

Chemical burns caused by trifluoroacetic acid

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Summary

Background. Trifluoroacetic acid is a very strong carboxylic acid. The acid has been suspected to have similar toxic effects as hydrofluoric acid on skin contact. Hydrofluoric acid is highly toxic, owing to skin penetration by fluoride ions. A spill of hydrofluoric acid on the skin may be fatal. As trifluoroacetic acid contains fluorine, patients with chemical burns caused by trifluoroacetic acid have been given particular attention when treated in the hospital.

Objectives. To gather the known cases of trifluoroacetic acid burns from our department to give an overview of how they were exposed, the clinical presentation, and treatment.

Methods. Five patients with chemical skin burns caused by trifluoroacetic acid were reviewed with regard to the extent of the burn, treatment, blood samples taken, and systemic effects.

Results. The chemical burns reported were limited (< 1% of the total body surface). The burns healed as expected for chemical burns caused by acids. None of the patients showed any symptoms or signs that are typical for hydrofluoric acid burns.

Conclusion. Localized chemical burns caused by trifluoroacetic acid should be regarded as being similar to burns from other acids, with the exception of hydrofluoric acid. To our knowledge, there are no indications that trifluoroacetic acid causes the same toxic effects as hydrofluoric acid.

Key words: acid; calcium gluconate; chemical burn; irreversible irritant reaction; toxic effects; treatment.

Concentrated strong acids are common and important chemicals that are used industrially on a large scale in the production of other chemicals, as well as in the laboratory for chemical syntheses and analysis. Strong acids should be handled with care, as exposure can cause severe chemical burns by damaging proteins via denaturation and hydrolysis, causing cell death

and necrosis. Handling of strong acids is common in industry, but exposure from their use in household products has also been reported (1). In industry, strong acids in large volumes are ideally handled in closed systems to minimize the risk of skin exposure. In the laboratory, however, where small volumes are handled, appreciation of the potential risks of acids may be limited.

During the last 6 years, the Department of Occupational and Environmental Dermatology in Malmö has seen 4 patients with chemical burns caused by trifluoroacetic acid (Fig. 1). Another patient with a similar injury was treated at the Department of Plastic Surgery at our hospital. The 5 patients all worked at the same medium-sized company, which uses trifluoroacetic acid in its production process.

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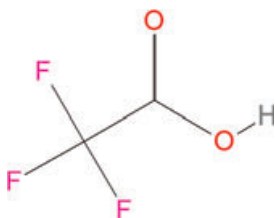


Fig. 1. Chemical structure of trifluoroacetic acid.

Case Reports

Case 1

A 22-year-old male with no previous skin disease was working as a process technician. He was exposed to trifluoroacetic acid when using a pair of tweezers to pick up an object from a reactor that had contained trifluoroacetic acid of unknown concentration. He wore protective clothes and gloves, but a leakage of condensed vapour occurred at the rim of the glove, and the skin on the right forearm was exposed. He immediately removed the glove and clothes, and treated the skin with polyethylene glycol, which is recommended by the available material safety data sheet (MSDS) for trifluoroacetic acid, and rinsed the arm with water for ~1 hr. Shortly thereafter, he was seen at our hospital, and the exposed arm was rinsed with water for another 45 min, and then treated with calcium gluconate gel (HF Antidote Gel; Crest Medical, Woolston, UK). After treatment, an erythema of approximately 6 × 10 cm was visible. Blood samples were collected for monitoring of liver status, creatinine, and electrolytes. All blood samples were normal. The patient was sent home, and re-examined 2 days later; no skin damage in the exposed area was observed.

Case 2

A 48-year-old woman placed a bottle of concentrated trifluoroacetic acid on her right thigh to date-mark it. Unfortunately, the cap was not closed, and a small amount of the acid spilled onto her leg. She immediately removed her trousers and rinsed the skin with water for at least 20 min. She was taken to hospital, where rinsing with water was continued. The progress of the rinsing was monitored with pH paper. The affected area was treated with calcium gluconate gel (HF Antidote Gel) and with hydrocortisone on the peripheral inflammatory area. On the skin where she was exposed to acid, a 2-cm² white–greyish surface developed, indicating necrosis (Fig. 2). The necrotic area was surrounded by an erythema, which was ~7 cm in width. The injured area was covered with a sterile dressing. Blood samples

were collected to monitor calcium and manganese. On re-examination after 18 hr, the condition of the exposed area had improved markedly. No erythema or signs of increasing necrosis were visible. Blood samples, including the calcium level, were normal. After ~1 month, the area exposed to trifluoroacetic acid was healed, but, in an area of ~1 cm² where necrosis had occurred, the skin was thin, hypopigmented, and slightly erythematous.

