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Case Report

A Rare Incidence of Ketorolac-induced Anaphylaxis: A Case Report

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Abstract

Anaphylaxis or type I hypersensitivity is a class of potentially life-threatening allergic reactions that may be caused by exposure to any drug or substance. These reactions are unpredictable, not dose-related and are not known adverse reactions. Medications as a cause or trigger of anaphylaxis are of concern to health practitioners not only because of the potentially deadly outcomes, but also that it may affect treatment efficacy and patient compliance. In resource-poor settings like ours, confirming anaphylaxis would be a challenge, requiring a high index of suspicion, and well-educated patients. Allergic reactions to analgesics are not common occurrences and ketorolac has been rarely implicated. We present a case of ketorolac-induced anaphylaxis in a 32-year-old man. We also discussed the contemporary scholarly literature.

Keywords: anaphylaxis, non-steroidal anti-inflammatory drugs, ketorolac

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1 INTRODUCTION

Non-steroidal anti-inflammatory drugs (NSAIDs), a class which ketorolac belongs, achieve their activity by inhibiting the cyclooxygenase I and II enzymes which are responsible for the synthesis of prostaglandins and mediate pain and inflammation[1]. NSAIDs are particularly indicated for moderate to severe musculoskeletal pain. Regarding pharmacodynamics, when taken via the oral route, the bioavailability of ketoralac is between 85-95% and is nearly 100% bound to plasma protein and reaches a peak plasma concentration between 1 to 2h after oral administration. Onset of action occurs within 30min to 1h. Ketorolac in all formulations is generally considered to have a good safety profile[2]. It has multiple uses, including controlling pain, reducing inflammation, and is also used for its anti-allergy activities and reversal of fentanyl-induced anaphylaxis[3]. However, paradoxically, it has been reported to cause anaphylaxis. Clinical features of such anaphylactic reactions may be related to angioedema, urticaria, shock, and bronchospasm, which are characteristic of type-I hypersensitivity[4].

In this case report, we described an anaphylaxis following the administration of a 10mg ketorolac tablet in a 32-year-old African male.

2 CASE PRESENTATION

A 32-year-old male reported experiencing musculoskeletal pain, a day after being involved in a minor road traffic accident. The pain was concentrated in the

quadriceps and gastrocnemius muscles. He did not have any other injuries or complaints. He did not have asthma but is known to have hypersensitivity reactions to NSAIDs such as diclofenac and ibuprofen, which was discovered 12 years ago. At that time he noticed difficulty breathing and facial swelling after taking ibuprofen, taking diclofenac had similar reaction. These symptoms were not noted when he took acetaminophen for pain occasionally. After examination, he was generally well. He weighed 64kg, blood pressure was recorded as 136/79mmHg, pulse was 82bpm, and indoor oxygen saturation was 100%. His examination was unremarkable, except for mild tenderness over the hamstring and calf areas bilaterally. He was prescribed oral ketorolac 10mg tablets, to be taken once daily for five days. On the second day, after taking the first tablet 8h earlier, he complained of difficulty in breathing and generalized facial swelling.

However, his condition remained stable with no sign of cardiopulmonary decompensation. His blood pressure was 140/75mmHg, his pulse was 73bpm and he had 100% indoor oxygen saturation. His respiratory rate was 24 cycles per minute and no wheezes on respiratory examination.

The clinical diagnosis was drug-induced hypersensitivity. He was detained at the emergency room and given 200mg of intravenous hydrocortisone. After about 4h, his general condition gradually improved facial swelling and urticaria were reduced and breathing became more tolerable (the respiratory rate had reduced to 18 cycles per minute). Subsequently, the patient was discharged on a prescription of oral cetirizine 10mg tablets to be taken once daily for five days and celecoxib 200mg tablets to be taken twice daily for five days to manage the residual pain. He had a follow-up one week later, and the pain together with the facial swelling had resolved.

3 DISCUSSION

Anaphylaxis or type I hypersensitivity is a life-threatening allergic reaction induced by several agents, including medications[5,6]. Medications are one of the most common causes of this reaction which mainly caused by the activity of mast cells and basophils[7]. Anaphylaxis exert its action primarily through the pathophysiologic mechanism of tissue ischemia and hypoxia induced by intercellular edema from inflammatory mediators.

