Carbamazepine Induced Severe Skin Eruptions: Dress Syndrome

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Abstract:

Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is a potentially fatal cutaneous reaction caused by therapeutic drugs. The pathophysiology of this disease is unknown, although it is induced by several precipitating factors such as genetics, viral reactivation, and specific drugs such as anticonvulsants, antibiotics, and so on. It is akin to cutaneous manifestations such as skin rashes, pruritus, and fever, but it also encompasses desquamation of the epidermis and other dermatological reactions and lymphadenopathy. Systemic involvement occurs depending on the organ affected. The European Registry of Severe Cutaneous Adverse Reactions to Drugs and Collection of Biological Samples (Regi SCAR) criteria for DRESS syndrome are used to diagnose the condition. The treatment consists of discontinuing the causative drug and treating the patient with antihistamines and emollients in the mild form, corticosteroids in the intermediate form, and plasmapheresis in the severe form, as well as various alternative medications. Healthcare providers should be more cautious of early signs of this condition, as early diagnostic and treatment enhance better outcomes significantly.

Keywords: DRESS syndrome, anticonvulsants, desquamation, cutaneous reaction, corticosteroids.

Introduction:

Drug Rash with Eosinophilia and Systemic Symptoms (DRESS syndrome) is an idiosyncratic adverse reaction where T cells mediate a hypersensitivity reaction (Type IV B). Depending on the internal organs involved, there may be fever, rash, lymphadenopathy, eosinophilia, and other systemic symptoms.[1]

Carbamazepine (Tegretol) is an anticonvulsant and analgesic medication used to treat seizures and pain due to trigeminal neuralgia, bipolar disorder. Carbamazepine inhibits neuronal stimulation by binding to voltage-dependent sodium channels.[2] Acting on these channels increases dopamine production and GABA transmission in the bipolar brain and alleviates the symptoms of mania and depression in disorder.[3] Carbamazepine is prescribed off-label to treat sleep disorders, alcohol withdrawal,[4] postherpetic neuralgia, restless leg syndrome[5], and schizophrenia. There have been serious and often fatal dermatologic reactions associated with carbamazepine treatment. The patient has an inherited variant of the HLA-B gene known as HLA-B*1502, usually found in Asian ancestry populations. Hypersensitivity reactions, Aplastic anemia, and agranulocytosis have been reported as adverse effects of carbamazepine

A long-term diabetic who received carbamazepine for neuropathic pain had fever and rashes all over the body and was hospitalized and treated at our facility. He acquired the symptoms relatively late after initiating Carbamazepine. This article describes the clinical aspects of the DRESS condition along with its immediate and subsequent treatments.

Case Report:

A 61-year-old male patient presented to our hospital with complaints of erythematous,

acute pruritus, and desquamation of the epidermis that began at the scalp and rapidly spread to all body surfaces for five days, despite the cessation of all medications. He is already a known case of Diabetes Mellitus (Type 2) and coronary artery disease on medications. He started using carbamazepine for neuropathic pain seven weeks ago. There is no history of any viral infections. The patient had a fever (above 38°C) at the time of the skin eruptions and was being treated with acetaminophen. The vitals were stable. On examination, the patient showed generalized erythematous eruptions with intense itching. There was significant erythematous desquamation of skin all over the body, except for the palms and plantar regions.

Additionally, the patient experienced mild anasarca and facial puffiness. He'd seen a dermatologist, and the diagnosis was DRESS syndrome. The patient was afebrile at the time of admission, and laboratory tests revealed leucocytosis (37000 cells/mm3, 20% with eosinophilia (2,400 cells/mm3), atypical lymphocytes, and other haematological findings that were normal. The liver function tests revealed a mild abnormality in the form of elevated AST – 80 U/L and ALT – 87 U/L. The Renal Function Test and other laboratory findings were found to be normal. Nonspecific intraventricular conduction delay was detected on the electrocardiogram. The USG of the abdomen showed mild prostatomegaly and a mild fatty liver, but other organs were normal.

The diagnostic criteria for DRESS syndrome were matched after evaluating those parameters. Carbamazepine at a dose of 300 mg HS for severe neuropathic pain was suspected of causing skin exfoliation in this patient.

The following images depict the epidermal lesions at the time of admission.

Figure 1 Skin eruption of all body surfaces of the patient at the time of admission.

