Case Report

The Tissue Distribution of Fluoride in a Fatal Case of Self-Poisoning

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Abstract

The purpose of this paper is to report a case of fluoride poisoning along with a discussion of poisoning characteristics, analytical procedures, and a review of previous reports of fatal intoxications with analytical data. A case of suicidal ingestion of 40 mL of a rust removal agent containing hydrofluoric acid and ammonium fluoride by a 33-year-old white male is presented. He had an organic personality disorder with residual schizophrenia and previous suicide attempts with therapeutic drugs and cleaning products. At admission, he presented with a Glasgow coma score of 3, third degree atrioventricular block, and asystole. Resuscitation efforts were performed during which the patient suffered two episodes of ventricular fibrillation followed by asystole. In spite of advanced resuscitation efforts and the administration of calcium chloride, he died 2.5 h after the ingestion. Analytical data in the hospital showed calcium levels of 3.1 mg/dL and metabolic acidosis. Internal findings were erosive gastritis, brain edema, and pulmonary and hepatic congestion. Quantitation of fluoride was performed using an ion-selective electrode for the anion. Disposition of fluoride in the different tissues was as follows: peripheral blood, 19.4 mg/L; urine, 670 mg/L; vitreous humor, 2.5 mg/L; liver, 40.0 mg/kg; kidney, 60.0 mg/kg; lung, 17.5 mg/kg; brain, 2.5 mg/kg; spleen, 30.0 mg/kg; bone, 0.5 mg/ kg; and gastric content, 1120 mg/L (67 mg total). Validation of the analytical method was performed using different spiked tissues, in a range of concentrations from 2.4 to 475 mg/L or mg/kg, and submitting them to dilution (1:25) to avoid the matrix effect and to bring these concentrations to the range of the aqueous calibration curve (0.19–19 mg/L). Limits of detection and quantitation were 0.02 and 0.1 mg/L, respectively. The linearity of the method, for all studies tissues, was excellent, with r^2 values of 0.999. Accuracy and precision were within 10.5% and 5.7%, respectively. Fluoride analyses using the ion selective electrode are simple, sensitive, and rapid. This report provides an extensive tissue distribution study of fluoride after a well documented case of acute poisoning. Based on the autopsy findings, patient history, toxicology results, and previously reported data the forensic pathologists ruled that the cause of death was due to a fluoride poisoning, and the manner of death was listed as suicide.

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Introduction

Hydrofluoric acid (HF) is known to be one of the most corrosive inorganic acids because of its strong affinity for protein and its hydratation and corrosion of tissues by free hydrogen ions. Moreover, the dissociated fluoride ions cause systemic poisoning because of their high affinity for cellular enzymes and divalent cations, mainly calcium and magnesium. The toxicity of each fluoride compound is related to the individual solubility, so some salts are practically nontoxic because the fluoride ion is tightly bound, whereas others such as sodium fluoride are highly soluble and easily dissociated and absorbed. Hydrogen fluoride is produced as a gas and then condensed into a liquid known as HF, which is soluble in water and has an irritating odor (1). The colorless property has resulted in the product being mistaken for water (2).

HF has a pK_a of 3.5, and in its non-ionized form, would be rapidly absorbed from the stomach. In the systemic circulation, dissociation of the molecule yield free fluoride and hydrogen ion. Fluoride is a low-molecular-weight anion that is easily absorbed in the gastrointestinal tract after ingestion. Volume of distribution is 0.5 to 0.7 L/kg. Fluoride is eliminated primarily and rapidly by renal excretion; about 50% is excreted within 24 h after ingestion. Renal clearance for fluoride is 48–147 mL/min, depending upon urinary flow and pH. After exposure ceases, urinary fluoride rapidly diminishes within 48 to 72 h. A small amount (5 to 10%) is excreted in feces. The elimination half-life of fluoride is 2–9 h (1,3).

