CASE REPORT

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Another Death Due to Ingestion of *Nicotiana glauca*

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ABSTRACT: Deaths attributed to ingestion of *Nicotiana glauca* are extremely rare. We report here a case where a 43-year-old man was found dead after apparently drinking a water extract of *Nicotiana glauca.* The primary alkaloid in the plant is anabasine. Toxicological analysis by capillary gas chromatography showed the deceased had a blood anabasine concentration of 2.2 mg/L. Clinically, the features of poisoning are nicotine-like and if death occurs it results from respiratory paralysis. The case further supports the view that, in the human, anabasine is considerably more toxic than nicotine.

KEYWORDS: forensic science, toxicology, *Nicotiana glauca,* plant poisoning, anabasine, nicotine, death

Nicotiana glauca (family Solanaceae) is commonly known as the Tree tobacco. It is native to South America and has been introduced to the warm dry areas of North America and Australia where it is found in all the mainland states. A perennial shrub 3 to 6 m tall, it has smooth green hairless branches and leaves that are often bluish in color. The rather unimpressive tubular flowers are yellow in color. It is now generally accepted that the primary alkaloid in the plant is anabasine (1) ($C_{10}H_{14}N_2$) although a small amount, less than 1%, of nicotine may be present. The percentage of anabasine is given as 1.3 from the dry plant and 1% from the root (1). Anabasine is similar in both structure and effects to nicotine but it appears to be more potent in humans despite a slower onset of action (2).

Two other species of *Nicotiana* occurring in Australia also contain anabasine as the primary alkaloid, namely *N. debneyi* and *N. rotundifolia* (3), both of which are Australian native species.

In the Western scientific literature there has only been one reported case of death attributed to ingestion of *Nicotiana glauca* (4). Here we report the pathology and toxicology findings in another death.

Case History

A 43-year-old man with no past medical history was found dead on the floor of his house. He had last been seen four days earlier by his neighbor. The deceased had told his neighbor that he had found a plant at local dockyards and planted it in his backyard. He claimed it was ''stronger than opium.'' Several days before the body was found his neighbor could smell something cooking with a ''funny smell'' and the deceased had told him he was cooking the leaves.

Police found a saucepan on the stove containing 250 mL of brown liquid with a green leafy sediment and a flagon with 1 L of amber liquid and leafy sediment in a cupboard by the back door. These two items were submitted for analysis along with the plant, which the police uprooted from the backyard. It consisted of a smooth shiny green trunk devoid of leaves with a 48 cm rootball. Submission of the plant remains to the Botanic Gardens of Adelaide and State Herbarium resulted in a provisional identification of family Solanaceae, possibly *Nicotiana glauca.* The identification was later confirmed following growing-on of the uprooted plant at the Botanic Gardens.

Autopsy Findings

The deceased was of muscular build, weighing 79 kg. The arms were tattooed. Early putrefactive changes were present with venous marbling over the chest and arms and a blood-stained discharge from the nose and mouth. All the internal organs were essentially normal apart from autolytic changes. The lungs weighed 1193 g and showed minor pulmonary oedema but no evidence of aspiration. The stomach contained a small quantity of cooked chicken but no identifiable leaf matter. The liver weighed 1593 g and histology showed a minor nonspecific focal polymorph infiltrate predominantly within portal tracts extending into adjacent trabeculae. There was no evidence of viral hepatitis and no stigmata of intravenous drug abuse.

Toxicological Analysis

Materials

Anabasine standard was obtained from Sigma Chemical Company (St. Louis, MD). Prazepam was used as the internal standard. Stock standard drug solutions were prepared in ethanol at a concentration of approximately 1 mg/mL as free base. Working standard drug solutions were freshly prepared by a 100-fold dilution with water. All reagents were analytical grade except for 1-chlorobutane, which was BDH HiPerSolv grade.

Instrumentation

Anabasine was screened for and subsequently identified using a Hewlett Packard 5890 series II gas chromatograph (GC) with a Hewlett Packard 5972 series mass selective detector [gas

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chromatography/mass spectrometry (GC/MS)]. The column was a 15 m DB-5MS 0.25 mm inside diameter, 0.25 μm film capillary column. The oven was held at 60°C for 2 min and then ramped at 15°C/min to 280°C and held for 5 min. The injection port temperature was 250°C and the mass detector interface temperature was 300°C. Under these conditions the retention time of anabasine was 8.7 min.

