H112 Death by Intracorporeal Fentanyl Extravasation During the Replacement of an Intrathecal Pump

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Learning Overview: After attending this presentation, attendees will be informed regarding an atypical overdose in a patient undergoing chronic therapy with intrathecal administration of fentanyl and the importance of correctly knowing the distribution and metabolism of fentanyl.

Impact on the Forensic Science Community: This presentation will impact the forensic science community by highlighting the difficulty of determining toxic values of fentanyl in subjects in chronic therapy and the lack of knowledge by clinical physicians regarding the metabolism of fentanyl and its difficulties in therapeutic management.

A 59-year-old woman with type I neurofibromatosis and chronic radiculopathy causing intense pain was treated with intrathecal fentanyl injection via a continuous-release pump implanted in the left abdomen in 2009. During a routine filling of the pump at 1.00 p.m. on December 7, 2017, there was an intracorporeal fentanyl solution extravasation of about 8.7ml (corresponding to 13,050ug of fentanyl). The woman was treated with immediate clinical monitoring and with naloxone therapy (both in bolus and in continuous infusion for anticipated bradypnea). The woman was then hospitalized for 24 hours of monitoring and administration of low doses of naloxone (0.1mg/h) and oxygen therapy. During hospitalization, there were episodes of bradypnea (with an episode below 10 breaths/minute), episodes of hypotension (68/54mmHg), and some periods of desaturation (average saturation 92%–93% with episodic 75% and 89% drops).

In the morning, the woman was visited and appeared well; the administration of naloxone and oxygen was stopped at 9:00 a.m., and the woman was discharged around 12.00 a.m. on December 8. Notably, at discharge a nurse had measured an oxygen saturation of 75% that was not reported to the doctor. For the passage of the woman from the bed to the wheelchair, a mechanical lift was used with belts located in the abdominal region. The woman returned home, reported being particularly tired and sleepy, and went to bed, where she was found dead at about 7:00 p.m. An autopsy was performed and revealed chronic cardiomyopathy, serous pleural effusions, splenomegaly, chronic liver disease, and multiple cutaneous neurofibromas. The pump for intrathecal infusion was positioned in the abdomen and surrounded by a fibrous envelope; transparent liquid was collected between the pump and the casing. Histologic examination confirmed the macroscopic data and showed microscopic alterations due to pulmonary arterial hypertension.

Interpretation of toxicologic results was complicated by multiple factors, including the absence of reference data regarding toxic/lethal fentanyl concentrations in patients chronically medicated via intrathecal administration. The compendium of all available data, however, ultimately led to certification of fentanyl overdose as the cause of the death. Per literature data, a blood concentration of fentanyl of 25µg/l (i.e., the concentration detected in a sample procured around 12 hours after death) was well above therapeutic values and within the range of toxic and/or lethal values. Furthermore, in this case, fentanyl concentrations detected in organs (i.e., brain, liver, and kidneys) were likewise found to fall into the toxic/lethal range. Analysis of samples taken near the pump (i.e., overlying liquid, fibrous tissue, and adipose tissue) likewise showed high concentrations of fentanyl. The highest tissue concentration was recorded in the adipose tissue underlying the pump (9.0mg/l); in sum, these findings would suggest substance redistribution from the extravasation point to the periphery was still in progress at the time of death. The pharmacokinetics of fentanyl in the present case was not comparable to those of intravenous therapeutic or accidental administration of the substance. It is suspected that drug accumulated initially between the pump and the fibrous tissue that covered it, and subsequently progressively distributed to the surrounding adipose tissue and the periphery—a distribution that was still ongoing at the time of death.

The Public Prosecutor then conducted a thorough investigation with reports by the doctors and nurses who treated the woman, highlighting a fundamental ignorance of the notion of a possible reservoir of the fentanyl in adipose tissue with subsequent progressive release into the body (as a lipophilic substance). The anomalous “delayed” release mechanism, not known in practice, has led to the filing of criminal proceedings against the operating medical staff.

Fentanyl, Chronic Therapy, Intrathecal Administration