HF is widely used in the petroleum industry; in etching and cleaning silicone, glass, metal, stone, and porcelain; in enameling and galvanizing iron; pickling stainless steel; in separating uranium isotopes; and in analytical and dye chemistry. It is used in the production of integrated circuits, plastics, germicides, and insecticides (1). As a result, occupational exposures by different routes to liquid HF or fumes are well-described (4–6). In addition, HF is present in domestic products such as cleaning solutions and rust removers at lower concentrations, although products consisting of 45 or 53% HF have been marketed (1); therefore, exposures in this environment are also documented (7–19).

Numerous fatalities have been reported following occupational accidents (20–26), suicides (27–31), homicides (32), and other accidents (2,9,19,33). In spite of this extensive literature, most authors have presented only blood fluoride data in lethal poisonings (2,20,29,33).

Because there are few data from extensive tissue distribution studies, a case of suicidal ingestion of fluoride from a commercial product is presented, including clinical data, autopsy findings, a complete tissue distribution study with validated analytical methodology, and a comparison with previously available data in the literature.

Case History and Autopsy Findings

A 33-year-old white man (56 kg, 166 cm) was admitted to the hospital of Galdakano (Vizcaya, Spain) at 14:27 h on April 2006. In the previous 2 h, he had voluntarily swallowed a commercial product contained in a plastic bottle. The victim took it from a housekeeping cart in the bathroom of the psychiatric hospital of Bermeo (Vizcaya, Spain) where he had lived for the last 6 years. At admission, he presented with a Glasgow coma score of 3, pulse of 80 beats/min, and oxygen saturation of 46%. No external burns were observed in the oro-pharynx. He was carefully monitored, and a third grade atrial-ventricular block and asystole was observed in the EKG. Resuscitation efforts were performed during which the patient suffered two episodes of ventricular fibrillation followed by asystole. Adrenaline, atropine, magnesium sulfate, and calcium chloride (5 ampoules) were administered. After 30 min of advanced reanimation maneuvers, he died. Analytical data in hospital showed glucose 176 mg/dL (normal range before meals: 90–130 mg/dL), amylase 242 U/L (normal range: 23–85 U/L), CPK 253 U/L (normal range for men: 38–174 U/L), chloride 89 mEq/L (normal range: 96–106 mEq/L), sodium 133 mEq/L (normal range: 15–250 mEq/L), and calcium 3.1 mg/dL (normal range: 8.5–10.2 mg/dL). The venous blood gases revealed pH 7.05 (normal range: 7.35–7.45), PCO_2 66.6 mmHg (normal range: 35–45 mmHg), PO_2 27 mmHg (normal range: 80–100 mmHg), bicarbonate 18.4 mEq/L (normal range: 20–26 mEq/L), oxygen saturation 28.5% (normal range: 95–99%), base excess –12.5 mEq/L (normal range: –2 to +2 mEq/L). The doctor in charge phoned our Poison Control Center at the National Institute of Toxicology and Forensic Sciences, where we informed him that the commercial product was a rust remover containing 5–10% hydrofluoric acid, 3–5% ammonium fluoride, and 80% water. The size of the container was 40 mL. Personal antecedents of the decedent included developmental disorder, an organic personality disorder, residual schizophrenia, and tricholeukemia. He had received multiple antipsychotic agents with poor results and had visited the emergency department in numerous occasions after simulated syncopal episodes and suicidal attempts with therapeutic drugs including lithium (needing hemodialysis) and cleaning products.

At autopsy, the description of the body was remarkable for the lack of burn evidence that was expected after the ingestion of a strong acid. Internal findings were erosive gastritis, brain edema, and pulmonary and hepatic congestion.

Peripheral blood (with and without fluoride as preservative), urine, vitreous humor, liver, kidney, lung, brain, spleen, bone, and gastric content (60 mL of a dark brown liquid) were collected during autopsy and sent to our laboratory (National Institute of Toxicology and Forensic Sciences) for analysis for a comprehensive toxicological screening, including fluoride determination.

