LAMOTRIGINE INDUCED DRUG REACTION WITH EOSINOPHILIA AND SYSTEMIC SYMPTOMS (DRESS) SYNDROME, DYSPHAGIA AND STEROID PULSE THERAPY. A CASE REPORT

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How to cite this article

Naz S, Ullah R, Haleema. Lamotrigine Induced Drug Reaction with Eosinophilia and Systemic Symptoms (Dress) Syndrome, Dysphagia and Steroid Pulse Therapy. A Case Report. J Gandhara Med Dent Sci. 2023;10(3): 90-92
https://doi.org/10.37762/jgmds.10-3.393

ABSTRACT

OBJECTIVES

Adverse drug reactions are common, and dermatological manifestation is a common indicator. The potentially lethal "Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome" is one example of severe drug reactions manifesting within weeks after drug intake. It is characterized by "fever, skin rash, lymphadenopathy, eosinophilia and systemic symptoms". We present a case of DRESS syndrome secondary to anticonvulsants lamotrigine associated with dysphagia and responding to steroid pulse therapy.

KEYWORDS: *Dress Syndrome, Eosinophilia, Drug Reaction, Hypersensitivity Reaction, Exanthema*

INTRODUCTION

DRESS syndrome is a peculiar drug reaction that occurs commonly after exposure to a variety of drugs like" allopurinol, sulfonamides, and aromatic anticonvulsants such as phenytoin, phenobarbital, carbamazepine, and lamotrigine".[1] DRESS Syndrome is considered a great Clinical Mimicker, mirroring other adverse drug reactions as well as many systemic disorders making it a diagnostic challenge. It has cutaneous and systemic manifestations. The systemic presentation may be esophagitis, Hepatic inflammation, nephritis, carditis, and neurological and endocrinological complications.[2] Apart from other manifestations, uncommon but many times the earliest clinical manifestation of DRESS is dysphagia which often goes unnoticed.[3] RegiSCAR criteria include at least 3 of the following seven characteristics: 1) skin eruption, 2) fever (>38°C), 3) lymphadenopathy at least two sites, 4) involvement of at least one internal organ, 5) lymphocytosis (>4×10^3/μL) or lymphocytopenia (<1.5×10^3/μL), 6) blood eosinophilia (>10% or 700/μL), and 7) thrombocytopenia (<120×10^3/μL). Patients were classified into definite, probable, possible or no cases according to the RegiSCAR scoring system.[4] Management relies on discontinuing the offending drug, supportive care, and administering systemic steroids or other immunosuppressive agents.[5] The mortality rate is approximately 10% to 20%. Dress syndrome usually requires continuous systemic steroids for 4-8 weeks. We present a case of dress syndrome associated with dysphagia and responding to steroid pulse therapy. Steroid pulse therapy is not described before in the management of DRESS syndrome.

CASE REPORT

A 17-year-old girl presented to the dermatology department with three weeks history of generalized pruritic urticarial papular rash after starting anticonvulsant lamotrigine for complex partial seizures (figure 1). It gradually became confluent into plaques. She reported fever, vomiting, food intolerance, dysphagia, and fever. The rash started around the neck and progressively became generalized following a waxing and waning course. She was febrile (100 F), tachycardiac and hypotensive on arrival. There was a generalized rash with plaque formation. She had acral and facial oedema with angular cheilitis without frank mucosal involvement (figure 2). Laboratory investigations are presented in the table that shows raised ALT and leukopenia (Table 1). Urine R/E and ECG were normal. Ultrasound abdomen showed mild splenomegaly with normal liver and kidneys. Lamotrigine was stopped, and high-dose oral prednisone, fluids and supportive treatment improved both the skin eruption and systemic symptoms. Consultation with a neurologist was done for safer medication for Seizures. The patient was discharged one week after stabilization, and an I/M bolus depot of methylprednisolone (80mg/2ml) was injected. She was planned for an outpatient follow-up after six weeks. Her investigations at follow-up were normal, along with

signs and symptoms.

