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Case Report

DRESS syndrome with carbamazepine and Epstein–Barr virus reactivation

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ABSTRACT

DRESS syndrome is a serious toxidermia, most often caused by anticonvulsants, including carbamazepine, which is responsible for a formidable clinical picture and which may be accompanied by viral reactivations, in particular of the herpes group. Herein, we report the case of a young girl affected by DRESS syndrome with the reactivation of EBV, in whom the evolution was favorable. Recurrent EBV infection is demonstrated by the presence of IgM antibodies to anti-EBV early antigen and IgG antibodies to anti-EBV nuclear antigen. Its pathogenesis suggests that viral reactivation is the consequence of a T-immune response directed against the causative drug in some patients. It is an unpredictable entity requiring immediate treatment, namely stopping the drug in question, monitoring the patient, searching for viral reactivation and notifying pharmacovigilance.

Key words: Dress syndrom, carbamazepine, EBV, rash, reactivation

INTRODUCTION

DRESS syndrome (*drug reaction with eosinophilia and systemic symptoms*) is a serious drug eruption most commonly associated with carbamazepine and other drugs. Its pathophysiology has been clarified by the demonstration of reactivations of herpes viruses. It has been postulated that virus infection may play a role in the development of this syndrome. Herein, we report carbamazepine-induced hypersensitivity syndrome with Epstein–Barr virus (EBV) infection in a nineteen-year-old girl with a favorable evolution.

CASE REPORT

A nineteen-year-old girl was hospitalized for diffuse pruritic erythematous rash with facial edema progressing one month after taking carbamazepine for an epileptic seizure. An examination found a febrile patient with diffuse maculopapular rash with facial erythro-edema (Fig. 1a and 1b) associated with a declining purpura. A blood test revealed hepatic cytolysis and eosinophilia. A skin biopsy revealed an inflammatory infiltrate rich in neutrophils and eosinophils. A pharmacovigilance declaration incriminated carbamazepine. The patient was put on topical corticosteroid with the discontinuation of the drug. Two days later, she presented a fever at 39.5°C with otitis put on amoxicillin, worsening of the rash, the appearance of basophilia with monocytosis, worsening of cytolysis hepatic, negative blood culture, negative CMV serology, positive MNI test, and positive EBV serology. Viral hepatitis serologies were negative. The patient was put on antihistamines and a topical corticosteroid, and amoxicillin was withdrawn, with good clinical and biological improvement. After one week the otitis was treated with amoxicillin without any complications or reactions.

DISCUSSION

DRESS syndrome, initially described by Bocquet et al. [1], is an acute and severe drug eruption that

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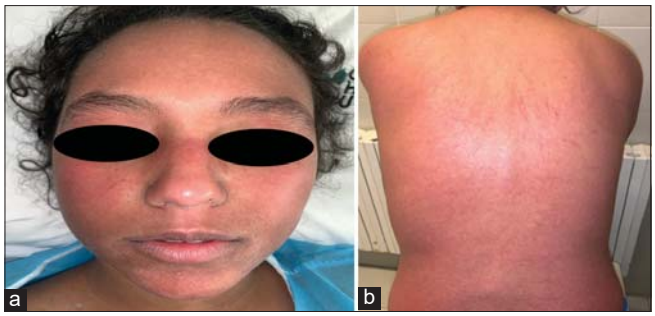

Figure 1: (a) Facial erythredema with desquamation.(b) Diffuse maculopapular rash on the body.

may be life-threatening [2]. The diagnosis is now well known and is based on a set of arguments associating, in a variable way, a generalized rash resembling a maculopapular exanthema, fever, periorbital facial edema, bilateral superficial polyadenopathy, hyperleukocytosis, blood hypereosinophilia, and multi-visceral failure, including the liver, kidney and lungs [2,3]. Recently, its physiopathology has been clarified by the demonstration of reactivations of herpes viruses, including Epstein–Barr virus (EBV), as well as cytomegalovirus (CMV) [4], human herpes virus-6 (HHV-6), and human herpes virus-7 (HHV7) [5-6], which explains the seriousness of the clinical manifestations, in particular, the systemic attacks, as well as the biological modifications of DRESS syndrome [7].

In our case, the delay, the clinical and biological data, the viral reactivation of EBV, and the aggravation by amoxicillin were in favor of DRESS syndrome with carbamazepine and EBV reactivation. In our patient, the reintroduction of amoxicillin did not modify the evolution of clinical or biological data. This is why it is necessary to know how to distinguish between a simple cutaneous reaction, infectious mononucleosis, and a true drug eruption with the reactivation of EBV [8].

The pathogenesis of this viral reactivation during this type of toxidermia remains poorly understood [9]. Several arguments exist to consider DRESS syndrome a mainly viral disease induced by a drug on a ground of genetic predisposition not yet determined: a similarity between the clinico-biological picture of DRESS syndrome and infections with herpes viruses, a demonstration viral reactivation, a possible immunomodulatory action of drugs associated with DRESS syndrome, favoring viral reactivation as well as a T-lymphocyte response directed against viral antigens with a T repertoire profile close to that observed in EBV infections. Some authors consider that viral reactivation is the consequence of a T-immune response directed against the causal drug [10].

The management of DRESS syndrome aims to monitor and possibly control the immune response. In some cases, no treatment is necessary while, in other cases, the immune response is deleterious requiring corticosteroid therapy [11].

Amoxicillin may be responsible for DRESS syndrome, yet may especially worsen it in the absence of a previous allergy to betalactamines [12].

CONCLUSION

DRESS syndrome is a rare and unpredictable entity, which is important to be aware of because of its potential seriousness, its progressive risk, and the necessary therapeutic sanction, namely the discontinuation of the drug in question and the search for a viral reactivation. The notification of these cases to the pharmacovigilance centers in addition to helping in identifying the suspected drug allows an inventory of these attacks and contributes to a better understanding of this iatrogenic pathology.

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

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