Drug hypersensitivity syndrome with lithium

Sir,

Drug hypersensitivity syndrome (DHS) is one of the more severe cutaneous adverse drug reactions. It is characterized by a clinical triad of fever, skin rash and internal organ involvement. It has been given different names like dapsone syndrome, febrile mucocutaneous syndrome, drug rash with eosinophilia and systemic symptoms (DRESS), and drug-induced delayed multi-organ hypersensitivity syndrome (DIDMOHS).[1] Sarantidis and Waters[2] (1983) did a review and controlled study of cutaneous conditions associated with lithium carbonate. They reported the overall incidence of cutaneous reactions possibly secondary to lithium as 34%. In their study, psoriasis and acneiform eruptions were more frequent followed by atopic dermatitis, alopecia areata, exfoliative dermatitis, icthyosis, prurigo nodularis, angular chelitis and unspecified eruptions. In their literature review they have also found the occurrence of other cutaneous conditions with lithium like maculopapular rash, ulcer, folliculitis, stomatitis and xerosis.[2] A review of the literature shows very few reports of patients developing hidradenitis suppurativa and DHS while receiving lithium.[3,4]

A 54-year-old married female with personal history of hypothyroidism and bronchial asthma without any significant family history of psychiatric illness presented to our outpatient center with a history suggestive of a depressive episode. She has had depressive episodes in the past and a diagnosis of recurrent depressive disorder, currently severe depression with psychotic symptoms was made. Patient was initially treated with tablet risperidone for six months following which the psychotic symptoms remitted. Due to persisting depressive symptoms, tablet sertraline was added and titrated up to 150 mg/day. In view of the lack of adequate response, the patient was admitted and tablet venlafaxine was started in place of sertraline. Tablet venlafaxine was titrated up to 300 mg/day and quetiapine (125 mg/day) was substituted in place of risperidone due to extra-pyramidal side-effects. As depressive symptoms did not remit patient was started on tablet lithium carbonate initially with 300 mg/day and later titrated to 600 mg/day. Her serum lithium level was 1.12 with 900 mg/day due to which the dose was reduced to 600 mg/day. The patient showed significant improvement and was discharged with advice for regular follow-up.

The patient presented after approximately four weeks with symptoms of fever and generalized skin rash. On examination the patient had fever (102 ^{0}F),

generalized erethematous maculopapular rash, xerosis, desquamation of skin, glossitis, oral cavity erythema, hepatomegaly, facial edema, mild pedal edema, crepitations in the left scapular pulmonary area and, cervical, epitrochlear and inguinal lymphadenopathy. The hematological report showed a total count of 12,600 with a differential count of neutrophils (60%) and lymphocytes (40%). The liver function tests were abnormal with elevated hepatic enzymes-AST: 113 U/L, ALT: 162 U/L, ALP: 746 U/L and GGT: 310 U/L. A routine urine examination was positive for protein and nitrate with specific gravity of 1.030. A clinical diagnosis of drug hypersensitivity syndrome was made and patient was treated in the medical/ dermatological ward as an in-patient. All psychotropic medications were stopped and she was treated with 4 mg dexamethasone intravenously eight-hourly for the first two days followed by oral prednisolone 40 mg per day, which was tapered at the rate of 10 mg once in four days. The final tapering of steroids was done with 10 mg on alternate days for a period of ten days. The patient's clinical condition improved and she was shifted to the psychiatric ward for further management of depression.

After approximately one week patient was started on tablet dothiapin for the treatment of depression. Due to persistent depression lithium was used as an augmentation agent with a dose of 600 mg/day while she was taking prednisolone 10 mg on alternate days. The patient developed generalized maculopapular rash with pruritus from the end of the second day of introduction of lithium carbonate. Dermatologists concluded that lithium was the causative agent for the DHS and it was decided not to challenge the patient with lithium for lifetime. The Naranjo Adverse drug reaction probability scale final score was 6 (probable).[5] On the introduction of oral escitalopram 5 mg/day patient reported significant improvement in depression that she has maintained during the follow-up period of one month.

DHS usually occurs on first exposure to the medication but with delayed onset. DHS as understood today, is an immunologically mediated symptom complex occurring in some genetically susceptible individuals exposed to an optimal dose of a specific drug for a specific duration of time.[1]

In conclusion, we report a case of DHS secondary to lithium carbonate. Recurrence of dermatological lesions on reintroduction of lithium strongly implicates lithium carbonate as the offending agent in our subject.

K. B. Shreedhar, J. Madhukara[1], J. Jessy, S. M. Manohari, K. Srinivasan

Departments of Psychiatry, [1]Dermatology, St. John's Medical College Hospital, Bangalore - 560 034, India

Address for correspondence: Dr. Shreedhar K. B., Department of Psychiatry, St. John's Medical College and Hospital, Johnnagara, Bangalore - 560 034, India.
E-mail: dr.shreedhar@gmail.com

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