Anabasine was subsequently quantitatively analyzed using a Hewlett Packard 5890 series II Plus GC equipped with a split injector, dual nitrogen/phosphorous detectors and a 7673A autosampler. The columns consisted of a 5 m phenyl-methyl deactivated 0.53-mm inside-diameter guard column split equally to a 10 m DB-1 0.32 mm inside diameter 1 μm film capillary column and a 10 m DB-17 0.32-mm-inside-diameter 0.5 μm film capillary column. The oven was held at 100°C for 0.5 min and then ramped at 10°C/min to 280°C and held for 8.5 min. The injection port temperature was 250°C and the temperature of the detectors was 280°C. Under these conditions retention times for anabasine were 5.4 min on the DB-1 column and 5.0 min on the DB-17 column.

Extraction

Our extraction procedure for anabasine was similar to that previously reported (4). Five grams of liver were finely macerated with 15 g of water. Five grams of stomach contents were diluted with 95 g of water. The brown and amber liquids were diluted 100-fold with water. This liquefied liver and the diluted samples were then treated in the same manner as the femoral blood, urine and bile samples.

To a glass screw-top tube was added 0.05 mL of a 5 μg/mL aqueous solution of prazepam as internal standard. Femoral blood or other specimen (0.5 mL), 1.75 mL 0.15% ammonia and 8 mL 1-chlorobutane were added to the tube, and the contents were rolled on a mechanical mixer for 10 min. After centrifuging, the solvent layer was transferred to a clean glass tube and evaporated to dryness in a Jouan centrifugal evaporator. The residue was dissolved in 0.1 mL ethanol for GC analysis. Quantitative GC analysis of anabasine was done by comparison of duplicate samples with a standard curve constructed by adding known amounts of the alkaloid to alkaloid free blood and following extraction and GC analysis, plotting the area-response ratio for anabasine and internal standard versus anabasine concentration. The calibration curve for the quantitative analysis included six concentrations in the range 0.2 to 8 mg/L and produced a linear correlation with a coefficient of regression (r) of 0.99. The limit of detection for anabasine was estimated to be 0.02 mg/L based on a 0.5 mL blood sample.

Toxicology Results

The mass spectrum of anabasine is shown in Fig. 1. Table 1 presents the results of the analysis. Full toxicological analysis of the blood using GC, high-pressure liquid chromatography and immunoassay techniques was done with the results shown in Table 2. None of these drug concentrations are significant in determining the cause of death. In particular, nicotine was not detected in the

TABLE 1—*Fluid and tissue concentrations of anabasine.*

Specimens	Anabasine Concentrations
Blood	2.2 mg/L
Urine	2.3 mg/L
Liver	1.7 mg/kg
Bile	2.7 mg/L
Stomach contents	18.9 mg/kg
Amber liquid	81 mg/L
Brown liquid	not detected

