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ANAPHYLACTIC SHOCK: SECONDARY TO INTRAMUSCULAR TRAMADOL INJECTION

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Abstract:

Opioid analgesics are commonly used in the hospitals. Tramadol is a synthetic opioid that is considered safe, and hypersensitivity reactions to this drug are rare. In this study, we report the first intramuscular tramadol-induced anaphylaxis case induced in an adult patient. This case indicates an important concept of detecting those reactions that include life threatening ones such as anaphylaxis in addition to the other commonly reported side effects.

Keywords: *Anaphylaxis, Hypersensitivity, Tramadol, Opioids, Analgesia.*

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INTRODUCTION:

Anaphylaxis occurs suddenly and is a severe life-threatening form of hypersensitivity with multisystem involvement [1]. Although food and medications are mainly considered responsible for this type of hypersensitivity, tramadol-related hypersensitivity reactions occur but are rare as it is considered to be a safe drug with fewer side effects compared to other opioids [2, 3]. Only one case has been reported for intravenous tramadol-induced anaphylaxis in a 15-year-old boy, and to the best of our knowledge, we are reporting the first case of anaphylactic shock in an adult due to intramuscular tramadol.

CASE SUMMARY:

A 43-year-old female presented to the emergency room complaining of acute right flank pain radiating to the groin. The patient was vitally stable, and her physical examination was unremarkable. A bedside abdominal ultrasound showed right sided hydronephrosis and bilateral renal cysts. She was given 50 mg intramuscular tramadol for pain after which she reported having a large watery bowel movement and feeling dizzy. She became pale, appeared to be ill, and her extremities became cold. Her blood pressure (BP) dropped to 60/30 mmHg, and an ultrasound RUSH protocol ruled out obstructive, cardiogenic & hypovolemic shock types. Distributive shock was most likely, thus our diagnosis was an anaphylactic reaction secondary to the tramadol injection. There was no history of prior allergies, and this was the first time the patient used tramadol. The patient was given epinephrine 0.5 mg IM twice and intravenous (IV) fluids along with hydrocortisone 200 mg IV and ranitidine 150 mg IV. After which her vital signs normalized transiently. She then started to develop urticaria, and after 30 min, her blood pressure dropped again at which point the third dose of epinephrine 0.5 mg IM was given followed by an epinephrine drip. The patient was moved to the intensive care unit (ICU) and intubated. Later, she developed acute disseminated intravascular coagulation (DIC) and acute kidney injury, requiring dialysis. The patient remained in the ICU for five days followed by three days in the ward. After she stabilized, she was discharged home in her baseline status.

DISCUSSION:

For the past two decades, tramadol hydrochloride, which is a synthetic analgesic drug, has been prescribed for the treatment of moderate to severe pain [1, 4]. It is an opioid drug that has both opioid and non-opioid properties and exhibits its action as a mu-opioid receptor agonist in addition to a serotonin and norepinephrine re-uptake inhibitor. Tramadol hydrochloride acts mainly on the central nervous system with multiple pharmacological forms available for different routes of administration serving as an analgesic to treat pain [1, 4].

In term of side effects, opioids such as morphine and pethidine are commonly associated with gastrointestinal upset in addition to sedation, nausea, vomiting, constipation, and lightheadedness or dizziness [2]. Moreover, respiratory depression and hypotension are notably seen when using large doses of such opioids; nevertheless, patients are more prone to addiction when taking morphine and pethidine [2, 3]**.** However, other than gastrointestinal upset and sedation, tramadol has been shown to have fewer side effects compared to other opioids, especially in term of respiratory depression, hypotension, and dependence as it is considered a safe synthetic opioid and favorable analgesic regimen [2, 3].

Despite the wide range of opioid use, allergic reactions to such medications are not usually reported, and tramadol-induced IgE-mediated hypersensitivity reactions such as anaphylaxis are rare since only one case of IV tramadol-induced anaphylaxis in a child was reported in the literature [1]**.** Anaphylaxis is a severe and life-threatening type of hypersensitivity reaction. It is an acute systemic syndrome usually on a background of an immunologic mechanism resulting from the rapid degranulation of mast cells and basophils mediators [5, 6]**.** Products of mast cell and basophil degranulation during the anaphylactic attack include histamine that acts on both histamine (H)1 and 2 receptors and is responsible for the manifestations accompany anaphylaxis. Tryptase is another product of mast cells, and its plasma levels correlate with the clinical severity of anaphylaxis [5]**.** Other products include chymase, heparin, and other cytokines [5].

Clinical manifestations of anaphylaxis can involve any organ. Cutaneous manifestations such as generalized urticaria and angioedema are the most common manifestations of anaphylaxis, but these cutaneous manifestations might be absent or delayed in sudden and rapidly developing anaphylaxis. Respiratory, cardiovascular, and gastrointestinal manifestations, including laryngeal edema, bronchospasm, hypotension, and hyperperistalsis are the next common manifestations to be present along with other nonspecific signs and symptoms [5,6].

Although anaphylaxis is a life-threatening reaction, it is not a commonly reported disease, and both the

mortality and morbidity of this type of hypersensitivity is underestimated. Food and medications are the most common known causes of anaphylaxis [5]**.** In terms of fatality, drugs, (commonly antibiotics) appear to be the most commonly reported causes of fatal anaphylaxis as the estimated rate of drug-induced fatal anaphylaxis had significantly increased from 0.27 to 0.51 per million people between the periods of 1999 to 2001 and 2008 to 2010 [7]**.** Drug-induced anaphylaxis was found to be the reason for emergency department visits for 1 in 4000 cases with an estimated incidence ranging from 0.04% to 3.1% [7]. In term of overall increase in anaphylaxis cases, drug-induced anaphylaxis and mortality rates had increased by 150% and 300%, respectively [6]**.** The reported incidence of tramadol-induced angioedema is 1 in 1,000 to 1 in 10,000 as only 11 cases of tramadol-related IgE-antibody-mediated angioedema have been reported in the literature, half of which needed treatment in an ICU [1].

We are reporting the first case of **intramuscular** tramadol-induced anaphylactic shock in a 43-year-old female. This diagnosis was made by exclusion supported by the time from tramadol injection and the development of patient's signs and symptoms.

CONCLUSION:

Opioids have been widely used in the practice of medicine, and tramadol is labeled as the safest among this group of medications. Tramadol is considered to be a safe drug, and immediate IgE-dependent hypersensitivity reactions to this drug occur but are rare. This case shows the importance of rapid detection of such cases even without the classical signs and symptoms of anaphylaxis and even for medications that have not been reported to cause an allergic reaction.

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