Case 3

A 29-year-old woman spilled concentrated trifluoroacetic acid when she opened a bottle of acid to prepare a dilute cleaning solution. Although she was wearing gloves, her right wrist was exposed to the concentrated acid. She immediately removed her gloves, and rinsed her arm with soap and water for ~30 min. At the hospital, the burn was rubbed with calcium gluconate gel (HF Antidote Gel) for ~30 min. On the exposed wrist, she had a red spot with a size of approximately 3 × 7 cm, which was centrally slightly oedematous. She experienced a smarting sensation at the site of the burn. The pain decreased after treatment with calcium gluconate and the burn site became less swollen, making it easier to extend the wrist. Blood samples were analysed for calcium, manganese, and albumin. All blood samples were normal. On re-examination the next day, the site of the burn was still slightly red and swollen, but there was no ulcer and there were no signs of necrosis.

Case 4

A 34-year-old woman came to the hospital emergency department after a spill of trifluoroacetic acid. At the workplace, she had rinsed the burns with water for ~15 min and applied polyethylene glycol before arrival at hospital. The patient had acid burns on her left arm and on the lower parts of her legs. From the emergency department, she was referred to the plastic surgery department for observation of the burns. The erosions were reminiscent of second-degree burns, but the total area was <1% of the body surface. She was treated with antibiotics to prevent infection. The patient was sent home after 24 hr, and re-examined 4 days later. On re-examination, the erosions had improved, and the patient was sent home without further measures being taken.

Case 5

A 46-year-old woman working as a laboratory technician preparing solvents for liquid chromatography, and used concentrated trifluoroacetic acid. When discarding excess acid, ~1 ml, she spilled the concentrated acid on the