Experimental

Toxicological analysis

A full toxicological analysis was performed on the deceased's peripheral blood and urine samples. The blood and urine were examined for ethanol and other common volatiles (methanol, acetone, isopropanol, etc.) using headspace with gas chromatography with flame-ionization detection (GC–FID). Urine from the case was also screened by immunoassay for propoxyphene, cocaine and benzoylecgonine, methadone, opiates, cannabinoids, benzodiazepines, amphetamine (and related compounds), barbiturates, and tricyclic antidepressants on a Hitachi 902 Automatic Analyzer (Tokyo, Japan) using Cedia® reagents (Microgenics, Fremont, CA). Then the blood and urine samples were extracted with Bond-Elut Certify columns (Varian Sample Preparation Products, Harbor City, CA), collecting together the acidic-neutral and basic eluates. The sample extracts were analyzed by GC with nitrogen-phosphorus detection (NPD) for screening analysis and by GC–mass spectrometry (MS) for confirmation analysis. Then an additional high-performance liquid chromatograph coupled to diode-array detector (HPLC–DAD) was used to complete the toxicological screening. All these procedures were performed following a routine analytical method described in our previous work (34). Finally, all the biological tissues were analyzed for fluoride using a selective electrode.

Quantitation of fluoride

Fluoride concentration was determined by potentiometry using a Mettler-Toledo fluoride ion selective electrode (model DX219-F, Urdorf, Switzerland) connected to a Crison pH/mV meter (model GLP22, Alella, Barcelona, Spain), that was calibrated to provide direct concentration readings. A CertiPur Merck (Darmstadt, Germany) sodium fluoride stock solution of 1000 mg/L was used as stock solution. Calibration of the equipment was achieved using fluoride standards of 0.19, 1.9, and 19 mg/L that were prepared in our laboratory by diluting the stock solution with water Milli-Q (Millipore, Billerica, MA). This Milli-Q water had a resistivity of 8.2 Mω.cm and 2 ppb of total organic carbon (TOC). A total ionic strength adjustment buffer type III (TISAB III) was obtained from Mettler-Toledo. The purpose of TISAB III is to buffer the samples at pH 5–5.5 to prevent formation of HF, as the electrode is sensitive only to free fluoride ion. TISAB III contains cyclo-hexylene-dinitrilotetraacetic acid, which forms stable complexes with aluminium (III) and iron (III), thus removing interferences by

freeing fluoride ions from complexes with these ions and brings the samples and the standards to a similar level of ionic strength for significant comparison.

All samples were diluted to bring its concentrations within the calibration range. Because of the size of the electrode, we needed a minimum volume of 25 mL of sample for measurements. All biological samples, including blanks of each one, and controls were diluted with Milli-Q water. The blanks were obtained from a case of a non-intoxicated individual.

Liquid samples. Blood and vitreous humor were diluted 1:25. Urine and gastric content were diluted 1:100.

Solid tissues. Liver, kidney, lung, brain, and spleen were homogenized using an electric tissue homogenizer model Ultraturrax® T-25 manufactured by IKA® Labortechnik (Staufen, Germany), and then 1 g of each tissue homogenate was diluted 1:25. Bone was pulverized with a Freezer Mill® model 6750 manufactured by Spex CertiPrep (Metuchen, NJ), and then 5 g was diluted with 25 mL Milli-Q water.

All samples were sonicated for 5 min before fluoride measurement. TISAB III (2.5 mL) was added to each 25 mL of tissue homogenate or standard. All fluoride concentrations were determined directly from the electrode meter. At these dilutions, no matrix effect was observed in any of the samples. This effect was previously investigated through the study of slopes in the linear regression lines of different matrices. The average calculated slopes of linear regression lines were –6.0 mV per mg/L for the diluted blood, urine, liver, kidney, and lung and –6.1 mV per mg/L for the aqueous standard with r^2 values, in all matrices, calculated to be ≥ 0.999. The similarity of these slopes allows the determination of all diluted tissues from the same aqueous calibration curve.

Results and Discussion

Assay characteristics

The validation of a bioanalytical method is required to demonstrate the performance of the method and the reliability of analytical results. In the field of clinical and forensic toxicology, it is essential to use well characterized and fully validated methods to yield reliable results that can be interpreted satisfactorily.

