neosensitization to imipenem and then to metronidazole/spiramycin following the manifestation of DRESS syndrome induced by metronidazole/spiramycin.

Keywords: DRESS Syndrome; Neosensitization; Adverse Drug Reaction; Pharmacovigilance

Introduction

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome is a rare and potentially life-threatening adverse drug-induced reaction. It is associated with skin eruption, fever and systemic involvement. Its evolution is unpredictable and it is characterized by a slow resolution, even after the withdrawal of the culprit drug. Exceptionally, Dress syndrome can induce multiple hypersensitivity reactions related to chemically unrelated drugs, without the reintroduction of the causative medication. This is neosensitization, distinct from cross reactions [1].

We report a case of hypersensitivity reactions to imipenem and then to metronidazole/spiramycin in a patient with a history of DRESS Syndrome with trimethoprim/sulfamethoxazole.

Case Report

A 45-year-old woman with a history of Widal triad (asthma, nasal polyposis and aspirin intolerance) was admitted to hospital with lumbar spondylodiscitis. Eight days after starting trimethoprim/sulfamethoxazole therapy (2.4g/0.48g per day), she developed a whole-body skin rash. Skin examination showed a generalized purpuric rash, facial edema and cervical lymph nodes associated with fever at 38.9°C. Laboratory tests revealed hyperleukocytosis (12x 103, with 27% eosinophils) associated with hepatic cytolysis. Viral serologies to herpes simplex human herpes virus 6 (HHV6), human herpes virus 7 (HHV7), Epstein Barr virus (EBV) and cytomegalovirus (CMV) were not performed. The outcome was favorable after 15 days of stopping the drug and under symptomatic treatment (methylprednisolone and ceftizidime). DRESS syndrome to trimethoprim/sulfamethoxazole was retained.

Three weeks later, the patient developed, immediately at the end of the first injection of imipenem, acute dyspnea associated with arterial oxygen desaturation (less than 90%). She was transferred to the intensive care unit where she received corticosteroid therapy, epinephrine and oxygen. The patient gets well in four hours.

One month after this episode, she started treatment with metronidazole/spiramycin for a tooth abscess. Three days later, she de-

veloped a maculopapular rash limited to the chest which resolved spontaneously 24 hours after stopping the drug.

Discussion and Conclusion

This patient experienced 3 episodes of systemic adverse events associated with 3 different classes of drugs.

In the first episode, it was about DRESS syndrome based on the criteria adopted by the European Registry of Severe Cutaneous Adverse Reactions (RegiSCAR) group [2]. The score was 5 (probable case): fever (0 point), typical rash (1 point), lymph nodes (1 point), hypereosinophilia (2 points) liver injury (1 point), resolution in more than 15 days (0 point). The responsibility of trimetoprim/sulfamethoxazole in inducing DRESS syndrome was evaluated as I2 according to the updated French method of assessment [3].

The two others events did not fulfill entirely the criteria of DRESS syndrome according the RegiSCAR score. However, the occurrence of hypersensitivity reactions with chemically and structurally unrelated drugs in a patient with a history of DRESS syndrome suggests a neosensitization. It is reported, mainly during the early phase or during the first months following DRESS syndrome [4]. This entity is different from cross-reactivity which occurs between drugs with chemical or antigenic similarities [5].

The mechanism of neosensitization is discussed. First DRESS episode may induce a massive non specific activation of the immune system, which will provide the enhanced expression of co-stimulatory molecules and proinflammatory cytokines. The latter allows for a more efficient presentation of chemical antigens to antigen-presenting cells which, consequently, decrease the level of tolerance to drugs, present at the time in the organism, and especially antibiotics such as amoxicillin [6-8].

The present findings suggest that clinicians should be aware of patient's drug history when prescribing drugs to a patient with a previous DRESS episode in order to ovoid multiple neosensitization.

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