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CASE REPORT

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The Analysis of an Intracerebral Hematoma for Drugs of Abuse

ABSTRACT: Toxicological investigations were performed on an intracerebral hematoma, antemortem blood, and postmortem blood of an individual who was found unresponsive in his home. The hematoma was found to have ethanol at a concentration of 0.05% (w/v), and benzoylecgonine (a cocaine metabolite) was also confirmed at a concentration of 0.43 mg/L by specific analysis using gas chromatography/mass spectrometry (GC/MS). These results enabled the pathologist to record the cause of death as intracerebral hemorrhage due to acute cocaine intoxication.

KEYWORDS: forensic science, intracerebral hematoma, cocaine, ethanol

In cases of prolonged survival following injury it is often difficult, at the time of autopsy, to determine whether an individual was under the influence of drugs or poisons at the time of the injury. It is particularly difficult when the drugs or poisons exhibit short circulatory half-lives and may be metabolized and/or eliminated prior to death. In such circumstances, there may be no drug or poisons detected in the blood or tissues collected at autopsy. In the absence of suitable antemortem specimens, which may be collected on admission to a hospital, an individual's drug use at the time of injury may never be known.

Some research has suggested that individuals with craniocerebral injuries often result in intracranial hemorrhages, which may be depositories of drugs or poisons subsequently isolated from circulation after the time of injury. The analysis of alcohol in such circumstances has been reported by several authors (1–4), but there is sparse literature available about the detection and analysis of other drugs and poisons in intracranial hemorrhages (5).

Hemorrhages, specifically intracerebral hemorrhages, can also result from acute use of stimulant drugs. Cocaine, for example, has been reported as a significant risk factor for fatal intracerebral hemorrhage (6,7). In this paper we present a case in which alcohol and cocaine (benzoylecgonine) were detected in an intracerebral hematoma, and we discuss how such hematomas may be used for drug testing in forensic cases.

Case History

Circumstances of Death

The decedent was a 51-year-old male who resided alone in an apartment. He was discovered unresponsive at home and paramedics were summoned. He was rapidly intubated and placed onto a cardiac monitor that revealed bradycardia and severe hypotension. He was transported by ambulance to the local emergency department for further evaluation and management.

Upon arrival, his vital signs were documented as a blood pressure of 105/96, pulse of 82, respiration rate of 20, and a temperature of 93.3°F. Suddenly his pressure dropped to 48/34, and he was placed on a dopamine drip. He remained comatose and was transferred to the imaging department, where a head CT revealed a hemorrhage in the left basal ganglia with a 3-mm herniation and extensive hemorrhage into the ventricles. Once stabilized, he was transferred to the Intensive Care Unit for further analysis. A urine drug screen for common drugs of abuse was positive for the presence of cocaine. He was placed on comfort care only. He remained comatose until his death some 30 h after initial admission.

Autopsy Findings

An autopsy was performed the following day, 17 h after death. The decedent was 69 in. and 142 lb. External injuries were limited to two small abrasions on the back and a faint, 1/8-in. abrasion on the left forehead. Two small possible old needle track marks were noted in the right antecubital fossa. Upon opening the cranium, a large blood clot fell from within the decedent's left cerebral hemisphere and was collected for toxicological testing. Examination of the brain confirmed the presence of a large intracerebral hematoma, which measured approximately 100 mL in total volume and was centered on the left basal ganglia with extension into the ventricular system. Brain swelling, subfalcine herniation, and Duret hemorrhages were also present. No scalp hemorrhage, skull fracture, subdural hemorrhage, or cerebral contusions were present.

The heart weighed 340 g and exhibited up to 70% atherosclerotic stenosis of the left anterior descending coronary artery and up to

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50% of the second diagonal branch. The kidneys were without nephrosclerosis. The liver exhibited slight to moderate mixed macrovesicular and microvesicular steatosis and developing cirrhosis. There were no other significant macro- or microscopic findings.