Table I shows comparative validation data of fluoride determination in water and non diluted blood from 0.1 to 19 mg/L at five concentration levels. Results show water and undiluted blood accuracies within 3.6% and 21.2%, respectively, and water and undiluted blood precisions within 7.6% and 3.7%, respectively. Limits of detection and quantitation in both materials were 0.02 and 0.1 mg/L, respectively. The linearity of both calibration curves was good, with r^2 values of > 0.998 in the studied range. The comparative study of the accuracies in water and undiluted blood revealed a slight matrix effect in the blood sample.

The procedure used for the determination of fluoride (dilution 1:25 or higher) has several advantages: first, it avoids the matrix effect; second, it brings the high tissue concentrations found in cases of acute poisonings to the range of measurements; and third, the dilution procedure is very useful when the size of the forensic specimen is very small, which is especially frequent with blood samples. Also, direct measurements (requiring minimum sample preparation) as conducted here are more convenient than other, more time-consuming and complex procedures reported by other authors (21,35–40). Thus, the addition standard method (31), microdiffusion (36), and a specific calibration curve for each matrix are not necessary.

Table II provides data of calibration curves in different materials obtained by plotting the responses in mV against fluoride concentrations (2.4, 4.8, 47.5, and 475) in milligrams per liter or milligrams per kilogram. The similarity of the slopes observed allows the determination of both aqueous material

Table I. Validation Data of Fluoride from Fortified Samples Using a Selective Ion Electrode*

Material	Level of Fortification (mg/L or mg/kg)	% Accuracy (n = 6)	Intraday Precision RSD† (%) (n = 6)	Linearity r^2 (0.1–19 mg/L) (n = 6)	Limit of Detection (mg/L)	Limit of Quantitation (mg/L)
Water	0.1	–0.8	7.6			
	0.5	1.4	1.3			
	5.0	0.8	2.5	0.998	0.02	0.1
	10	0.5	3.2			
	19	–3.6	3.6			
Blood	0.1	–2.0	3.7			
	0.5	–21.2	2.4			
	5.0	–13.7	2.2	0.998	0.02	0.1
	10	–14.5	1.8			
	19	–15.7	1.1			

* Measurements performed without dilution of the samples and using a water calibration curve (0.19–19 mg/L).
† RSD: relative standard deviation.

Table II. Data of Calibration Curves in Different Materials Obtained by Plotting the Responses in mV Against Fluoride Concentrations in mg/L or mg/kg

Material	Range (mg/L or mg/kg)	Slope	Intercept	Linearity (r^2)
Blood*	2.4–475	–6.2	120.4	0.999
Urine*	2.4–475	–6.0	114.9	0.999
Liver*	2.4–475	–6.0	116.7	0.999
Kidney*	2.4–475	–5.9	114.7	0.999
Lung*	2.4–475	–6.0	115.4	0.999
Water	0.1–19	–6.1	116.9	0.999

* Measurements performed on spiked biological samples diluted with deionized water (1:25). The calibration curves were obtained with three determinations in one day.

and diluted tissues from the same aqueous calibration curve, which is simple and desirable in a forensic laboratory.

Table III shows accuracies and precisions of fluoride determination in different tissues at four concentration levels from 2.4 to 475 mg/L or mg/kg following the mentioned procedure (dilution 1:25). They were within 10.5% and 5.7%, respectively, considering all the different tissues.

Disposition of fluoride in the different tissues of our case is showed in Table IV. Despite numerous reports of fatal poisoning cases with inorganic fluoride salts and/or HF, only few authors have presented an extensive body tissue distribution study in acute poisoning (Table V). Concentrations of fluoride in tissues and body fluids vary among individuals depending on diet, age, and extent of fluoridation of water. The work of Gettler and Ellerbrook (41) published in 1939 remains, even today, a primary reference for toxicologists concerned with fluoride tissue distribution in normal and poisoned subjects. The fluoride concentrations found in the present case are many orders of magnitude above published figures for the normal range (41). The distribution in different organs throughout the body strongly suggests systemic dissemination and the values observed are consistent with the concentrations previously reported following fatal exposures. Approximately 95% of the total body burden of fluoride is stored in bone. Interestingly, bone fluoride in our case was low, and it is similar to the bone concentration obtained in the nonexposed individual used for comparison. This fact can be justified simply because this is an acute poisoning case; therefore, there was no time following the exposure in the current case for the incorporation of fluoride into bone to occur. Higher concentrations observed by Gettler and Ellerbrook (41) could be explained by a high exposure of fluoride in that population or, more probably, the different techniques employed that could have overestimated the normal tissue concentration.

