G131 Anaphylaxis After the Injection of Buprenorphine

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After attending this presentation, attendees will become aware of the possibility of an anaphylactic reaction due to the intravenous use of buprenorphine, and attendees should consider analysis for tryptase in cases of its misuse.

This presentation will impact the forensic science community by increasing the awareness of the possibility of an anaphylactic reaction following the injection of abused prescription medications.

Buprenorphine is a partial opioid agonist that was developed for pain management in the 1970s and in 2002 became available for opioid substitution therapy (OST) in the United States. The formulations designed for OST are sublingual and include Subutex®, a tablet that contains only buprenorphine, and Suboxone®, a formulation of buprenorphine and naloxone in a 4:1 ratio designed to reduce the diversion and misuse of buprenorphine by causing withdrawal symptoms when administered intravenously. Despite the addition of naloxone to buprenorphine formulations, the drug is still diverted and misused. Buprenorphine is relatively safe when used appropriately, however multiple deaths have been reported due to buprenorphine use and misuse both with and without concomitant use of other drugs. In several of the cases reported, the levels of buprenorphine were not considered to be toxic; however, in many of these cases, since there was no other identifiable cause of death, buprenorphine toxicity was still listed as the cause of death. Two cases of anaphylaxis in decedents who had injected buprenorphine formulations just prior to death and suggest that anaphylaxis should be considered in individuals who misuse buprenorphine via intravenous administration regardless of the postmortem buprenorphine concentration are presented.

In 2009 and 2010, autopsies were performed on two individuals who were witnessed to die suddenly after the injection of buprenorphine. Initial thoughts were that the deaths were due to buprenorphine intoxication, however toxicologic analysis showed elevated tryptase. The first case was a 29-year-old woman with a history of asthma, drug abuse, and an allergic reaction in the past. Investigation showed that she and her boyfriend had bought 20 tablets of alleged 0.2mg buprenorphine via the internet from a Philippine based pharmacy. They soaked the tablets in water, filtered them and prepared two syringes each with a 1mg dose. After purging the air from the syringe, she injected the solution and was witnessed to immediately gasp for air and collapse. Her boyfriend administered two puffs of her albuterol inhaler without benefit. She received multiple doses of naloxone and epinephrine from EMS and in the ER. Analysis of the contents of the syringes revealed no buprenorphine. Autopsy showed hyperinflated lungs with mucous plugging of the airways, peribronchial smooth muscle hypertrophy and eosinophilic infiltration. Postmortem toxicology screen was positive for naloxone (22 ng/mL) and elevated serum tryptase concentration of 179ng/mL. The cause of death was Anaphylactic reaction complicating asthma and the manner was Accident. The second case was a 30-year-old woman who was three months postpartum with a history of heroin abuse. Investigation showed that her boyfriend witnessed her complain of not feeling well after injecting herself with Suboxone® from a 8mg/2mg strip that she had purchased on the street. She then went to her bedroom was found to be unresponsive five minutes later. Autopsy showed rare polarizable foreign material in the pulmonary macrophages, scattered multinucleated giant cells in the lungs and focal interstitial hemorrhage and edema of the larynx; however, no mast cells were identified. Postmortem toxicology screen was positive for buprenorphine (17ng/mL), norbuprenorphine (7.6ng/mL), and naloxone (96ng/mL). Postmortem serum tryptase concentration was elevated at >200.0ng/mL. The cause of death was Anaphylactic reaction due to intravascular injection of Suboxone®, and the manner was accident.

Anaphylaxis is an acute immunologic systemic reaction an allergen via IgE receptor activation on mast cells and basophils with the release of inflammatory mediators including histamine, tryptase, prostaglandins, and leukotrienes. Anaphylactic reactions can be elicited by many substances; therefore it is possible that any constituent in either formulation abused in these cases elicited the anaphylactic reactions. The postmortem diagnosis of anaphylaxis depends upon a complete investigative history with focus on the details of the reaction and the event surrounding it as there is individual variation in symptomatology. Investigation should include questions on how the decedent reacted immediately prior to death, how the person has reacted before from exposure to the substance, and a complete medical history including history of asthma or allergies. Autopsy should include gross and microscopic evaluation of the airway and toxicologic analysis for serum for tryptase. Postmortem tryptase concentration has generally been considered elevated when greater than 10ng/ml. It has also been reported that postmortem tryptase can be elevated in the absence of anaphylaxis but usually not to the degree seen in these cases.

Given the increasing use of buprenorphine in opioid replacement therapy and the recent increase in the quantities of diverted buprenorphine being seized by law enforcement, the possibility of an anaphylactic death should be considered when the drug is misused. Serum tryptase concentration should be assessed prior to assigning the cause of death as buprenorphine intoxication in these types of cases. Elevation of tryptase is particularly useful in confirming the diagnosis of anaphylaxis triggered by injection of a medication or agent that is not normally used intravenously.

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