G15 Exploration of Non-Cardiogenic Pulmonary Edema With Chronic Opiate Use: Case Studies and Scientific Review

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After attending this presentation, attendees will learn how to characterize non-cardiogenic pulmonary edema during autopsy caused by opiate use. Additionally, attendees will learn about alternative opiate sources which may lead to cases of non-cardiogenic pulmonary edema. Such cases may present during autopsy and potentially lead to classification of a secondary cause of death or change in the classification of manner of death.

This presentation will impact the forensic community by providing potential answers to cases in which underlying chronic opiate use potentiates mortality. Chronic opiate use may synergistically lead to fatal pathology not readily recognized when secondary to diseased states in the lung. The presentation focuses on the reliability of diagnosing cause and manner of death during autopsy with the goal of increasing the validity of techniques, processes, and methods used in forensic medicine.

Use of opiate variants, including pain management medications such as morphine and street drugs such as heroin, have all been implicated in causing acute respiratory distress marked by non- cardiogenic pulmonary edema (NCPE). Despite efforts to treat patients who develop NCPE through chronic use or acute over-dose; presentation of NCPE stills has a mortality rate of 30-50%. With significant mortality and the rise in cases, development of NCPE is increasingly significant to the forensic community. The molecular and cellular mechanisms by which opiates induce non-cardiogenic pulmonary edema (NCPE) remain elusive. NCPE is a clinical hallmark of opiate use in long-term drug users as well as patients treated with narcotics for chronic pain. Sporadic cases of NCPE were recently reported with use of other medications: primarily drugs used to treat other forms of edema, regulate blood volume, or blood pressure.

Although the pathogenesis of NCPE is largely unknown it thought to be dose related—thus maybe a presentation of an abhorrent cardiorespiratory response. Acute or chronic opiate use causes acute respiratory distress syndrome (ARDS) marked with pulmonary capillary leak and exudation leading to NCPE. Data shows us of opiates, primarily heroin, is the primary cause of NCPE in patients under 40. As many as 50% of these patients are clinically defined as an overdose with as much as 20% of these cases will be fatal. Previous animal models and marginal human studies identified three active opioid receptors ($\delta\mu\kappa$) varying in distribution throughout the respiratory tract. The lung is a very complicated microenvironment. Several hypotheses regarding the pathogenesis of NCPE indicate involvement of various cell and tissue types throughout the respiratory tract. Local changes may cause alterations to the alveolar epithelium direct or have effects on the pulmonary capillary bed resulting in NCPE. The lung parenchyma co- exists with the alveolar terminal air space where gas exchange occurs. Studies indicate there are two distinct H^3-morphine binding sites—with the most abundant binding localized within alveolar walls. Therefore, this is the site implicated as responsible for fluid clearance in the lungs. The exact mechanism by which activation of opiate receptors in this region leads to fluid influx is largely unknown. It is possible alveolar tissue plays a role in the release of soluble mediators or recruitment of inflammatory cells leading to a cascade of events contributing to the pathogenesis of NCPE. Dysregulation of solute and fluid clearance by the alveolar epithelium itself may be altered by opiate receptor activation. Finally, long-term or acute aactivation of opiate receptors with may lead to significant alterations in the epithelial surface that are the basis local changes conducive to the onset of NCPE.

With underlying disease in the lungs or other chronic conditions which require use of opiates, these changes may not be easily recognizable during autopsy. The goal of this poster is to demonstrate how opiate toxicology may induce local effects in the respiratory tract which ultimately results in direct changes to the pulmonary alveolar epithelium contributing to underlying disease. Secondary pathology may contribute to cause and manner of death in forensic cases. Understanding how opiates contribute to altered pathology will enhance the methods by which forensic pathologists diagnose NCPE postmortem.

Autopsy, Forensic Pathology, Pulmonary Toxicology

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