Table III. Precision and Accuracy of the Assay in Different Tissues Using the Dilution Procedure

Material	Level of Fortification (mg/L or mg/kg)	% Accuracy (n = 6)	Intraday Precision RSD* (%) (n = 6)
Blood	2.4	-3.3	5.7
	4.8	-4.7	2.9
	47.5	0.9	1.9
	475	4.4	0.6
Urine	2.4	-0.5	0.1
	4.8	-4.7	2.9
	47.5	0.6	1.7
	475	2.7	1.0
Liver	2.4	-3.3	5.7
	4.8	-3.3	3.3
	47.5	-3.3	2.6
	475	0.1	1.3
Kidney	2.4	8.8	4.7
	4.8	5.0	4.3
	47.5	-0.2	1.5
	475	2.2	1.1
Lung	2.4	10.5	0.1
	4.8	-1.9	2.8
	47.5	-0.3	1.7
	475	3.2	1.5

* RSD: relative standard deviation.

In our case, the highest concentrations of fluoride were observed in the gastric contents and in the urine. Normal urinary fluoride concentrations range from 0.2 to 3.2 mg/L depending upon dietary intake. Urinary fluoride concentration in our case exceeds the normal maximum by a factor of approximately 200. This may be due to a rapid start of elimination and is comparable with cases in which the sample was taken at similar times (13). When the patient dies later, as in most of the reported cases, low urine fluoride concentrations may be due to urine loss during emergency treatment (31).

On the other hand, blood fluoride concentrations have been higher than ours in both fatal (2,26,37,39) and nonfatal cases (11,14) and could depend on the time of sampling after the ingestion as can be exemplified with the cases reported by Greendyke and Hodge (20) and Menchel and Dunn (37). An average postmortem blood fluoride concentrations of 15 mg/L has been reported by Baselt (3).

Routine screening in the urine sample by immunoassay was positive for benzodiazepines. Ethanol and other volatiles were present neither in the blood nor in the urine samples. HPLC–DAD was used for quantitation of quetiapine and 10-monohydroxycarbazepine (MHD) (oxcarbazepine active metabolite) because these drugs are partially decomposed in the heated injection port of the GC. Nordiazepam was also quantitated using the same technique. Results are shown in Table I. All these pharmaceutical drugs were within therapeutic ranges (3).

The pH of the deceased's gastric content was 4.5. As re-

Table IV. Fluoride Concentrations in Tissues from the Forensic Case

Material	Fluoride*	
Peripheral blood (mg/L)†	19.4	(0.5)
Urine (mg/L)†	670	(3.0)
Vitreous (mg/L)	2.5	(0.5)
Liver (mg/kg)	40.0	(0.5)
Kidney (mg/kg)	60.0	(0.7)
Lung (mg/kg)	17.5	(0.9)
Brain (mg/kg)	2.5	(0.5)
Bone (mg/kg)	0.5	(0.5)
Gastric content (mg/L)	1120	(2.0)
Total amount (mg)‡	67.2	

* Fluoride measurements in parentheses were obtained from a non-intoxicated individual used for blank samples.
† Other toxicological findings. Peripheral blood (mg/L): nordiazepam: 0.5; quetiapine: 0.1; and 10-hydroxy-oxcarbazepine: 22. Urine (mg/L): nordiazepam: 0.4; quetiapine: 4.2; and 10-hydroxy-oxcarbazepine: 30. Drugs quantitated using HPLC–DAD.
‡ Total amount of fluoride (mg)/total amount of gastric content.