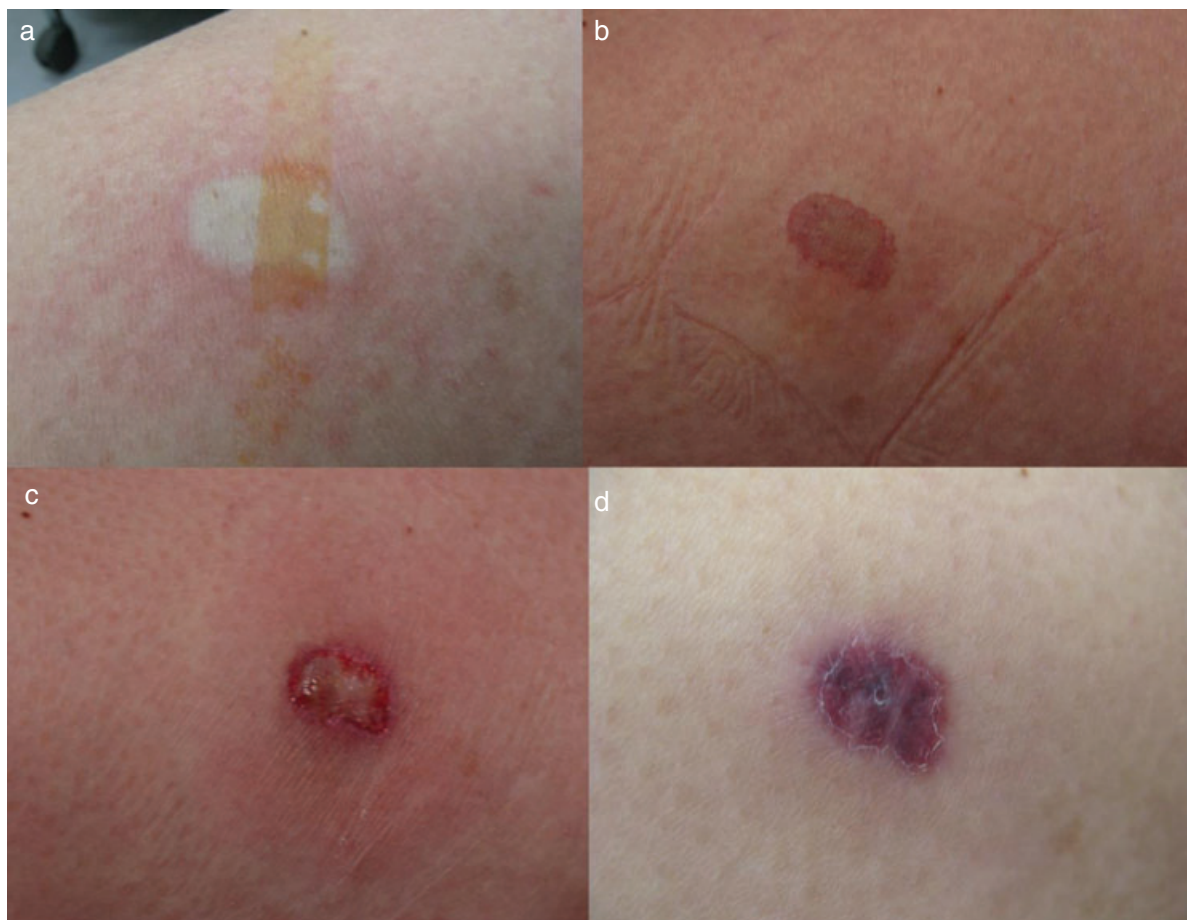


Fig. 2. A chemical burn caused by trifluoroacetic acid on the thigh in case 2. (a) Immediately after rinsing with water at the hospital. The discolouration across the injury is from the pH paper used for monitoring the rinsing. (b) Twenty-four hours after exposure. (c) Seven days after exposure. (d) Seven weeks after exposure.

arm of her laboratory coat, covering her left wrist. She immediately felt a burning sensation on the skin, and pulled up the arm of her coat to rinse the burn with water. Unfortunately, the acid remaining on her coat arm caused a second burn close to her left elbow. The laboratory coat was removed, and rinsing with water was started at the workplace. When she arrived at the hospital, the burn on the forearm measured approximately 1×5 cm. The central parts of the burn were white, and were surrounded by an erythema. Rinsing with water was continued for 1 hr. The pH on the skin surface was monitored with pH paper. After rinsing, the exposed area was rubbed with calcium gluconate gel (HF Antidote Gel). Blood samples were collected to monitor electrolytes, including calcium and albumin. All blood samples were normal. The wound was covered with a sterile dressing. The patient was sent home. On re-examination the following day, the central parts of the burns were brown and

necrotic. A weak steroid ointment was prescribed for treatment of the inflammation, and chlorhexidine/fusidic acid was prescribed as prophylactic treatment for bacterial infection. After ~ 1 month, no necrosis remained, and the burns were completely healed.

Discussion

Trifluoroacetic acid is used industrially in organic synthesis for the production of peptides. In the laboratory, trifluoroacetic acid is also widely used in low concentrations in eluents for liquid chromatography. The acid is easily soluble in both water and organic solvents. The total annual consumption of trifluoroacetic acid in Sweden has varied between 1 and 10 tonnes in the last 10 years (2). The company where the reported patients work used ~ 4 tonnes of trifluoroacetic acid in 2009.

Like all strong acids, trifluoroacetic acid can cause severe chemical burns. To describe the strength of an acid, the acid dissociation constant (K_a) or logarithmic acid dissociation constant (pK_a) is used. A high K_a or a low pK_a indicates that the acid is strong and easily loses a proton. Trifluoroacetic acid is one of the strongest carboxylic acids, with a pK_a of 0.3. It is structurally similar to acetic acid ($pK_a = 4.8$), but the electron-withdrawing effect of three fluorine atoms in the molecule more strongly favours the release of the proton. No animal toxicity data for skin exposure have been presented in the literature. The median oral lethal dose (LD_{50}) for the rat is 200 mg/kg, and the median lethal air concentration (LC_{50}) for the rat is 10 g/m³ (3).

It has been suspected that trifluoroacetic acid could have a similar toxic effect as hydrofluoric acid. Hydrofluoric acid ($pK_a = 3.2$) above a concentration of 60% causes severe, extremely painful skin burns, which are deep and heal slowly. Hydrofluoric acid is toxic to cells, as fluoride ions interfere with calcium metabolism and enzyme mechanisms (4). Hydrofluoric acid burns are severe injuries; fatalities have occurred following exposure (5), and exposed persons should always be treated at hospital, owing to the risk of systemic effects. A visibly small burn can still cause serious internal damage through the effects of fluoride ions. As an antidote for hydrofluoric acid exposure, calcium gluconate is used for the formation of insoluble fluoride salts, preventing the fluoride ions from penetrating into the tissue. Calcium gluconate can be applied as a gel or injected at the site of the burn.