It has been reported that aside from anaphylaxis, ketorolac also causes serum sickness. Anaphylactic allergic reactions induced by ketorolac will present variably. Similar to this case report, respiratory distress may be caused by respiratory hypersecretion bronchospasms, laryngeal irritation, or laryngeal spasms[6,8]. Respiratory distress in the index case might be induced by laryngeal edema, as he did not have the typical wheeze of bronchospasm or a cough associated with laryngeal hypersecretion like reported by Goetz et al[9]. Hypotension and tachycardia might also occur in some patients[4,5], due to the increase in plasma into the extracellular space[5], although that was not noticed in the index case. It might also be attributable to the relatively lower ketorolac dosage administered compared to the nearly 20-fold intravenous dosage given in the case of Chung et al.[5], which did not achieve a wide circulation. Palpebral edema is also a feature that may occur especially in children, for unknown reasons[4]. The onset of symptoms varies, ranging from seconds to hours. The evident contributing factor is the route of administration, with intravenous, intrathecal and intramuscular routes having a faster onset, whereas oral, dermal, and conjunctival formulations have a delayed onset. This explains why onset of symptoms was reported to be shorter in some of the cases[6] than the presentation in this report. Although the 2h lag between oral ingestion and symptomatology appeared to be very delayed compared to other case reports.

In resource-poor settings like ours, diagnosis of a ketorolac hypersensitivity reaction could be daunting, when equipment was lacking to measure serum tryptase levels[9]. However, as we have done, a good history and keen patient observation for clinical symptoms following administration of intervention medications may be crucial for diagnosis[9]. Supportive investigations such as *in vitro* allergen specific IgE tests have been used in other cases and may delay the diagnosis but can be more useful for chronic cases where the allergens are unknown. In our specific case, we relied on the temporal relationship between drug administration and symptom onset.

The treatment of drug-induced hypersensitivity reactions involves various interventions, depending on the severity and the major body system involved. Firstly, discontinuing the use of triggering medication or allergen. Secondly,a quick assessment of the Airway, Breathing, and Circulation, the so-called ABC's. Furthermore, actions are determined by the results of this assessment. Pharmacological interventions may be required contingent upon the rise of symptoms and complications, such as epinephrine, histamine-1 receptor antagonists, corticosteroids, beta2 agonists, glucagon, and oxygen[4,6,8,9]. Early intervention can be life-saving for patients experiencing severe forms of anaphylaxis[6]. Since predictors of anaphylaxis may be unknown, as a general warning, people can avoid using drugs to which precipitants belong[2]. However, not all drugs within specific categories can cause anaphylaxis[1] as we experienced with celecoxib, another NSAID, even though the patient reacts to ibuprofen and diclofenac. This further confirms that the allergen was ketorolac in this case.

We acknowledged a critical limitation in this case. This related to the absence of serum tryptase levels to corroborate the diagnosis through laboratory evaluation[10] and our inability to assess his immunological status. However

we relied on the consistency of the pharmacokinetics, the temporal relationship between symptoms onset and administration, as well as the patient's awareness of ibuprofen and diclofenac allergies to aid in rapid documentation of the reaction. This clarified the diagnosis which was difficult to resolve due to unavailability of serum tryptase testing at our facility and other nearby primary facilities.

4 CONCLUSION

Anaphylaxis after oral intake ketorolac is rare but could be fatal if it occurs. Therefore, awareness possible side effects of ketorolac and signs evident of ketorolac-induced anaphylaxis is essential for physicians, pharmacists, and nurses. We recommend educating patients and clinical staff to the awareness that any medication can potentially lead to this life-threatening condition.

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Not applicable.

Conflicts of Interest

The authors declared no conflict of interest.

Author Contribution

Gyasi AF conceptualized, drafted and reviewed the manuscript. Asante F drafted and reviewed the manuscript. Yambah JK and Ackah NB reviewed the manuscript. All authors approved the final submitted manuscript.

Abbreviation List

NSAIDs, Non-steroidal anti-inflammatory drugs

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