Table V. Comparative Review of Reported Fatalities from Fluoride Poisoning with Analytical Data

Age (years)/ Gender	Samples (mg/L or mg/kg)								Other Samples	Case History	Technique used for Fluoride Measurement	Author(s), Year, and Reference
	Blood	Urine	Vitreous	Bile	Liver	Kidney	Lung	Gastric				
unknown/ unknown	0.64	0.56	–	–	0.70	0.78	0.42	–	0.56 brain, 0.60 heart, 0.30 spleen, 141 bone	Normal tissue (maximun concentrations) obtained from healthy individuals (n = 3–5)	Titration	Gettler et al., 1939 (41)
unknown/ unknown	15.5	–	–	–	15.0	11.6	–	–	–	Five poisoning cases (maximum concentrations are shown here). Two victims were found dead; the other three died in less than 24 h in the hospital	Titration	Gettler et al., 1939 (41)
27/female	–	–	–	–	1.65	–	–	–	–	Suicidal ingestion of an iron-mould remover (1.5 g HF)	Unknown	Curry, 1962 (27)
37/male	4	–	–	–	–	–	–	–	–	Accidental dermal exposure. Extensive burns. The patient expired in the hospital 4 h after the accident	Titration	Greendyke and Hodge, 1964 (20)
29/male	3	–	–	–	–	–	–	–	–	Accidental dermal exposure. Co-worker of the previous victim. The patient expired in the hospital 10 h after the accident	Titration	Greendyke and Hodge, 1964 (20)
28/male	0.50	–	–	–	N.D.*	–	0.57	–	0.43 bone	Accidental dermal exposure in an alkylation unit in a petroleum refinery. The patient died at the scene 30 min after the accident.	Microdiffusion	Watson et al., 1973 (21)
3/male	2.6	–	–	–	1.8	2.1	–	18	3.2 stomach, 12 jejunum contents	The patient died 5 h after ingestion of an unknown amount of sodium fluoride and heavy metals	Microdiffusion	Craston et al., 1975 (35)
57/male	16	320	–	–	–	–	–	260	–	Suicidal ingestion. The victim was found dead after he ingested a rodenticide	Microdiffusion and fluoride selective electrode	Speaker, 1976 (36)
unknown/male	3.0 (serum)	–	–	–	4.2	6.2	–	–	–	Accidental dermal exposure. The patient died in the hospital approximately 10 h after the accident	Unknown	Tepperman, 1980 (43)

* N.D.: Not detected.
† Spectrophotometric measurement using lanthanum-alizarin complexone.

Table V. (continued) Comparative Review of Reported Fatalities from Fluoride Poisoning with Analytical Data

Age (years)/ Gender	Samples (mg/L or mg/kg) Blood	Urine	Vitreous	Bile	Liver	Kidney	Lung	Gastric	Other Samples	Case History	Technique used for Fluoride Measurement	Author(s), Year, and Reference
31/female	85 (antemortem), 48 (postmortem)	–	–	–	37	–	–	5 g (total)	37 cerebro-spinal fluid	Suicidal ingestion. The patient (a dental assistant) died 2 h after ingestion of 56 g of sodium fluoride	Microdiffusion, spectrophotometry†	Kaa et al., 1986 (39)
33/male	56.2	17.0	–	–	81.2	68.4	–	5.6 g (total)	–	Suicidal ingestion. The patient died 45–60 min after ingestion of 3–4 fl. oz. of "Erusticator"	Microdiffusion, spectrophotometry†	Menchel and Dunn, 1984 (37)
23/male	4.2 (serum)	–	–	7.25	16	–	19 (max.)	–	14.2 heart, 20.4 brain, 18.0 muscle (psoas), 303 skin (burn site)	Accidental dermal exposure. The patient died in the hospital 17 h after the accident	Microdiffusion and fluoride selective electrode	Mayer and Gross, 1985 (38)
29/male	35.2 (antemortem), 56.2 (postmortem)	–	–	–	–	–	–	–	–	Accidental ingestion. The victim ingested a mouthful of an unknown "rust remover", mistaking it for water. He died 90 min after the exposure	Fluoride selective electrode	Manoguerra and Neumann, 1986 (2)
33/female	–	295	–	3.4	8.6	16	–	225	–	Suicidal ingestion of 1 lb of a roach powder containing 95% sodium fluoride	Microdiffusion and spectrophotometry†	Poklis and Mackell, 1989 (40)
51/male	18.6	–	11.9	–	–	–	–	–	–	Accidental dermal exposure in a sanitation worker after the rupture of a garbage canister containing 80% HF	unknown	Hung et al., 1998 (25)
56/male	19	–	–	–	–	–	–	–	–	Accidental ingestion. The victim ate a tablespoon of a glass etching compound, having mistaken it for peanut butter	Fluoride selective electrode	Randall and Fraser, 1994 (33)
43/male	13	–	–	–	–	–	–	–	–	Suicidal ingestion of an unknown quantity of "Erusticator"	Fluoride selective electrode	Bost and Springfield, 1995 (29)
65/male	63.8 (serum)	61.7	–	–	–	–	–	–	61.7 pericardium fluid, 53.7 toracity cavity fluid	Accidental dermal exposure while cleaning iron pipes of a cooling apparatus	Fluoride selective electrode	Takase et al., 2004 (26)
43/male	–	5.0	4.5	6.5	–	10.0	–	39.0	4.5 squeletal muscle	Suicidal ingestion of a 10-fl. oz. bottle of "Whink Rust Stain Remover"	Fluoride selective electrode	Cordero et al., (2004) (31)

