Case Report

Severe angioedema induced by tomato soup with alprazolam and muscle relaxant drug: A rare and complex drug-food interaction

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ABSTRACT

Molecular interactions at the level of drug and food may lead to the reduced or enhanced effect of a concomitantly given drug or food nutrient. The resultant effects of such interactions may sometimes be severe to life-threatening. Here, we present a rare case of a 40-year-old male patient who developed severe angioedema secondary to drug-food interaction. The patient presented in emergency with complaints of angioedema face, rashes, and difficulty in breathing. History revealed that the patient had been prescribed analgesic muscle relaxant Flexon MR (t.i.d) for severe backache 1 day before. On day 2, the patient self-medicated with tablet alprazolam for inducing sleep followed by intake of hot concentrated tomato soup (350 ml). Within ½ h, the patient took Flexon MR. Following Flexon MR, the patient went drowsy and developed angioedema face and rashes on the whole body with difficulty in breathing. The patient was given injection adrenaline (i.m) injection followed by an injection of chlorpheniramine (i/m) stat. After stabilization of vitals, the patient was discharged.

Key words: Angioedema, Muscle Relaxant, Tomato Soup

Physicians have to face many challenges in clinical practice with the advent of new drugs coming in the market. Despite advancements in knowledge of adverse drug effects and interactions, still there are lacunae to be filled by exploration of mechanisms of such interactions. Drug-food interactions are the interferences in pharmacokinetics or pharmacodynamics of either drug or food, leading to treatment failure or adverse effects [1]. Face angioedema accounts for almost 85% of among total angiomatous cases and obstruction of respiratory passages accounts for 30% mortality if not managed in time [2]. We are presenting the first-ever case of complex drug-food interaction in a male patient who developed severe allergy manifesting as angioedema face following alprazolam, tomato soup, and muscle relaxant.

CASE REPORT

A 40-year-old male was brought to the Emergency Department of a Government Hospital in Delhi with complaints of generalized urticaria and angioneurotic edema of the face and tongue along with breathlessness and drowsiness. History of the patient revealed that he had been prescribed Flexon MR t.i.d. (ibuprofen 400 mg, paracetamol [PCM] 325 mg, AND chlorzoxazone 250 mg) 2 days before for severe lower backache. At night, the patient self-medicated with tablet alprazolam (0.5 mg). After 10 min, he consumed hot tomato soup about 350 ml. Within 30 min of the intake of tomato soup, he took tablet Flexon MR and immediately went to bed. The patient started complaining of generalized itching 20 min after intake of Flexon MR. He noticed spreading rashes all over the body. Gradually, he started having swelling of the face, especially around the eyes and lips (Fig. 1). He was barely able to speak and felt difficulty in breathing. Hence, he immediately rushed to our hospital.

On clinical examination, there were generalized rashes on the body with redness, swelling, and pruritis. The vitals of the patient were as follows: Blood pressure of 100/60 mm of Hg, pulse rate of 88/min, respiratory rate of 24/min, and oxygen saturation of 94% as measured by a pulse oximeter.

The patient was immediately put on oxygen. Intramuscular injection of 0.5 ml of diluted epinephrine (1:1000) was given followed by a slow intravenous injection of Avil (Chlorpheniramine) 20 mg. Blood samples for routine blood tests, including the liver function tests (LFTs), were collected and sent for investigations. The LFTs showed moderately raised aspartate

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aminotransferase 800 IU/L, alanine transaminase 680 IU/L, and total bilirubin 2.1.

The patient was discharged following improvement in clinical condition and stabilization of the vitals. On discharge, the patient was prescribed tablet methylprednisolone 4 mg once daily along with tablet fexofenadine 180 mg once daily for the next 3 days and was advised to report after 5 days. On follow-up, the patient was stable without any sign of an allergy. The patient was advised to avoid the offending drug combination and tomato soup/fruit juice. The patient refused to take the skin atopy or drug provocation test to rule out the cause of allergy.