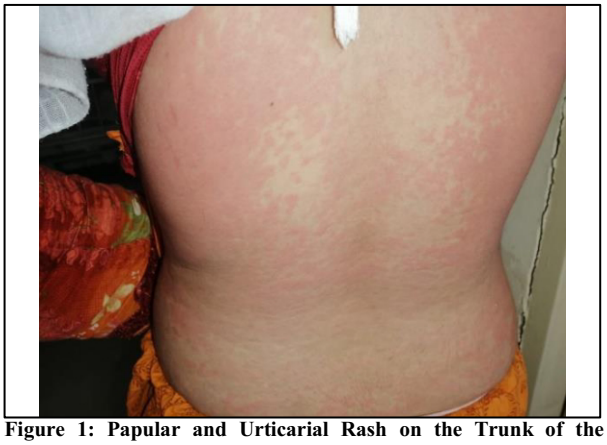

Figure 1: Papular and Urticarial Rash on the Trunk of the Patient

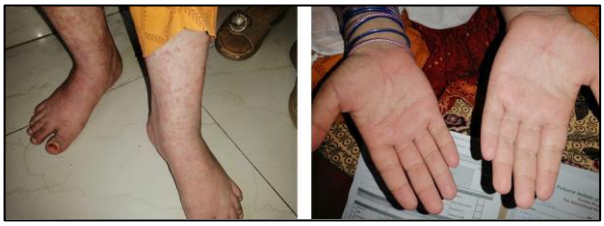

Figure 2: Acral Rash with Oedema of Hands and Feet

Table 1: Laboratory Investigations

Investigation	Result
Haemoglobin	11.6 g/dl
Total leukocyte count	2.26 x 10^9/L
Anti-HCV	Negative
HBs Ag	Negative
HIV*	Negative
Serum amylase	56 U/L
Alanine transferase	71 U/L
ANA*	Non-reactive

*HIV: human immunodeficiency virus
*ANA: antinuclear antibody

DISCUSSION

DRESS syndrome is a rare, uncommon, but potentially fatal severe drug reaction, and it is difficult to estimate its true incidence.[7] Only one study in the literature has reported the estimated incidence of this syndrome, and the values are in the range of 1 case per 1,000 to 10,000 drug exposures.[8] Prospective studies would provide better estimates but may be too long to be feasible. The clinical manifestations of DRESS syndrome usually appear within two months after introducing the causative drug. Common features include skin rash, fever, haematological abnormalities, lymphadenopathy, and systemic organ involvement like pneumonitis, carditis, pancreatitis, and hepatic renal and neurological complications.[2] Diagnosing DRESS syndrome sometimes becomes very challenging as there is no reliable standard for diagnosing DRESS Syndrome. Diagnosis is based on a mixture of clinical and laboratory abnormalities. Labelling a patient with DRESS Syndrome Diagnostic Criteria must be addressed.[5,6] Our patient fulfilled the diagnostic criterion by scoring 5 points confirming DRESS syndrome i.e.

1. The extent of rash >50 %of body surface area
2. Papular urticarial Rash suggestive of DRESS
3. Systemic involvement (hepatitis, pancytopenia and esophagitis)
4. Relevant 3 Negative serological tests (Hepatitis B, C and ANA)

Although there is high variability in the clinical presentation of DRESS syndrome. The presence of exposure to a high-risk medication(lamotrigine), skin rash with progression to the commonly affected areas and is associated with oedema (facial, hands, feet) and systemic symptom organ involvement (fever, malaise, abnormal liver function tests, esophagitis, splenomegaly) and laboratory abnormalities (raised ALT, leukopenia) were consistent with the diagnosis. This case also highlights that eosinophilia is not mandatory for diagnosis, as 10---50% of patients do not show it. Few other studies also demonstrate lamotrigine-induced Dress syndrome.[9] within three weeks, especially after the dose increases, indicating crossing the threshold above the body's metabolic capacity. Apart from other manifestations, dysphagia is often the earliest clinical manifestation of DRESS syndrome, which often goes unnoticed. Professor Descamps also reports the association of DRESS syndrome with dysphagia and facial oedema.[3] Dysphagia in DRESS syndrome has been reported in association with herpes virus infection.[10] Overall, early withdrawal of the offending drug and the administration of systemic steroids and supportive treatment proved helpful in successfully managing this life-threatening drug reaction, as described by other studies.[4] Steroid pulse therapies are used in various inflammatory and autoimmune diseases as they are cumulatively less toxic. Pulse therapy is the administration of supra therapeutic administration of steroids intermittently. This therapy has given excellent treatment response with few side effects in many dermatological conditions and immediate, profound anti-inflammatory effects with fewer side effects. Compared to daily oral steroids, a faster clinical response lasts about three weeks after one pulse without any prolonged suppressive effect on the hypothalamic-pituitary axis.[11,12] This clinical case responded to the more feasible I/M pulse steroid therapy (methylprednisolone 80mg/2ml) instead of prolonged daily systemic steroid therapy. After three weeks, the patient was discharged in a vitally stable and

symptomatically improving clinical status with an outpatient follow-up visit. The patient was followed for two months, complete clinical and biochemical resolution of signs and symptoms. The patient is still on six monthly follow-up plans for developing any autoimmune association (alopecia areata, thyroid disorder) as described previously in the literature.[13] The role of steroid pulses instead of prolonged oral or IV steroids is more convenient and cost-effective, decreases the need for tapering steroids and has fewer compliance issues. Similar studies should be done on a large scale to validate it further before switching the practice towards depot injections. Additionally, patients recovering from dress syndrome must be monitored closely over the next few years for subsequent development of autoimmune diseases like alopecia areata and thyroid disorders.

CONCLUSIONS

In conclusion, this case highlights the importance of considering DRESS syndrome as a possible adverse reaction to medications, even in the absence of typical symptoms. Additionally, it suggests that early recognition and prompt initiation of appropriate treatment, such as steroid pulse therapy, may lead to favorable outcomes for patients with DRESS syndrome.

CONFLICT OF INTEREST: None

FUNDING SOURCES: None

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CONTRIBUTORS

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