* N.D.: Not detected.
† Spectrophotometric measurement using lanthanum-alizarin complexone.

ported, normal pH value in gastric contents is about 2.0, our data are in accordance with the effect in the stomach of the ingestion of a weak acid such as HF.

Poisoning characteristics

The case reported here illustrates many of the clinical features of previously reported fatal fluoride poisoning. Systemic manifestations can be observed after exposure to fluoride by different routes. For instance, hemorrhagic pulmonary edema has been observed after significant inhalation, ingestion, and dermal exposures (2,4,14,21,26). Persistent nausea, vomiting, and diarrhea were reported following dermal exposure to 70% HF as well as after ingestion (2,13,37) and histologic myocardial damage has been described in fatal exposures both orally or dermally (20,38).

Ingestion of HF may cause painful necrotic lesions of the oral mucosa and the gastrointestinal tract, depending on the concentration. In fact, significant gastrointestinal burns are not expected after taste ingestions of low concentration products, but they may occur after ingestion of high concentration (greater than 20%) solutions or deliberate ingestions (i.e., suicide attempts by adults). In our case, ingestion of about 40 mL of a low concentration rust removal agent resulted in erosive gastritis, similar to other cases reported in the literature (16,37).

Cardiac toxicity generally manifests within 6 h of an exposure. Hypocalcemia, hyperkalemia, and hypomagnesemia (5,28,42) with ventricular dysrhythmias and cardiac arrest have been reported following ingestion and dermal exposure (2,10,11,13,22,25,31,43–48). There are several mechanisms underlying the cardiotoxicity seen in fluoride intoxications, including the electrolite abnormalities and the direct cardiotoxic effect of the fluoride ion on the myocardial adenylate cyclase. In our case, there was a rapid onset of asystole and ventricular arrhythmias, within the first 2 h. We also observed metabolic acidosis, which is an important marker of fluoride toxicity, and is likely to be an important determinant of the subsequent course. Besides metabolic acidosis increases the tissue/intracellular delivery of fluoride and decreases renal elimination of fluoride.

The rapid onset of severe toxicity and death that occurs following the ingestion of low concentrations of HF such as in our case is not often described (2) because, on other occasions, treatment with calcium salts was effective (17,18). On the other hand, in our case, the estimated dose of fluoride could be calculated as 2.5–5 g, which is at least twice the estimated lethal dose of 1.5 g or 20 mg/kg (27,37).

Conclusions

This is the first case we are aware of that provides an extensive and characteristic tissue distribution study of fluoride after a fatal and acute case of self-poisoning including a validated analytical method and a literature review. Based on the autopsy findings, patient history, toxicology results, and previously reported fluoride poisonings, the forensic pathologists ruled that the cause of death was fluoride poisoning, and the manner of death was listed as suicide.

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