G26 Antiepileptic Drug Intoxication: Report of One Case and a Forensic Pathologist's Approach

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After attending this presentation, attendees, will learn a better forensic approach in investigating fatal cases where there is suspicion of antiepileptic drug misusage.

This presentation will impact the forensic science community by showing a fatal case of intoxication with valproic acid. In addition, further discussion is made in order to clarify and systematize forensic approaches (crime scene investigation and autopsy procedure) in cases involving suspicion of antiepileptic drug misusage, fatal consequences of antiepileptic drug, particularly valproic acid, including its direct toxic effects, adverse reactions and interactions with others drugs, possible mechanisms, causes and manners of death in these type of cases, and promotion of prevention measures with physicians to avoid fatal cases in patients taking antiepileptic drugs.

Valproic acid is formally an antiepileptic drug but currently it has wider clinical uses, including treatment of some psychiatric disorders, such as bipolar and affective disorders. Since prescription of valproic acid has been growing, it is becoming an increasingly common agent to be used in intentional overdoses. Although considered a relatively safe drug, it is known to cause hepatotoxicity and pancreatitis, amongst other adverse reactions. In patients co-ingesting other medications, specifically, those acting as CNS depressants, side effects and toxicity can become more dangerous and even fatal for the patient.

This study presents a 45-year-old blind female, who was found dead by her husband inside their house. The forensic pathologist called to the scene, found five empty blisters-packs of valproic acid. Previous pathologic history included epilepsy, bipolar disorder, and chronic alcohol abuse with prior suicide threats. At autopsy, external and internal examination didn't reveal significant traumatic lesions. The organs showed generalized congestion, the liver was significantly enlarged, the pancreas showed no macroscopic abnormalities and a whitish substance was present in the stomach.

Histological ancillary investigation confirmed congestion in the lungs and kidneys, and also, mild hepatic steatosis. Toxicological results revealed high concentrations of valproic acid (556.0 µg/mL); therapeutic concentrations of other psychiatric drugs (tiapride, mirtazapine, nordiazepam, and oxazepam) and blood ethyl alcohol concentration of
1.34 g/L.

After excluding death due to natural or traumatic causes, a direct toxic effect by valproic acid was considered. Taking into account the autopsy, histopathology and toxicological findings, along with the circumstantial evidence, the cause of death was attributed to suicide by intoxication with valproic acid in association with other CNS depressants.

In conclusion, this case illustrates that is crucial for forensic pathologists to: (1) participate or have detailed information from the crime scene, prior to autopsy; (2) know the deceased´ complete medical history and prescribed medication; (3) do a careful postmortem examination to exclude natural and traumatic causes of death; (4) study target organs of valproic acid action by macroscopic and microscopic approach; and, (5) do toxicological studies and exclude other causes of death.

When prescribing multiple CNS depressant drugs to patients with alcohol abuse and suicidal ideation, physicians should always be

particularly aware of the risk of valproic acid toxicity, interactions with other drugs and possible adverse reactions, besides the potential accidental or intentional intoxication.

Forensic Pathology, Antiepileptic Drug Intoxication, Valproic Acid

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