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Chlorpromazine Induced Angioedema- A Case Report

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ABSTRACT:
Introduction: Angioedema is an uncommon side-effect of antipsychotics. The literature on association of angioedema with Chlorpromazine is less compared to other antipsychotics. Here, we describe a patient, who developed angioedema following five days of treatment with chlorpromazine and resolution of angioedema with removal of Chlorpromazine.
Methods: A 19 years old female, case of Bipolar affective disorder, came with manic symptoms without psychosis. While on Chlorpromazine, patient developed angioedema within a week along with fever and eosinophilia. As there was a temporal relationship between starting the drug and development of angioedema, after ruling out other causes, Chlorpromazine was tapered and stopped.
Results: Angioedema started to subside while tapering the dose of Chlorpromazine and completely settled within 2 days of stopping the drug. Repeat blood counts were normal and Naranjo's algorithm for ADR probability scale showed a score of 7, indicating probable association.
Conclusion: Antipsychotic-induced angioedema is a transient and self-limiting condition but still it is a cause of distress to the patient. So, it is important to be cautious about this rare occurrence.
KEY WORDS: angioedema, chlorpromazine, antipsychotic
Key messages: There are very limited evidences which have reported the association of angioedema with antipsychotics. Chlorpromazine has the least amount of evidence to support its association with angioedema. Here, we have reported a case of 19-year-old girl who developed angioedema with chlorpromazine.

I. INTRODUCTION:

Chlorpromazine is a typical/first generation antipsychotic, belonging to class of phenothiazines[1]. Chlorpromazine has antagonistic properties at various receptors like dopaminergic (D_1, D_2, D_3 and D_4), serotonergic (5-HT_2, 5-HT_6 and 5-HT_7), muscarinic (M_1 and M_2), histaminergic (H_1 receptors) and alpha adrenergic (α_1- and α_2) receptors. It blocks the postsynaptic dopamine receptors in cortical and limbic areas of the brain, and prevents the excess of dopamine in the brain.[1,2] By this mechanism it leads to a reduction in psychotic symptoms, such as hallucinations and delusions. Thus, it is used in disorders like Schizophrenia, Bipolar affective disorder etc. It is also used for nausea, vomiting and chronic hiccups. Weight gain, sedation, cholinergic side effects like dry mouth, constipation, urinary retention and extrapyramidal side effects like tremor, dystonia are the common side effects seen with Chlorpromazine. Angioedema is usually seen with blockers of the renin-angiotensin-aldosterone system probably caused by elevated bradykinin levels. Other drugs commonly associated are beta lactam antibiotics and non-steroidal anti-inflammatory drugs.[3] With typical and atypical antipsychotics, angioedema is an uncommon side-effect. Here, we present a case of a 19-year-old female, who developed angioedema following 5 days of treatment with Chlorpromazine.

II. CASE REPORT:

A 19-year-old single female, college student, belonging to lower middle socioeconomic status came with complaints of pervasive irritability, increased psychomotor activity, increased energy levels, reduced sleep and anger outbursts, 6 months after she had discontinued her medicines. She was diagnosed to be having mania without psychotic

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symptoms a year back. She improved within one month of treatment. She was on regular medications for 6 months and after which she stopped taking them which resulted in her current episode. Considering the good response during her previous episode, she was started on Oral Olanzapine 10mg HS (subsequently increased to 20mg), Sodium valproate 750mg and Lithium 800mg in divided doses. One dose of parenteral Haloperidol 5mg and Lorazepam 4mg was given. On day 2, Oral Chlorpromazine 300mg in divided doses was added for sedation and control of symptoms. On day 5, she developed facial puffiness, swellings of eyelids, nose, cheeks, lips and had one spike of fever. Her vitals were within normal limits. Systemic examination was normal. Blood counts revealed eosinophilia (12.3%). Urine examination, electrolytes, renal, hepatic and thyroid function tests were all normal. There was no history of similar episodes or drug allergies in the past and no family history of angioedema. There was also no change in dietary/ fluid intake or intake of angioedema associated drugs. Following this, Chlorpromazine was reduced to 200mg and then stopped. As an alternative, Oral Quetiapine 100mg was started. Angioedema started to subside with reduction of dose and it completely settled in 2 days following removal of the drug. Repeat blood counts were normal. Naranjo's algorithm for adverse drug reaction (ADR) probability scale showed a score of 7, indicating probable association between Chlorpromazine and angioedema.



III. DISCUSSION:

Angioedema refers to swelling of the lower layer of skin and tissue just under the skin or mucous membranes. It is not usually seen as a side-effect with administration of typical and atypical antipsychotics. Typical antipsychotics like Haloperidol[4], Trifluoperazine[5] and atypical antipsychotics like Risperidone, Quetiapine[6], Clozapine[7] have evidences to suggest their association with angioedema but Chlorpromazine has only limited evidence. One study[8] reported that, when chlorpromazine was titrated from 150mg to 450mg for a patient, there was development of angioedema within 14 days. Another study[9] reported, that a 45 years old woman, known case of schizophrenia for 25 years, developed persistent edema of face, breasts and pedal edema for 2 years with chlorpromazine. In both the studies, all the possible causes were considered and ruled out. Angioedema resolved only when chlorpromazine was removed. In our case, angioedema started within 5 days of treatment with Chlorpromazine. Chlorpromazine was attributed to angioedema because of temporal relationship between starting the drug and onset of angioedema and also resolution with reduction and stoppage of the drug. All other possible causes were also ruled out. The possible mechanism behind this, could be an allergic reaction or an immune reaction to the drug. It can be explained through various inflammatory processes mediated by kinin-dependent processes, IgE-related hypersensitivity etc.

IV. CONCLUSION:

Antipsychotic-induced angioedema is often transient and self-limiting, but sometimes it can be life-threatening when it involves the airways and also it can cause significant distress to the patient. So, clinicians should be mindful about this rare occurrence to prevent any such adverse events.

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