Methods

Toxicological Analyses

Toxicological analyses were conducted on antemortem (admission) whole blood (EDTA), which was stored refrigerated; postmortem peripheral blood and an intracerebral clot collected at autopsy using radioimmunoassay (RIA) screening for drugs of abuse; gas chromatography (GC) for the analysis of alcohol (forensic alcohol analysis by gas chromatography; method approved by the State of California, Department of Health Services, United States); and capillary gas chromatography with mass spectral confirmation (GC/MS) for basic/neutral substances.

Cocaine, Benzoylecgonine, and Cocaethylene Analysis

Drug Stock Solutions—Drug stock solutions of cocaine (1 mg/L in acetonitrile), benzoylecgonine (1 mg/L in methanol), and cocaethylene (1 mg/L in acetonitrile) were purchased from Cerilliant Corporation (Round Rock, Texas). Internal standards cocaine-D3 (100 μg/L in acetonitrile), benzoylecgonine-D3 (100 μg/L in methanol), and cocaethylene-D3 (100 μg/L in acetonitrile) were also purchased from Cerilliant Corporation. Working standards were prepared by serial dilution of the stock solutions with deionized water to give concentrations ranging from 0.02 to 1.0 mg/L for each analyte. The limit of quantitation was 0.02 mg/L for each analyte.

Instrumentation—A Hewlett-Packard gas chromatograph (Model No. 6890) with a mass selective detector (Hewlett Packard Model No. 5973) was used for the analysis of cocaine and metabolites. The inlet temperature was set at 240°C, and the oven was programmed at: 75°C, 0 min, 20°C/min; 250°C, 0.2 min, 50°C/min; 300°C, 4.0 min. The MS Aux was at 280°C.

An HP-1 capillary, 15-m, 0.25-mm diameter, 0.25-μm film thickness was used for analyte separation at a constant flow mode of 1.0 mL/min.

The mass selective detector was in SIM mode with solvent delay at 5.0 min. Cocaine was monitored with ions 182*, 272, 303, benzoylecgonine with 82*, 361, 240, and cocaethylene with 196*, 272, 317 (*quantitation ions). The deuterated internal standards were monitored with ions 185 (cocaine), 85 (benzoylecgonine), and 199 (cocaethylene). The dwell time was 30 for each ion.

Extraction—Calibrators (blank, standards), controls, and unknown bloods were added to screw cap culture tubes. Porcine blood was used for blank blood and preparation of standards. One mL of blood was added to 0.5 mL of the working internal standards in each tube and mixed well by vortexing. Five mL of 5% zinc sulfate solution was added to each tube and mixed by vortexing. All tubes were then centrifuged at 3000 rpm for 5 min. Solid-phase columns (Bond Elut, Certify LRC, Varian, Inc., Walnut Creek, California) were prepared by adding sequentially 2.0 mL of methanol, 2.0 mL of 0.1 *M* acetate buffer pH 6.0. The supernatant was poured into the columns and 2.0 mL 0.1 *M* acetate buffer, pH 6.0 added. A vacuum was used to aid the flow of reagent through the columns. These were then washed with 3.0 mL deionized water and 3.0 mL 0.1 *N* HCl, then dried under maximum vacuum. Following additional washing with 9.0 mL methanol, columns were again dried. The VacElut apparatus (Varian, Inc., Walnut Creek, California) was then placed into the "collect" position and eluted with 2.0-mL elution solvent (2% ammonium hydroxide in dichloromethane/isopropanol; 80/20). The eluate was then evaporated with nitrogen in a 40°C water bath. Eighty μL of acetonitrile and 50 μL BSTFA/1% TMCS were added to each tube, transferred to autosampler vials, capped, and derivatized at 70°C for 40 min on a Reacti-Therm heating block (Pierce Chemical, Rockford, Illinois). After allowing vials to cool to room temperature, 1.0 μL was injected for analysis by GC/MS.

Quality Control Samples—Whole blood controls (Drugs of Abuse WB Level 1, product No. 98818) containing 0.100 mg/L of cocaine, benzoylecgonine, and cocaethylene were purchased from UTAK Laboratories (Valencia, California) and extracted with each assay. The average results obtained over a six-month period were: cocaine 0.09 (range 0.08 to 0.10 mg/L), benzoylecgonine 0.10 (range 0.09 to 0.12 mg/L), and cocaethylene 0.09 (range 0.08 to 0.10 mg/L).

