Galore International Journal of Health Sciences and Research
Vol.5; Issue: 2; April-June 2020
Website: www.gijhsr.com
Case Report *P-ISSN: 2456-9321*

Disulfiram Induced Exanthema- Case Report

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ABSTRACT

Disulfiram is an FDA approved drug for the treatment of Alcohol dependence syndrome. It is a deterrent and produces unpleasant symptoms due to accumulation of acetaldehyde in the blood. Dermatological side effects with the drug are rare, but can be severe enough to warrant hospitalization. We present a case of exanthema induced by disulfiram in a patient with alcohol dependence syndrome and multiple comorbidities.

Keywords: Disulfiram, Exanthema, Intermediate Risk.

INTRODUCTION

Adverse Drug Reactions (ADRs) with disulfiram treatment occur with an intermediate frequency (1 in 200-2000/year) often affecting the gastrointestinal and nervous systems. [(1)] Effects on the skin are rare, with two case reports published on disulfiram induced toxic pustuloderma and hyperpigmentation. [(2,3)] We present a case of disulfiram induced exanthema in a patient with alcohol dependence syndrome and multiple medical comorbidities.

CASE ILLUSTRATION

A 36 years old graduate, working as a Project Manager in the Middle East presented to the Psychiatric OPD with history of alcohol use over 23years. His symptoms fulfilled the ICD-10 criteria of Alcohol Dependence Syndrome and Nicotine dependence syndrome. Past history of intravenous use of heroin was present until 12years back. He also had a history of multiple falls under intoxication.

He underwent surgery for pilonidal sinus in 2007, during which he was diagnosed with Hepatitis C and allergy to sulfa drugs and penicillin. He was commenced on insulin injections in 2014 for Type II Diabetes mellitus. Nine months ago, he developed Stroke and was treated conservatively. Following this, he was advised strict abstinence from alcohol and nicotine, but was unsuccessful in his attempts to quit. He was subsequently admitted to a deaddiction facility and his detoxification phase was uneventful. He was started on 125mg of disulfiram. On the fifth day of commencement, he complained of itching. Erythematous lesions were noted on his forearms, which progressed to the neck and face over the next two days. He had no history of any new chemical exposure around the time of eruption.

His mental state examination was unremarkable and cognitive functions were intact. On General Physical Examination, he was afebrile with a pulse rate of 76/minute, blood pressure of 120/70mm Hg (sitting and lying), and BMI-22.2. There was no pallor, icterus, cyanosis, clubbing, lymphadenopathy and oedema. He had a tattoo inscribed on his left forearm, but no tracklines, sinus or scars. In addition to this, he had multiple erythematous papules over forehead, trunk and extremities, erythema with scaling and crusting over cubital and popliteal fossa, erythematous crusted plaques over bilateral groin folds and thighs, erythema and hyperpigmented plaques over both the palms, crusting and fissuring over lips and crusting and erythema of nasal mucosa. His oral cavity and genitals were

normal. Systemic examination was within normal limits, except for slurring of speech.

His investigations revealed raised levels of eosinophils and absolute eosinophil count. His blood sugars were elevated, but other blood parameters and electrocardiogram were normal. Ultrasound abdomen and pelvis showed hepatomegaly. His neuroimaging and EEG were normal.

Disulfiram was stopped and he was referred to the Department of Dermatology, where he was treated with hydroxyzine, oral and topical steroids and antibiotics. His lesions abated after cessation of disulfiram and was then shifted to the deaddiction ward. The repeat investigations were within normal limits.

DISCUSSION

A diagnosis of disulfiram induced exanthema was made based on the temporal relationship between the onset of rash and administration of disulfiram, [4] the incubation period (i.e., peak incidence of cutaneous reactions within 7days of initiation of disulfiram), [1] the clinical pattern of the eruption (bilaterally symmetrical and associated with severe itching and fading with desquamation) and improvement on drug withdrawal. However, we did not re-challenge the patient with disulfiram for ethical reasons and patient's unwillingness for the same. [4] The score on the Naranjo's adverse reaction (ADR) scale suggested probable ADR. [5] This was due to the ethical limitations when applied to our patient (such as increase of dose, administration of placebo, re-challenges etc. which couldn't be carried out).

The disulfiram induced maculopapular rash was differentiated from viral exanthema by the absence of fever, lymphadenopathy or prodromal symptoms, typical clinical pattern with bilaterally symmetrical lesions, raised eosinophils on investigations, improvement of symptoms with stoppage of disulfiram and treatment with anti-histaminic drugs and steroids. Resolution of lesions was seen in our patients with steroids as opposed to predisposition to secondary bacterial infections in patients with viral maculopapular rash. [6]

A clinically significant Ig-E mediated (immunologic) cross reactivity in patients with confirmed penicillin allergy to cephalosporins has been established. [7] Our patient had previous adverse drug reactions to antibiotics (sulfa and penicillin) and could have been genetically predisposed to ADR with disulfiram. The maculopapular drug eruptions are also considered to bea T-cell-mediated delayed hypersensitivity (Type IV) reaction. Drug-specific CD4+ T cells expressing cytotoxic granule proteins such as perforin and granzyme B are critically involved in killing activated keratinocytes present in and contribute to the generation of vacuolar alteration and destruction of basal keratinocytes. [6] The pre-existing illnesses in our patient (Diabetes Mellitus, Hepatitis C, Stroke, Substance dependence) and drug interaction with insulin may have predisposed our patient to develop exanthema. [8]

CONCLUSION

ADRs are seen in 2-3% of hospitalised patients and the estimated prevalence rate of disulfiram induced rash in men is about 1%. [1,4] Clinical manifestations of cutaneous ADRs can range from transitory exanthematous rash to the potentially fatal Toxic Epidermal Necrolysis (TEN). [4] Despite its adverse effect profile, disulfiram is still widely used due to its efficacy in particular patient groups. [8] Though dermatological adverse effects are uncommon, patients and their family members should nevertheless be made aware of these while obtaining informed consent to commence disulfiram.

DECLARATION OF PATIENT CONSENT:

The authors certify that they have obtained all required patient consent forms. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

ACKNOWLEDGEMENT

We would like to thank the Faculty and Post graduate residents. Dept of Dermatology, Father Muller Medical College for their support and co-operation.

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How to cite this article: Mascarenhas JJ, Rao PV. Disulfiram induced exanthema- case report. Gal Int J Health Sci Res. 2020; 5(2): 1-3.

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