TABLE 2—*Results of blood toxicological analysis.*

Analyte	Concentration
Paracetamol	6 mg/L
Caffeine	2 mg/L
Alcohol	0.03%

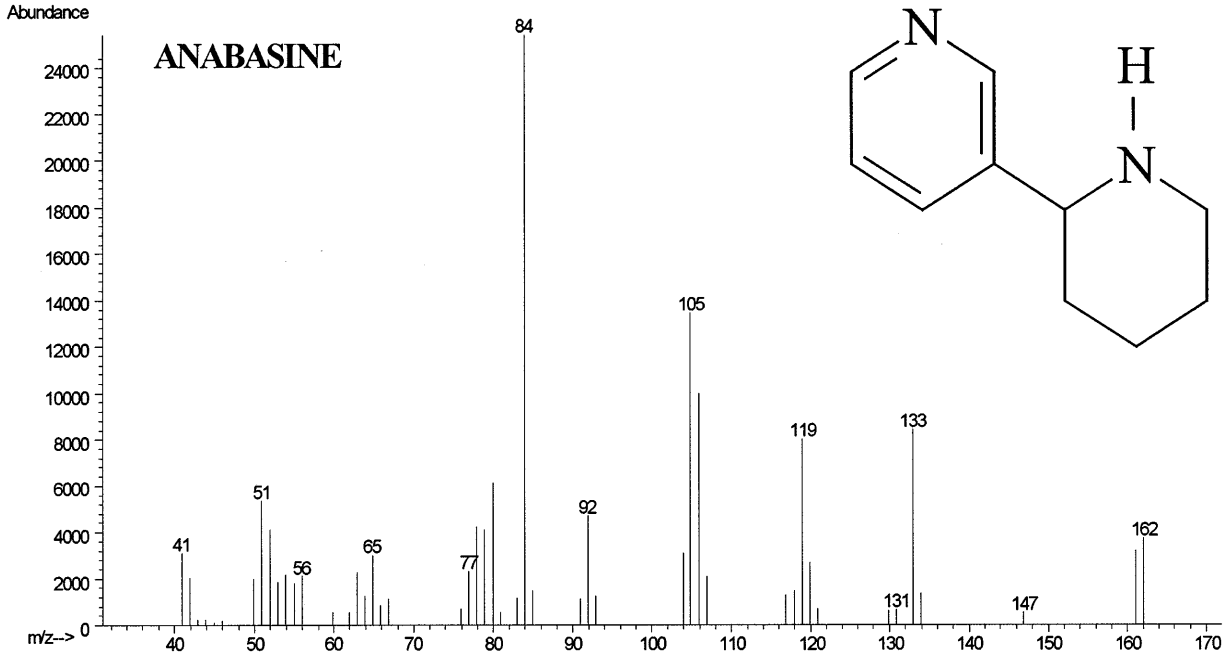

FIG. 1—*Mass spectrum of anabasine.*

liquids or postmortem specimens. Caffeine was the only substance of interest found in the brown liquid.

Discussion

The mechanism of action of nicotinic alkaloids appears to be generalized stimulation of nicotine receptors, including sympathetic and parasympathetic ganglia and the adrenal medulla with central effects on the limbic, midbrain and brain stem regions (5). The effects at low levels may be considered desirable by tobacco smokers. At the neuro-muscular junction initial stimulation may be followed by blockade, leading to paralysis of skeletal muscles and respiratory failure.

Clinically the features of poisoning are again nicotine-like. The speed of onset varies with the form of use. The drug is rapidly absorbed in liquid form with the onset of toxic features in about 30 min. With whole leaves there may be a delay of up to 90 min. Symptoms may persist for up to 72 h (2). Initially there may be hypersalivation, vomiting and later diarrhea. Cardiovascular effects include hypertension and tachycardia. Central nervous system effects include headache, dizziness, auditory and visual hallucinations, twitching and paralysis if neuro-muscular blockade occurs. If death occurs it results from respiratory paralysis.

There have been many deaths from nicotine poisoning, most resulting from ingestion of horticultural pesticides now not generally available. Other cases resulted from ingestion of tobacco or tobacco enemas in the treatment of intestinal worms or constipation (6). The half-life of nicotine is reported to be 24 to 84 min and shorter in smokers (7). In adults 40 to 60 mg of nicotine may be toxic or lethal but severe toxic symptoms may occur in children with as little as 1.4 mg/kg (8). In fatal cases, blood concentrations have varied between 5 to 600 mg/L (7).

There are very few reports in the literature relating to *Nicotiana glauca* toxicity and only one death has been verified (4). The reported death was of a young man in a field. Green leafy material in his mouth and stomach was identified as *N. glauca.* The only positive finding was anabasine with a blood concentration of 1.15 mg/L and a leaf anabasine concentration of 2 mg/g. The reported body tissue concentrations were about 10 times greater than the blood concentration which is often the case in poisonings with basic drugs. In this report the blood and other body fluids and tissues contain similar concentrations of anabasine which was unexpected. The reasons for this remain uncertain but may involve the different mode of ingestion of the anabasine, the dose, the survival time and the postmortem interval. The neighor's statement and the scene suggest the deceased may have consumed the *N. glauca* extract over a period of days. However, it is to be noted that in a report of 24 suicidal poisonings with nicotine, the blood and liver concentrations were similar (7).

Another report described an elderly man who developed severe alkaloid toxicity after eating *N. glauca* leaves with a meal (6). He had neuro-muscular blockade with respiratory failure and recovered with treatment. Included in this report is the newspaper-reported death of a 7-year-old girl who allegedly died after ingesting boiled leaves from a plant identified as *N. glauca.*

A description has been given of a 50-year-old woman who developed involuntary limb jerking, paraesthesiae of the feet, blurred vision and diarrhea one hour after eating three steamed leaves from a plant identified as *N. glauca* (2). She recovered the next day in hospital. No toxicology was reported.

The plant is also poisonous to animals (1,9), including cattle, ostriches, sheep and rabbits although cases of poisoning are rare due to apparent unpalatability of the plant. Animals develop the typical features of nicotine toxicity with a staggering gait, jerking of the head, stupor and death within hours.

There is a paucity of toxicology data after anabasine poisoning. The previously reported case blood concentration of 1.15 mg/L compares with the blood concentration of 2.2 mg/L in this case. This case supports the suggestion that anabasine is much more toxic for humans than nicotine.

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