

Clozapine Induced Skin Rash – a report of two cases

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ABSTRACT

Atypical antipsychotics are known to cause cutaneous reactions but are very rare. There have been individual cases of different skin reactions with olanzapine, risperidone and olanzapine. Herewith we have presented two cases of cutaneous rash following clozapine use.

Keywords: clozapine, rash, skin, atypical antipsychotic.

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INTRODUCTION

Antipsychotic drugs causing adverse cutaneous reactions have been reported in almost 5% of patients which can be exanthematous eruptions, skin pigmentation changes, photosensitivity, urticarial, pruritus, etc [1]. Atypical antipsychotics are known to cause fewer dermatological reactions compared to typical ones but there have been reports of skin lesions associated with risperidone, olanzapine and aripiprazole. [2-4]. The majority of cutaneous lesions are benign and are easily treated [5]. Herewith we are presenting two cases of patients who had cutaneous rash following clozapine use.

CASE 1

A 87 year old female was brought to us with complaints of irrelevant talking and seeing things invisible to others since 15 to 20 days. She would occasionally tell that she can see pins and needles all over her bed; she would occasionally feel that these have been kept to harm her. She would get angry, occasionally abusive towards family members due to this. She would feel that they are trying to harm her. In spite of everyone convincing that there are no pins and needles on her bed she would not agree. There was no previous such history. Gradually her condition started worsening and she had stopped eating food and also her sleep was reduced. Hence her family members brought her to us. On examination there was no memory or orientation problem. Only the patient complained of seeing pins and needles and that family member have kept them to harm her.

We diagnosed as having late onset psychosis and started on tablet olanzapine 5 mg at night. All her routine blood investigations including electrolytes and serum ammonia came to be within normal limits. As there was no improvement after 7 days dose of olanzapine was increased to 10 mg and later on gradually to 20 mg. But still after 3 weeks there was no improvement so tablet clozapine was added

12.5mg at night. The relatives found 10% improvement after 7 days so the dose was increased to 25mg at night.

The patient was much better for next 4 weeks; so we continued her on tablet olanzapine 20mg and tablet clozapine 25mg. But 2 weeks later the patient was brought back to us with complaints of rash on her body and itching all over body. These rashes were of maculo papular type and at some places bullous in nature. [Figures 1 & 2] The general physician had given some local applications which didn't help much. So we consulted our dermatology department and they diagnosed her as having drug induced rash. So we stopped both the antipsychotics, and gave only antihistaminics and skin emollient cream advised by the dermatologist.

After 6 to 7 days the skin rashes disappeared and patient was better. But her visual hallucinations recurred. So we decided to start on tablet clozapine 12.5mg as she had responded to it in the past. But the rash recurred after 2 days and it was stopped. After stopping clozapine, rash disappeared. Currently she is on tablet haloperidol 1.5mg twice a day only.

CASE 2

A 41 year male studied till 10th standard and working as labourer was brought to us with complaints of suspiciousness towards other and hearing of voices inaudible to others, angry abusive behaviour and reduced sleep since 10 years and the complaints have increased since 1 month.

He would have suspiciousness towards 6 of his family members that they will kill him and are always against him. Due to this he would get abusive and assaultive towards them to the extent that he had lodged a police complaint against them. His condition gradually started worsening; he would feel that they had some machines to keep a tab on his daily activities. They talk amongst each other via the antenna; they can remove his thoughts and insert their thoughts in his mind through these machines. He also would hear voices inaudible to others of unknown males and females giving bad words to him and even ordering him to die on railway tracks.

For the above complaints he was admitted to our hospital in the past several times and he would get better with medications. But after discharge he would be non-compliant to medicines and again complaints would start.

This was his 6th admission. We started him on tablet olanzapine 20 mg, haloperidol 10mg tablet trihexyphenidyl 4mg in divided doses. As he did not respond well to medicines after 10 days, we added tablet clozapine 25mg at night. After 7 days he started complaining of itching all over the body and rash which were described as urticarial plaques on upper limb and abdomen by dermatologist. [Figures 3 & 4] We stopped all the psychotropic medications and gave antihistaminics and calamine lotion along with tablet prednisolone. The dermatologist gave the risk of drug allergy to our medications as follows: Clozapine 2%, olanzapine >2%, haloperidol <1%, trihexyphenidyl <1%. We diagnosed as clozapine induced drug rash as it was the only new medicine added, rest all he was taking in the past too. Once he was stabilised we started him on tablet haloperidol 5mg twice a day and trihexyphenidyl 2mg twice a day. Gradually the doses were up titrated and patient gradually became better.

DISCUSSION

Clozapine is a dibenzodiazepines antipsychotic and interacts with several different subtypes of dopamine receptors (D1, D2, D3, D4), serotonin receptors (5-HT1A, 5-HT2A, 5-HT2C, 5-HT3, 5-HT6, 5-HT7), adrenergic receptors (alpha-1, alpha-2), histaminergic receptor (H1), and muscarinic receptor (M1). The commonly reported adverse effects are central nervous system reactions (sedation, dizziness/vertigo, headache, and tremor), cardiovascular reactions (tachycardia, hypotension, and syncope), and autonomic nervous system reactions (hypersalivation, weight gain, drooling, sweating, dry mouth, and visual disturbances), and gastrointestinal reactions (constipation and nausea). Antipsychotics can lead to varied degrees of severity of skin reactions ranging from generalized cutaneous rashes (50–95%) and urticaria (5–22%) to more severe lesions warranting emergency treatment like angioedema, acute generalized exanthematous lesions, toxic epidermal necrolysis and 'Steven-Johnsons' syndrome [6]. There have been

individual cases of clozapine induced cutaneous reactions like pruritus, exanthematous reactions, urticaria, photosensitivity, drug-induced pigmentation, erythema multiforme, Stevens-Johnson syndrome/toxic epidermal necrosis and drug hypersensitivity vasculitis. The exact etiology for these reactions is not known but can be by direct toxic reaction or indirect pathways related cytokine release [7]. Cutaneous skin reactions though rare with atypical antipsychotics, we need to be aware of them. If they are picked up at the earliest severe life threatening allergic reactions can be avoided.

Figure 1 - Maculo popular rash in case 1



Figure 2 – Bullous lesions in Case 1



Figure 3 - Skin rash over abdomen in case 2



Figure 4: Skin rash over forearm in case 2



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