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Carbamazepine Induced Drug Rash with Eosinophilia and Systemic Symptoms

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ABSTRACT

Stabilizes inactivated state of sodium channels, thereby making neurons less excitable may reduce activity of nucleus ventralis of the thalamus or decrease synaptic transmission or summation of temporal stimulation leading to neuronal discharge.A adult of 68 years old patient came to dermatology department with chief complaints of neuralgia over scalp to relieve the symptoms physician prescribed carbamazepine 200mg Po OD. During his 2nd week of treatment patient developed pain,fever,sore throat followed by skin rash.Better vigilance is necessary for implementation of safe and effective treatment for each individual patient.in order to prevent serious adverse drug reactions of this drug,close monitoring drug treatment course, creating awareness, recognition of the problem and careful management of all the patients who receive medication are essential,because use of carbamazepine causes thrombocytopenia, leukopenia, leukocytosis, eosinophilia, anemia, pruritic and erythematous rashes, urticaria, photosensitivity reactions, alterations in skin pigmentation, exfoliative dermatitis, erythema multiforme and nodosum, purpura, aggravation of disseminated lupus erythematosus,Abnormalities in liver function tests, cholestatic and hepatocellular jaundice, hepatitis; very rare cases of hepatic failure, Pancreatitis ,Pulmonary hypersensitivity characterized by fever, dyspnea, pneumonitis, or pneumonia

Keywords: Carbamazepine, Induced Drug Rash with Eosinophilia and Systemic Symptoms, adverse drug reaction.

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Introduction

Drug rash with eosinophilia and systemic symptoms (DRESS) syndrome is a rather distinct severe adverse drug reaction. However, use of the term DRESS has been inconsistent, because eosinophilia is not a constant clinical finding, cutaneous and systemic signs are variable. The estimated incidence of this syndrome ranges from 1 in 1000 to 1 in 10,000 drug exposures, Adults are more affected than children [1]. The main culprit drugs are carbamazepine and allopurinol, even though 50 drugs can induce DRESS [2]. Another drug was reported particularly sulfa derivatives, antidepressants, non steroidal anti-inflammatory drugs, and antimicrobials. DRESS syndrome including a severe skin eruption, fever, hematologic abnormalities (eosinophilia or atypical lymphocytes), and internal organ involvement, usually 2-6 weeks after the initiation of drug therapy, with a possibility of persistence or aggravation of symptoms despite the discontinuation of the culprit drug. Given the potential morbidity, wide differential diagnosis, and relatively simple treatment, it is important for emergency physicians to consider this entity in patients with severe rashes. Severe cases of DRESS often require aggressive treatment; however, current pharmacologic treatment options are limited

Case report

A adult of 68 years old patient came to dermatology department with chief complaints of neuralgia over scalp to relieve the symptoms physician prescribed carbamazepine 200mg Po OD. During his 2nd week of treatment patient developed pain,fever,sore throat followed by skin rash.On general examination, patient was conscious and coherent.on physical examination PR-92/min,RR:16/min,spo_2: 97% with RA,Resp: BAE+, CVS: $S_1 S_2$ +. Dermatological examination: skin- multiple, discrete purpuric popular, macular rash over trunk, thighs, upper limbs, lower left cervical

lymphadenopathy, left axillary lymphadenopathy, laboratory investigations CBP:Eosinophils- 101 (14%), LFT: aspartate aminotransferase (AST)- 84 U/L (10-35 U/L), alanine aminotransferase (ALT) 67 U/L (10-40 U/L), ultrasound abdomen shows splenomegaly,prostatomegaly,Lymph node enlargement>2,Patient was referred to physician of head of the department to confirm the ADR was due to phenytoin high dose .On analysis compared to all other drugs prescribed,phenytoin pharmacology and literature support the occurrence of irritability. In order to confirm the relationship between the effect and drug we have also done dechallenge test i.e.drug was withdrawn from treatment regimen

Discussion

The acronym "drug rash with eosinophilia and systemic symptoms" was first introduced in 1996 by Bocquet, to describe patients exhibiting a drug-induced condition characterized by an extensive rash, fever, lymphadenopathy, hematologic abnormalities, hepatitis, and involvement of the kidneys, lungs, heart, or pancreas [3]. Usually presents within 8week. Aromatic anticonvulsants (phenytoin, phenobarbital, and carbamazepine) are the most common cause of DRESS. In the review of 172 cases reported as DRESS or drug hypersensitivity syndrome in the literature by using the Regis CAR scoring system [4], carbamazepine remains the mostly reported (27% of cases). But a variety of other drugs, such as allopurinol, minocycline, dapsone, sulfasalazine, and mexiletine, antiretrovirals have also been associated with DRESS. Cross-sensitivity is as high as 75% among the aromatic anticonvulsants [5].

The pathogenesis of DRESS syndrome is partially understood. Different mechanisms have been implicated in its development, including detoxification defects leading to reactive metabolite formation and subsequent immunological reactions slow acetylation, and reactivation of human herpes, including Epstein-Barr virus and human herpesvirus (HHV)-6 and -7. The detection of HHV-6 reactivation has even been recently proposed as a diagnostic marker for DRESS. Other types of viral infection were reported, such as cytomegalovirus reactivation and paramyxovirus infection. It is increasingly apparent that there is a genetic predisposition to adverse drug reactions. Studies have found that HLA-B*1502 is associated with carbamazepine induced Stevens-Johnson syndrome /toxic epidermal necrolysis in some Asian populations, but the same association does not occur in hypersensitivity syndrome (HSS) / DRESS. It is hoped that further research may define pharmacogenetic disease susceptibility markers to identify people at high risk of developing HSS / DRESS, Regis CAR and Japanese consensus group have developed specific criteria for making the diagnosis of DRESS. To meet the definition of DRESS, patients must have three of the four main Regis CAR criteria: an acute rash, fever above 38° C, lymphadenopathy at two sites, involvement of at least one internal organ, and abnormalities in lymphocyte and eosinophil counts. Additional criteria include hospitalization and that the reaction is suspected to be drug-related. Concerning Japanese consensus group the diagnosis requires meeting seven of the nine criteria in this system or all of the first five: a maculopapular rash developing > 3 weeks after drug initiation, clinical symptoms continuing > 2 weeks after stopping therapy, fever > 38° C, liver abnormalities (ALT > 100 IU/L) or other organ involvement, leukocytosis, atypical lymphocytes, eosinophilia, lymphadenopathy, or HHV-6 reactivation. Although an association with HHV6 is of interest, definite confirmation that herpes viruses are central to the hypersensitivity reaction is currently lacking. An ambiguous role for virus reactivation coupled with low availability of the relevant assay reduces the worth of HHV6 as diagnostic criteria.

The patient described here met the majority of criteria according to Regis CAR scoring guidelines for a diagnosis of DRESS induced by carbamazepine.

Conclusion

Although the mechanisms underlying DRESS syndrome remain poorly understood. This is a growing case reported in literature. The diagnosis of dress should be highly suspected with the presence of skin rash, liver involvement, fever, hypereosinophilia, and lymphadenopathy particularly in starting any new anti-epileptic. The use of systemic corticosteroids is classically reported in case of organ- or life-threatening disease. However, this remains controversial and may lead to activation of HHV- 6. Besides the prompt withdrawal of causative drug as standard of care, further studies are needed to recommend specific treatment guidelines.

Competing Interest

The authors declare no competing interest.

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