

## A case report of Olanzapine induced DRESS Syndrome

Prosenjit Ghosh<sup>1</sup>, Ankur Bhattacharya<sup>2</sup>

<sup>1</sup>Assistant Professor, Department of Psychiatry, Silchar Medical College & Hospital, Silchar.

<sup>2</sup>Postgraduate Trainee, Department of Psychiatry, Silchar Medical College & Hospital, Silchar.

**Corresponding author:** Prosenjit Ghosh

**Email** – p\_ghosh72@yahoo.com

### ABSTRACT

DRESS syndrome (Drug reaction with eosinophilia and systemic symptoms) is defined as a drug-induced complex of symptoms consisting of fever, rash, lymphadenopathy, eosinophilia and a wide range of mild to severe systemic presentations. Here we report a case of a 24-year-old female who developed a severe generalized Anasarca, skin erythema, facial puffiness, reddish discoloration over the body, fever, eosinophilia, leukocytosis and hepatitis 30 days after ingestion of olanzapine. Considering the occurrence of fever, eosinophilia, enlarged lymph nodes, typical skin rash and internal organ involvement, a “ Probable diagnosis “of DRESS syndrome was made using the RegiSCAR Criteria. DRESS induced by psychotropic medications have been scarcely reported. Extensive reporting and educating clinicians as well as patients regarding DRESS will lead to decreased morbidity as well as mortality. Further research is warranted in elucidating its pathogenesis with the aim of designing personalized treatment plans.

**Keywords:** DRESS Syndrome, Olanzapine, Psychosis, Eosinophillia.

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### INTRODUCTION

Cutaneous adverse reactions represent an important group of adverse events caused by psychotropic medications. Severe cutaneous adverse reactions(SCARs) affect about 1 of every 1000 inpatients, TEN and SJS being the most widely reported SCARs [1]. Recently, another SCAR has caught attention due to unique clinical features and unknown pathogenesis: drug reaction with eosinophilia and systemic symptoms (DRESS). Apart from other classes of drugs, the psychotropic medications that have been implicated as offending agents include amitriptyline, clomipramine, lamotrigine, mirtazapine, bupropion, benzodiazepines, carbamazepine, oxcarbazepine, olanzapine etc. [1-3]. DRESS syndrome is considered to be an immunological reaction to a drug or to its metabolites. Although still unclear, the following mechanisms have been suggested as the pathogenic process: (a) immunological hypersensitivity reaction (type IV), with genetic vulnerability determined by HLA types; (b) viral reactivation (particularly HHV-6); (c) expansion of regulatory T-cells [4]. Typically occur 2-6 weeks after drug intake [5]. Usually starts with high grade fever and rash, followed by other systemic reactions such as lymphadenopathy, arthritis, or general malaise. Multiple organ involvement is another distinct feature: liver (50%-87%) and kidney (10%-53%) are most frequently involved [1, 6-7].

### CASE REPORT

The patient was a 24-year-old married Muslim female of a nuclear family belonging to lower socioeconomic status hailing from rural background was brought to the casualty department with erythematous lesions all over the body along with facial puffiness. At the time of presentation, she was drowsy, had icterus, axillary

lymphadenopathy, Anasarca, tachycardia with normal blood pressure, normal breath sounds and heart sounds, with no focal neurological signs.



The patient was then admitted under the dermatology department and subsequently examined by the dermatologists and it was later found that the patient was on some antipsychotic medication for last one month. She was then examined by the psychiatrist. Her history revealed that she had fearfulness, suspiciousness, hallucinatory behaviours, wandering tendencies, decreased sleep and appetite for last 3

months. She was diagnosed as a case of paranoid schizophrenia and was treated on OPD basis from a private psychiatrist with oral olanzapine 10mg and lorazepam 2mg per day. Her symptoms started improving with the above medications. But, around 4 weeks after initiation of medications, she developed high grade fever followed by rashes all over the body. Within next 3 days, she developed facial puffiness and erythematous lesions and was then brought to the hospital.