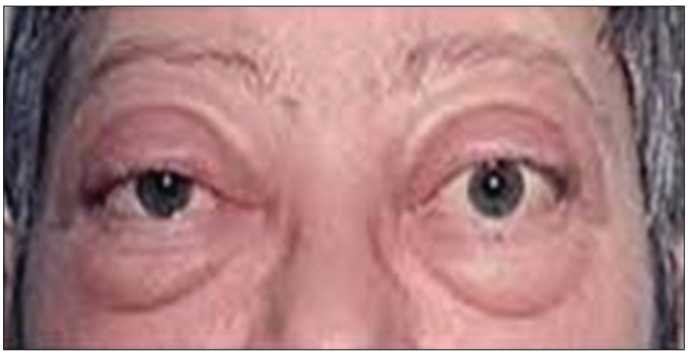

Figure 1: Patient showing angioedema around eyes

DISCUSSION

Chlorzoxazone, a centrally acting muscle relaxant, has some known adverse effects, for example, dizziness, drowsiness, and headache, and dose-dependent hepatotoxicity as encountered in the present case. Both analgesic muscle relaxants (chlorzoxazone, PCM, ibuprofen) and alprazolam (anti-anxiety drug) being metabolized by hepatic cytochrome enzymes tend to produce hepatotoxicity. Raised plasma levels of both centrally acting drugs tend to produce drowsiness when combined together, as seen in the present case [3,4]. History of the patient revealed intake of concentrated hot tomato soup in-between two types of medications mentioned above.

Many studies found that red-colored fruits and vegetables, for example, tomatoes, watermelons, guava, etc., contain an anti-oxidant carotenoid known as lycopene. Lycopene has an inhibitory effect on various cytochrome P450 (CYP 2E1) enzymes. Muscle relaxant Flexon MR (ibuprofen, PCM, and chlorzoxazone) and alprazolam are metabolized in the liver through cytochrome enzymes. When taken with concentrated tomato soup, lycopene present in soup has a tendency to inhibit cytochrome enzymes of the liver, thereby reducing the metabolism of Flexon MR as well as alprazolam. That could have lead to raised plasma levels of both drugs. Excess levels of Flexon MR and alprazolam are responsible for drowsiness. However, the severe allergic response seen in the patient may be an idiosyncratic reaction [5,6]. In general, when all chemicals (drug and food) are being metabolized by the same set of liver enzymes, they are likely to saturate metabolizing enzymes, leading to excess free levels of drugs and their metabolites. Few metabolites generated may act as haptens, which might be responsible for triggering a severe allergic response by direct histamine release, as seen in the present case. Such interactions may manifest as Type-1 hypersensitivity (IgE-dependent) reactions [7].

As per the Food and Drug Administration classification of severity of the adverse event, our patient falls into grade 3, that is, serious adverse event of medical significance requiring hospitalization and emergency management [8]. Skin atopy test or drug provocation test has been proved useful to determine the possible cause of allergic reactions [9]. However, our patient refused to take the skin atopy or drug provocation test to rule out the cause of allergy.

There is a need to explore the molecular mechanisms of complex drug-food interactions. The present drug-food interaction may be the result of hepatic microsomal enzyme inhibition by lycopene, a carotenoid in tomato, leading to increased plasma levels of mentioned drugs. Physicians should keep in mind the possibility of weird allergic reactions and interactions before prescribing. Moreover, the patient should refrain from self-medication, especially for a new drug, never experienced earlier.

CONCLUSION

Drug-food interactions manifesting as severe allergic responses are one of the most important challenges in modern medicine. Inadequate reporting of drug-drug and drug-food interactions among the Indian population is an important cause of unawareness among clinicians regarding the possibility of such severe allergic reactions. Therefore, healthcare workers need to be made aware regarding weird interactions. The health system and the general public should be sensitized to report such incidences. Adequate reporting would help in minimizing patient hospitalization and would further reduce the burden on the healthcare system.

DECLARATION OF PATIENT CONSENT

Authors certify that they have obtained the patient's informed consent for reporting all relevant clinical information, including image.

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