Results

Initial screening of the admission antemortem blood detected the presence of cocaine metabolites (RIA screen). Ethanol and other simple volatiles were not detected, and no other therapeutic agents or poisons were detected by the basic drug screen (GC/MS). Screening of the intracerebral clot detected cocaine metabolites (RIA) and ethanol at a concentration of 0.05% (w/v) (GC). No other therapeutic agents or poisons were detected by the basic drug screen (GC/MS).

As shown in Table 1, specific cocaine quantification analysis confirmed the presence of benzoylecgonine in the admission antemortem blood (0.41 mg/L), the intracerebral clot (0.43 mg/L), and in a postmortem peripheral blood sample (0.17 mg/L). Cocaine was detected only in a trace amount in the postmortem peripheral sample (<0.02 mg/L). Cocaethylene was not detected in any specimen.

Discussion

Although the estimation of blood ethanol concentrations at the time of injury may have been complicated by postmortem diffusion of ethanol from the hematoma into surrounding tissues (3), the finding in the present case confirms the use of alcohol prior to injury (hemorrhage). Buchsbaum et al. (4) also commented on the usefulness of ethanol testing in subdural hematomas, concluding that these analyses provide pertinent forensic information. Cassin

TABLE 1—*Concentrations of alcohol and cocaine/metabolites.*

	Specimen		
Drug	Admission (Antemortem) Blood	Intracerebral Clot (Hemorrhage)	Postmortem Peripheral Blood
Ethanol	ND	0.05	ND
Cocaine	ND	ND	Trace (<0.02)
Benzoylecgonine	0.41	0.43	0.17
Cocaethylene	ND	ND	ND

ND = Not detected.
NOTE: Drug concentrations presented as mg/L.
Ethanol concentration presented as % (w/v).

and Spitz (8), however, warned that in cases of prolonged survival following injury, initially positive concentrations of alcohol might become negative. In other words, a negative ethanol result in a subdural hematoma should not imply that there was no ethanol in the circulation at the time of injury.

There have been very few reports of the analysis of drugs (other than ethanol) in hematomas, which have become isolated from the circulation and recovered at autopsy. Moriya and Harimoto (5) reported findings for six cases in which intracranial hematomas were found to contain drugs and chemicals. They reported drugs such as norephedrine, phenytoin, phenobarbital, toluene, lidocaine, and diazepam. They further reported that, although several drugs were self-administered prior to injury, some drugs diffused from circulating blood during medical treatment. They concluded that this phenomenon might become more obvious in cases of a slow formation of subdural hematomas occurring at the time of hospitalization and administration of therapeutic medications. This could obviously lead to a false interpretation of self-administration by victims prior to injury.

In the present case we report, for the first time, the detection and confirmation of cocaine (benzoylecgonine) in an intracerebral hematoma. The concentration of benzoylecgonine in the admission of blood and hematoma were essentially equivalent. These findings indicate that the individual was under the influence of both ethanol and cocaine at the time of the hemorrhage. Furthermore, as there was no ethanol detected in the antemortem specimen, it may also be concluded that the hemorrhage occurred several hours prior to the individual being discovered unresponsive in his home. Although the benzoylecgonine concentrations remained unchanged, there was sufficient time for elimination of alcohol prior to hospital admission. The detection of a trace concentration of cocaine, together with the benzoylecgonine metabolite in the postmortem peripheral blood, is most likely a result of postmortem re-distribution, a phenomenon now widely reported for many compounds (9,10).

Similar to subdural and other intracranial hematomas, therefore, intracerebral hematomas are the postmortem specimens of choice, especially for detecting drugs with short circulating half-lives, in individuals who survive several hours after intracranial bleeding. As reported previously in subdural hematomas, such analyses are useful to determine whether an individual was under the influence of ethanol at the time of injury (hemorrhage). In addition, toxicologists can now be confident of detecting and confirming illicit drug use (at least cocaine) despite a survival time of many hours or even days in the hospital. In the current case, the individual survived 30 h after initial hospital admission.

These findings enabled the pathologist to record the cause of death as intracerebral hemorrhage due to acute cocaine intoxication.

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