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Case Report

Clonazepam induced maculopapular rash: a case report

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ABSTRACT

Clonazepam is a benzodiazepine with prominent anticonvulsant action than other members of the group at equisedating doses. It especially blocks pentylenetetrazole-induced seizures. Other important actions include anxiolysis. Common adverse effects to Clonazepam include drowsiness and lethargy. In this submission we report a case of Clonazepam induced maculopapular rash in a 30 year old female treated for panic disorder.

Keywords: Clonazepam, Adverse cutaneous drug reaction, Maculopapular rash

INTRODUCTION

Clonazepam is a benzodiazepine with prominent anticonvulsant action than other members of the group at equisedating doses.[1] It especially blocks pentylenetetrazole-induced seizures and also effective in akinetic and myoclonic seizures. It is used as a second line drug for treatment of primary generalized epilepsy and for status epilepticus. It is also used in the treatment of panic disorder.[2] It is a well tolerated drug and common adverse effects include drowsiness and lethargy.[1] In this submission we report a case of clonazepam induced maculopapular rash in a 30 year old female treated for panic disorder.

CASE REPORT

A 30 year old female presented to the psychiatry OPD with complaints of unknown fear, dizziness, feeling of impending doom, sweating and palpitations which are episodic in nature each lasting for 3 to 5 minutes. Patient was suffering with these symptoms for the past one month. There were no specific aggravating or relieving factors. History from husband had confirmed patient's complaints. She was not receiving any other medications and denied having a history of drug allergies, substance abuse and caffeine usage. She was diagnosed with panic disorder (as per ICD -10.F41.0) for which she was advised clonazepam 0.5mg twice a day. Eight days after starting clonazepam treatment, an itchy rash developed which progressed during the next 24 hours. She returned to the psychiatrist with pink red eruptions on her extremities (Figure 1). These rashes were associated with burning and itching. On examination, symmetrical erythematous maculopapular rash was observed on both upper limbs and lower limbs. The rash was also seen on palms. She was afebrile and had no blisters, purpura, or pustules; there was also no involvement of the mucous membranes. There was no involvement of face, trunk and back. All routine blood investigations were within normal limits.

An adverse cutaneous drug reaction to Clonazepam was suspected from the history and clinical examination. The causality assessment score carried out using the Naranjo's algorithm suggested a probable causality for Clonazepam[3] (Total score was 6). A diagnosis of Adverse Cutaneous Drug Reaction [ACDR] to clonazepam was

made and the patient was instructed not to take same drug again. The patient was treated with hydroxyzine 25mg TDS for 6 days and topical calamine lotion advised. The rash gradually resolved over the next 6 days.

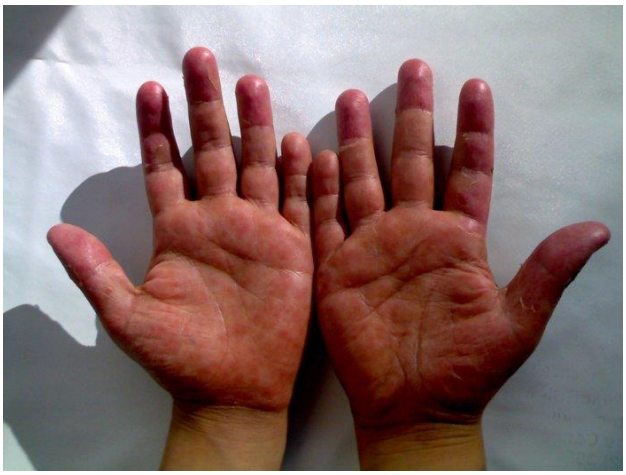

Figure 1: Maculopapular rash involving palms.

DISCUSSION

Adverse drug reactions are most commonly manifested as cutaneous eruptions and are observed in about 1% of patients taking any particular medicine. The most common type of drug-induced cutaneous eruption is a maculopapular exanthem.[4] Maculopapular rash is often referred to as moribiliform rash that exhibits the combined characteristics of macules and papules. The rash typically begins on the trunk and pressure-bearing areas and then progresses becoming confluent and covering large areas of the body. They are distributed symmetrically with lesions appearing on the upper torso or head and neck. The pink to red papules often coalesce and yield a rough or coarse texture. Patients may also experience moderate to severe pruritus and fever. The rash usually appears 8-10 days after initiation of drug therapy (but can be earlier or later) and fades within a similar period after medication withdrawal.

Common risk factors for drug eruption include the type of drug, female gender, older age, and immunosuppression. Delayed immunological hypersensitivity to the drug or a metabolite involving both humoral and cell-mediated mechanisms are implicated in etiology of drug eruptions. The reactions are often unpredictable, dose-independent, and idiosyncratic.[4]

Differential diagnoses for a maculopapular rash include anaphylaxis, drug eruptions (particularly in adults), viral exanthems (particularly in children), rickettsial infections, bacterial infections, rheumatological diseases, and systemic diseases. The correct diagnosis can be made by eliciting proper history and from the case scenario.

Clonazepam was introduced specifically as an anticonvulsant.[1] Clonazepam has a wide spectrum of activity, having a place in the management of the motor seizures of childhood, particularly absence seizures and infantile spasms. It is used intravenously in status epilepticus. It is also useful in complex partial seizures and myoclonic epilepsy in patients who are not adequately controlled by phenytoin or carbamazepine. However, its value is limited by development of tolerance to the therapeutic effect within one to six months or so. Oral treatment is usually started with a single dose at night. The dose is gradually titrated upwards until control is achieved or adverse effects become unacceptable.

The other uses include adjunctive treatment in acute mania, psychogenic pruritus, and panic disorder with or without agoraphobia. Panic disorder is characterized by the occurrence of unexpected panic attacks and associated concern about having additional attacks, worry about the implications or consequences of the attacks, and/or a significant change in behaviour related to the attacks.

The most common and important adverse effects of clonazepam are lethargy, somnolence and dizziness.[1] These can be minimized by starting with a low dose and then titrating upwards. Sedation often disappears during chronic treatment. More serious and less common effects include muscular incoordination, ataxia, dysphoria, hypotonia and muscle relaxation, increased salivary secretion and hyperactivity with aggressive behaviour.

Skin reactions to clonazepam are not well reported. A single case of Clonazepam induced Erythema multiforme has been reported by Amichai et al 1998.[5] These mild cutaneous reactions gain attention as they also represent the early manifestation of rare, severe drug-induced cutaneous reactions, such as Stevens - Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) that have high rates of morbidity and mortality.[6] Also upon occurrence of dermatological manifestations, the patients may become noncompliant, which is one of the common causes for treatment failure. Therefore, withdrawal of the offending treatment and further change in drug therapy is imperative in patients with maculopapular exanthem where drug involvement is suspected, particularly when fever or influenza like symptoms are also present or where there is mucosal involvement.

CONCLUSION

To the best of our knowledge, skin reactions to clonazepam are not well reported. Practitioners should be aware of this rare adverse event, since clonazepam is a common drug used in psychiatric disorders. Upon occurrence of dermatological manifestations, the patients may become noncompliant, which is one of the common causes for treatment failure. The patients undergoing treatment on an outpatient basis should be counseled for the early recognition of dermatological manifestations to prevent severe reactions.

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