Owing to the solubility of trifluoroacetic acid in both organic solvents and water, trifluoroacetic acid can easily penetrate the skin (6). Burns caused by trifluoroacetic acid heal slowly. Trifluoroacetic acid has been suspected to cause hypocalcaemia by the release of fluoride ions, possibly because of metabolism in the skin. However, there is no report indicating that the fluorine atoms of trifluoroacetic acid are released by metabolism. According to one manufacturer of trifluoroacetic acid, the trifluoromethyl group is inert to *in vivo* metabolism (6). Trifluoroacetic acid itself is a metabolite in the biotransformation of 1,1,1,3,3-pentafluoropropane (HFC-245fa), a hydrofluorocarbon (HFC) used as a blowing agent for polyurethane. Trifluoroacetic acid can be detected in urine after exposure to this HFC (7). The fact that the body metabolizes an HFC to trifluoroacetic acid is an indication that trifluoroacetic acid is a stable substance that is excreted in the urine. For the patients reported here, blood samples showed that the calcium levels were normal, and no late symptoms were reported, indicating that fluoride ions are not released from trifluoroacetic acid.

No reports where concentrated trifluoroacetic acid was the cause of burns have been found in the literature. Cases have been reported where trifluoroacetic anhydride was the cause of severe chemical burns (8, 9). Trifluoroacetic anhydride is the corresponding anhydride of trifluoroacetic acid. This anhydride is often used in organic analysis as a derivatizing agent for amine groups before chromatographic analysis. Upon hydrolysis, this anhydride forms trifluoroacetic acid. The injuries caused by trifluoroacetic anhydride were probably a combination of the corrosive effect of the acid formed upon hydrolysis and the high reactivity of the anhydride. Nakamura et al. treated the trifluoroacetic anhydride burns with calcium gluconate, as a precaution, because they suspected that the acid could form fluorine ions (8).

The immediate treatment for chemical burns caused by acid is rinsing the exposed skin site with large amounts of water. Clothing, watches and jewellery should be removed. If suitable, removal of clothes could be performed with scissors. Pulling-up of clothes can give rise to secondary burns if the clothes are soaked with acid, as shown in one of our cases.

As trifluoroacetic acid contains fluorine, calcium gluconate gel was used as a precaution in 4 of the cases reported here, and is also for burns caused by trifluoroacetic anhydride (8, 9). However, treatment with calcium gluconate probably has no effect on trifluoroacetic acid burns. When calcium gluconate was used for the treatment of burns caused by trifluoroacetic anhydride, it was reported that the pain increased at the site of the burn (8, 9). For hydrofluoric acid burns, the pain should decrease upon treatment with calcium gluconate, as a sign of successful treatment. The patients treated with calcium gluconate gel for trifluoroacetic acid burns in our department showed no signs of pain being increased or decreased by the treatment.

In some MSDSs for trifluoroacetic acid, for example those found at the company where the accidents occurred, it is stated that burns should be treated with polyethylene glycol (PEG) 400. According to one manufacturer of chemicals that included this information in the MSDS, PEG 400 should have good ability to 'pull out' substances from the skin. PEG 400 is sometimes recommended for the treatment of phenol burns (10). One can only speculate why PEG 400 has been recommended for trifluoroacetic acid burns. Trifluoroacetic acid is soluble in several organic solvents, and it is therefore possible that PEG 400 has been suggested because of the lipophilic properties of the acid. However, trifluoroacetic acid is also completely miscible with water, and copious rinsing may therefore be better than a special decontamination solution. We have

found no evidence in the literature that PEG 400 is an effective antidote for trifluoroacetic acid burns.

From the cases reported here, it seems like that the emergency treatment for trifluoroacetic acid burns should be the same as for other strong acids, that is, immediate rinsing with large amounts of water. To monitor the progress of rinsing, the pH of the skin can be determined with pH paper. If possible, hard soap could also be used for more efficient neutralization. In our department, blood samples are nowadays always routinely collected to monitor the blood status, including calcium, magnesium, and potassium. Chemical burns should always be examined by a physician. Burns involving large areas

require hospitalization independently of the cause of the chemical burn. If necrosis occurs, excision may be necessary. For follow-up of the necrotic lesions, the injuries were photographed and the healing process was followed for ~ 1 month.

In the reported cases, the burns were limited to < 1% of the total body surface. No symptoms reminiscent of hydrofluoric acid burns were observed. It is important to remember that, even though trifluoroacetic acid does not cause the same types of injury as hydrofluoric acid, it is still a very strong acid, being ~ 100 000 times more acidic than acetic acid, and requires handling with great care whenever it is used.

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