The patient is subsequently given intravenous Methyl Prednisolone Sodium Succinate 60 mg BD, Inj. Ceftriaxone (1000 mg) + Tazobactam (125 mg) BD, Inj. Hydroxyzine hydrochloride TID was maintained on the first day, followed by oral pills and additional coronary artery disease treatments. Basal bolus insulin treatment was used to achieve glycemic control. IV steroid was administered for three days, followed by oral steroids at the dose of 1mg/kg of prednisolone at the time of discharge. The test results revealed normal leucocytes and eosinophils.

Discussion:

DRESS syndrome (Drug Rash with Eosinophilia and Systemic Symptoms) is a severe life-threatening hypersensitivity reaction to certain medications. The etiology is idiopathic, although it is induced by one or more causes such as genetic factors (lack of detoxifying enzymes for metabolism, resulting in metabolite accumulation), HLA, and its moieties for the chemical structure of the drug), and viral reactivation (viral-drug interaction).[6] Anticonvulsants (carbamazepine, phenytoin, phenobarbital, and lamotrigine), sulphonamides (dapsone, sulfasalazine), antibiotics (specifically beta-lactams), allopurinol,[7] and less well-known medicines such as Captopril, mood stabilizers, and antiretrovirals are all known to cause this syndrome.[8] However, certain viruses such as

human herpesvirus–6 and human herpesvirus–7, Epstein-Barr virus, cytomegalovirus, and hepatitis C virus have been speculated to reactivate DRESS syndrome.[9]

The incidence of DRESS syndrome with anticonvulsants has been reported to be one in every 10^3 or 10^4 patients. DRESS syndrome typically appears 2 to 8 weeks following exposure to the offending drug substance, with a 10% mortality rate.[10]

In the early stages, common symptoms include fever, malaise, and skin eruption. The skin eruption's most prevalent symptom is a morbilli form rash on the face and upper extremities. The rash frequently causes lymphadenopathy and facial oedema. In most cases, the rash develops into widespread, confluent erythema that covers almost half of the whole-body surface area (BSA).[11] The symptoms can range from a moderate exanthem to significant blistering and skin loss, but the most common is pruritic, macular erythema with papules, pustules, or vesicles. Typical signs of systemic involvement include lymphoma, hepatitis, pericarditis, interstitial nephritis, and pneumonitis.[12]

The inclusion criteria for prospective cases of the European Registry of Severe Cutaneous Adverse Reactions to Drugs and Collection of Biological Samples (Regi SCAR) must have at least three of the following: a) Hospitalization, b) Drug-related reaction, Acute skin rash, c) Fever around 38° Celsius, d) Enlarged lymph nodes at two sites, involvement of at least one internal organ, e) Blood count abnormalities such as low platelets, elevated eosinophils, or aberrant lymphocyte count.[13]

In this study, carbamazepine administration is significantly associated with typical clinical symptoms for DRESS syndrome, such as severe skin rashes, the presence of significantly elevated eosinophils, atypical lymphocytes, leucocytosis, and lymphadenopathy, the elevation of liver enzymes, and improvement in those clinical manifestations after carbamazepine discontinuation.

Questions	Response	Score
Are there previous conclusive reports of this reaction?	Yes	+1
Did the adverse event appear after the suspected drug was administrated?	Yes	+2
Did the adverse event improve when the drug was discontinued or a specific antagonist was administrated?	Yes	+1
Did the adverse reaction reappear when the drug was readministered?	Yes	+2
Are there alternative causes (other than drug) that could on their own have caused the reaction?	No	+2
Did the reaction reappear when a placebo was given?	Don't know	0
Was the drug detected in the blood (or other fluids) in concentrations known to be toxic?	Don't know	0
Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	Don't know	0
Did the patient have similar reaction to the same or similar drugs in any previous exposure?	Don't know	0
Was the adverse event confirmed by any objective evidence?	Yes	+1
Total		+9

Figure-2 Naranjo algorithm for Adverse Drug Reaction Probability Scale score of 9 indicates carbamazepine was a highly probable cause of this patient's presentation.

The Naranjo Adverse Drug Reaction Probability Scale score was assessed in our patient with a score- 9 (as shown in Figure-2), indicating that carbamazepine was a potential cause of DRESS syndrome. The case report also has certain limitations, such as lack of serum concentration of carbamazepine and the absence of biopsy data for Human Leucocyte Antigen (HLA B*-1503).

Conclusion:

This case report is being published due to the limited availability of distinct condition presentations. This paper emphasizes the need to consider DRESS disease when assessing any generalized rash, particularly erythroderma. If eosinophilia is found, the patient should be evaluated for DRESS syndrome. Physicians must be aware of this condition to identify and treat patients.

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