K67 Fatal Intravenous Injection of Oral Therapeutic Drugs in an Elderly Patient

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After attending this presentation, attendees will be more conscious of the potential lethal effects following adverse reactions due to erroneous intravenous administration of oral therapeutic drugs.

This presentation will impact the forensic science community by promoting awareness of rare lethal therapeutic errors.

A 77-year-old male resident in a retirement home, suffering cardiac failure, severe neurological diseases, and dysphagia, died immediately after intravenous administration of a mixed compound, obtained by manual fragmentation of one tablet Respicur® 200mg (theophylline), one tablet of Dintoina® 100mg (phenytoin sodium salt), one tablet Luminale® 100mg (phenobarbital sodium), and a few milliliters of water. The nurse, educated in an Eastern European country and recently employed in Italy, intentionally injected the compound into a jugular catheter to bypass daily difficulties in oral administration, since the patient's parents had refused gastrostomy. A few minutes after the drug-blend injection, the patient showed convulsions, loss of consciousness with cardiac arrest.

Autopsy showed myocardiosclerosis and previous myocardial infarction, pulmonary emphysema, exogenous lipid pneumonia, interstitial fibrosis due to previous repeated gastric aspirations, remarkable congestion in the residual alveolar septa, and no emboli in the pulmonary vessels.

Toxicological analyses on the jugular catheter and syringe revealed extremely high concentrations of all three drugs, as expected from the unusual administration procedure. Toxicological analyses on biological specimens showed drug levels below the maximum therapeutic concentration (left ventricular blood: phenobarbital 15.33mcg/mL; theophylline 1.97mcg/mL; phenytoin 3.70mcg/mL; right succlavian artery blood: phenobarbital, 18.60mcg/mL; theophylline, 2.92mcg/mL; phenytoin, 5.26mcg/mL; left jugular cath residual blood: phenobarbital, 492.3mcg/mL; theophylline, 1395mcg/mL; phenytoin, 463.3mcg/mL). In fact, some degree of postmortem redistribution is expected to have occurred, considering the autopsy was performed three days after death.

Death was caused in this elderly patient by acute phenobarbital, phenytoin, and theophylline toxicity, following erroneous intravenous administration of oral therapeutic doses.

Severe theophylline-related arrhythmias happened very quickly after inoculation of the drug-blend, since the immediate and complete bioavailability produced extremely high concentrations, incomparable to any model of toxic overdose. The total lack of drug metabolism due to first hepatic passage was also responsible for this huge concentration. Moreover, intravenous injection at the left jugular site realized an exceptional condition inoculating theophylline very close to the heart, target of toxicity, and obtaining a sort of topic toxic effect at dramatically high concentrations.

The unusual way of administration also suggests phenytoin-related arrhythmias, as discussed for theophilline. Phenytoin is an anticonvulsant drug usually administered in tablets for chronic therapy, and intravenously at higher dosages for the treatment of acute epileptic seizures. In these cases, rapid parenteral injection can induce cardiac arrhythmias, while oral overdoses usually produce only neurological toxic effects.

Theophylline dose-related toxicity on the central nervous system should also be considered in the mechanism of lethality. On the contrary, the role of phenobarbital neurotoxicity is ruled out, since death rapidly took place and this barbiturate needs a longer time span to cross the hematoencephalic barrier.

Other possible lethal effects related to chemico-physical properties of excipients contained in the micro-fragments of injected tablet-mixture have been considered, but no relevant toxicological or hystopathological findings were noted.

In conclusion, this is the first case in the forensic literature reporting fatality by erroneous parenteral administration of oral therapeutic drugs. This study also points out that in similar occurrences postmortem analytical data have limited value. For this reason, the forensic scientist takes advantage in the diagnosis by the application of uses an appropriate methodology evaluating a complex of elements (circumstantial data; pathology; analytical data), but mainly inquiring/discussing evaluating the pharmacodynamic of each drug in relation to this bizarre irregular method of administration.

Teophylline Toxicity, Phenytoin Toxicity, Therapeutic Error

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