Blood investigations revealed raised absolute eosinophil count (AEC) ( $3010 \text{ cells/mm}^3$ ), high serum bilirubin levels (Total:  $12.6 \text{ mg/dl}$ ; I:  $1.8 \text{ mg/dl}$ ; D:  $10.8 \text{ mg/dl}$ ), raised Aspartate Transaminase (AST) ( $444 \text{ mg/dl}$ ) and also increased Alanine transferase (ALT) levels ( $359 \text{ mg/dl}$ ) with peripheral smear revealing no malarial parasites. Other blood and urine examination were all negative for bacterial (Leptospiral Antibody), parasites (plasmodium vivax and plasmodium falciparum) and viral markers (HbsAG, Anti-HCV, Anti-HAV, Anti-HEV). Her ECG and Chest X-ray revealed no specific changes. However, her USG Whole abdomen revealed peritoneal fluid ( $120 \text{ ml}$ ).

A provisional diagnosis of DRESS syndrome was considered. All Psychotropic medications were stopped initially. She was started on systemic corticosteroid (intravenous dexamethasone  $16 \text{ mg/day}$ ), antihistaminic agent (levocetirizine  $10 \text{ mg/day}$ ), topical steroid (clobetasol lotion). Lorazepam  $2 \text{ mg}$  at bedtime was added on 3<sup>rd</sup> day. She gradually improved symptomatically, and by the 7<sup>th</sup> day, her blood investigations came out to be near baseline value (AEC:  $208 \text{ cells/mm}^3$ ; Serum bilirubin: T:  $1.2 \text{ mg/dl}$ , D:  $1.1 \text{ mg/dl}$ , I:  $0.1 \text{ mg/dl}$ ; AST:  $72 \text{ mg/dl}$ ; ALT:  $54 \text{ mg/dl}$ ). Dexamethasone was gradually tapered off. At the time of discharge, oral haloperidol  $5 \text{ mg/day}$  was added, while the patient and the caretakers were informed regarding any red flag signs of possible adverse reactions.

After 2 weeks, and then after 4 weeks of discharge, the patient was reviewed and was found to be maintaining well with the prescribed medications. Currently, she is on oral haloperidol  $5 \text{ mg/day}$ . She is free of the psychotic symptoms and with normal biological functions. No particular adverse reaction to haloperidol including EPS have developed so far.

## DISCUSSION

Considering the occurrence of fever, eosinophilia, enlarged lymph nodes, typical skin rash and internal organ involvement, a "Probable diagnosis" of DRESS syndrome was made using the RegiSCAR Criteria. [8]. As there was a clear temporal association between development of the symptoms of DRESS syndrome with initiation of Olanzapine and thereafter withdrawal of the drug Olanzapine leading to symptom improvement, hence, Olanzapine was considered to be the offending agent in this case.

This case presents a typical feature of onset in 4 weeks which was similar to mean onset of DRESS syndrome of 3.9 weeks (S.D=2.3) reported in a review of 172 cases following initiation of the offending agent [9]. In our case, single drug was found to be etiological agent, contrast to both Valproate and Olanzapine had been postulated to be the offending agents [10-11]. The principles of management include stopping the notorious agent, judicious use of corticosteroids and supportive care [3].

This case had management challenges. Firstly, several second generation antipsychotics have been found to cause DRESS syndrome [3]. Hence, we are left with limited options of antipsychotics to manage this case of paranoid schizophrenia. Haloperidol was finally decided to be used in this case as it was found to be effective in such cases [11-13]. Secondly, DRRESS syndrome has got a significant morbidity and mortality with about 10 % cases succumbing to it, requiring high index of precision and prompt management [5]

## CONCLUSION

Although a rare occurrence, DRESS represents a significant and potentially devastating adverse reaction to psychotropic drugs. DRESS induced by psychotropic medications have been scarcely reported. Extensive reporting and educating clinicians as well as patients regarding DRESS will lead to timely intervention and decreased morbidity as well as mortality. Further research is warranted in elucidating its pathogenesis so that vulnerable patient groups can be identified with the aim of designing personalized treatment plans.

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