Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) Syndrome in a Patient with Bipolar Disorder: A Case Report

Dear Sir,

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) is a severe drug reaction characterized by mucocutaneous rash, fever, multi-organ involvement, and hematologic abnormalities.[1] Incidence is about one in 1000–10,000 individuals exposed to offending drugs, with 10%–20% mortality.[2] Drugs such as allopurinol, sulfasalazine, and anticonvulsants have been associated in existing reports.[1,2] Very few reports, however, exist in psychiatric literature.[3–6] PubMed-based MeSH search [("Drug Hypersensitivity Syndrome"[Majr]) AND "Psychotropic Drugs"[Majr]] and search terms restricted to the title/abstract returned less than 10 case reports, inclusive of cross-reference search.

Mr X, 58 years, a known case of hypertension for 6 years (well-controlled on amlodipine 5 mg and telmisartan 80 mg), with a family history of unipolar depression in his mother, with no history of allergies, had treatment-naive bipolar-II disorder for >15 years. He had a severe depressive episode with psychotic symptoms in February 2015, which necessitated seeking treatment. He was initiated on lithium (900 mg), fluoxetine (20 mg), and olanzapine (5 mg) in daily doses at a private hospital with which there was a significant improvement. Six weeks later, he developed fever, generalized maculopapular erythematous changes with minimal edema of the skin and fine scaling, associated with the respiratory difficulty, and status epilepticus. The rest of the systemic examination was noncontributory. Investigations revealed raised transaminases (SGOT: 120; SGPT: 156 units/L), leucocytosis (13,000/μL), eosinophilia (2000/μL) along with hyponatremia (102 mEq/L). MRI brain and CSF examination were normal.

The patient visited our institute in May 2015. Dermatological opinion was sought for the skin lesions; a diagnosis of DRESS was considered as per RegiSCAR (score 4) and Bouquet's criteria.[7,8] The causality by the offending agents was established as per the Naranjo Algorithm (score: 10, definite probability), and severity of adverse drug reaction was rated as per Hartwig's Severity Assessment Scale (score: 5, severe).[9,10] All psychotropic drugs were discontinued. Any possible consumptions of ayurvedic or homeopathic preparations were ruled out. He was started on an infusion of sodium valproate for 24 hours and inj. dexamethasone (12 mg), which was continued for five days and later shifted to oral prednisolone (40 mg/day), with improvement in the systemic symptoms over 2 weeks. However, after 1 week of discontinuation of psychotropic medications, his hypomanic symptoms resurfaced, which was managed with the quetiapine (100–200 mg/day). He was discharged after 2 weeks of hospitalization. A subsequent attempt at slow taper of prednisolone (5 mg fortnightly) led to re-emergence of generalized rashes; however, they responded again to 40 mg/day.

After a month of euthymia, he started experiencing depressive symptoms while on quetiapine and prednisolone. In August 2015, escitalopram (5–10 mg/day) was added, and prednisolone was slowly tapered to 30 mg/day. After a week, he developed similar rashes (in face and upper extremities), with fever. Escitalopram was immediately stopped, and prednisolone increased to 40 mg/day, with improvement. Relevant investigations for fever (malarial, typhoid, and dengue serology; viral markers; and blood and urine culture) were unremarkable.

Given the severity of depressive symptoms and the caregiver's initial refusal for modified electro-convulsive therapy (MECT), nortriptyline was added cautiously and built up to 125 mg/day, over his other medications (prednisolone 40 mg, quetiapine 200 mg/day, clonazepam 1.5 mg/day, amlodipine 5 mg, telmisartan 80 mg). Given nonimprovement, he finally received 10 sessions of MECT. The patient maintained euthymic till October 2015, when nortriptyline was stopped due to hypomania. He was euthymic on quetiapine (600 mg/day) by November 2015.

Prednisolone was successfully tapered off very slowly (by February 2016). A subsequent depressive episode (2016) was managed by the addition of nortriptyline for a few months only. As of March 2020, he continues to remain euthymic on quetiapine monotherapy (400 mg/day) and is in regular follow-ups.

This treatment-naive patient of BD-II developed DRESS on multiple psychotropics. It is difficult to delineate the precise culprit out of the three drugs (lithium, fluoxetine, and olanzapine). Each has very few (1–3) reports in indexed literature, despite their widespread use. Further, a sequential rechallenge was deemed to be out of question, given the serious life-threatening risks and a long lag period to develop DRESS.

The choice of subsequent medication for severe depression posed a management dilemma. It was decided not to rechallenge with lithium or SSRIs (as a class), given their prior temporality. Anticonvulsants were not considered due to a strong association in the literature. Finally, nortriptyline (selective for norepinephrine transporter) and quetiapine were found to be safe in this patient.

The use of steroids, though lifesaving, could have exacerbated the mood symptoms in this case. The available literature on DRESS is unclear on the recommended duration of steroid use, ranging from 3–4 weeks to several months.[2,6] In this patient, DRESS developed after 6 weeks of exposure; this is in concurrence to the literature (mean exposure: 35.6 days; range: 7–120 days).[2] Hyponatremia is not commonly associated with DRESS but has been described in a few reports.[2,6]

Hypothesized mechanisms for DRESS include defective metabolic enzymes, sequential virus activation, and certain HLA alleles (e.g., HLA-B*15:02 with carbamazepine).[2,6] No specific allele

associations are known for psychotropic drugs. Patch and lymphocyte transformation testing might help to identify the drug, but neither is widely used or accepted.[11,12]

This article adds to the scarce reports describing psychotropic-drug-induced DRESS, along with the subsequent clinical-psychiatric management and a safe trial on quetiapine and nortriptyline. The report emphasizes the need for awareness about this rare yet potentially life-threatening drug reaction.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical Statement

Written informed consent and anonymity have been ensured.

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Gastaut-Geschwind Syndrome in a Patient of Bipolar Disorder: A Case Report

To the Editor,

Gastaut-Geschwind Syndrome (GGS) is a constellation of symptoms commonly seen in patients with temporal lobe epilepsy. GGS can be interpreted as a manifestation of the temporo-limbic neuropsychiatric syndrome. It is characterized by personality changes and behavioral changes like hyper-religiosity, hypergraphia, compulsive documentation, an exaggerated philosophical concern, atypical sexuality (usually decreased), interpersonal stubbornness, and circumstantial thought process.[1,2] Here, we present a rare case report of GGS in a patient of bipolar disorder (BD) without any evident neurological finding, which adds to the current scientific literature.

Case Discussion

Mr M, a 37-year-old married craftsman, was brought by his wife to the department of psychiatry in a tertiary care