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Case report

Critical care management of major hydrofluoric acid burns: a case report, review of the literature, and recommendations for therapy

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1. Introduction

Hydrofluoric acid (HFA), the inorganic acid of elemental fluorine, is a colourless gas or fuming liquid with a strong, irritating odour. It is produced from the reaction between calcium fluoride and sulphuric acid. When present in its purified form (>99%) it is referred to as anhydrous HFA, as aqueous HFA in its more diluted forms [1]. Since its first use to etch glass and dissolve silica in the seventeenth century, HFA has become an ubiquitous industrial agent [1–3].

Most burns are considered to be minor, involving only small parts of the body surface area [4]. When larger parts of the skin are burnt, morbidity and mortality significantly increase. If more than 20% of the body surface area is burnt with high concentration HFA mortality approaches 100% [5–9]. In major HFA burns, death almost always results from severe electrolyte imbalance [1–3,8]. *Exitus letalis* has been reported after a burn with 70% HFA involving as little as 2.5% of the body surface area [8]. Although no clear definition exists, it is reasonable to define major HFA burns as HFA exposures with a high risk for lethal electrolyte imbalances (Table 1).

Unlike most minor HFA burns, which can be successfully managed by topical and regional therapy as well as close monitoring [10], major HFA burns require immediate critical care treatment. Currently, however, most therapeutic recommendations focus on therapy of minor HFA burns [11,12]. Although it is inadequate and possibly dangerous to apply guidelines of minor to major HFA burns, no therapeutic strategy for the management of major HFA burns has yet been defined.

This work presents the successful treatment of a patient with a major HFA burn. Additionally, it reviews the literature for treatment of major HFA burns, and tries to suggest recommendations for critical care management.

2. Case report

A 45-year-old white male (90 kg) suffered from a 70% HFA II–III burn of 30% of his body surface area involving both hands, forearms, parts of the upper arms, the chest, back, and in particular the scalp and neck. The patient was immediately showered at the workplace for 10 min, and then taken to a regional hospital. After intravenous, intraarterial, subcutaneous, and topical calcium gluconate application, as well as fluid and pain management, the patient was transferred to the surgical intensive care unit of our university hospital. At admission, serum electrolyte concentrations were as follows: calcium, 1.35 mmol/l; magnesium, 0.67 mmol/l; potassium, 4.5 mmol/l. Electrolyte therapy was performed with continuous intravenous infusion of calcium gluconate 10%, magnesium gluconide 10%, and potassium chloride 10% according to two hourly measured serum concentrations (Fig. 1). Bilateral intraarterial continuous calcium gluconate 2% infusions (Aa. brachiales) were titrated according to pain as well as tenderness, and carried on for 3 days. Additionally, calcium gel and calcium gluconate 10% solution (in soaked gauzes) were topically applied to all burnt areas; calcium gluconate 5% was used to infiltrate the scalp, back, and chest. During the first 24 h, the patient received 21,200 ml of fluids due to significant polyuria (18,000 ml/24 h) using a fluid control system (Equaline®;

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Table 1
HFA burns with a high risk to develop lethal electrolyte imbalances

1% BSA burn with anhydrous HFA
5% BSA burn with >70% concentrated HFA
7% BSA burn with 50–70% concentrated HFA
10% BSA burn with 20–50% concentrated HFA
20% BSA burn with <20% concentrated HFA
Prolonged exposure or long delay for treatment in minor HFA burns
Ingestion of HFA at concentrations >5%
Inhalation of HFA at concentrations >5%

HFA, hydrofluoric acid; BSA, body surface area.

Brady, Vienna, Austria). During the first 72 h on the intensive care unit, the patient received 239 mEq calcium, 223 mEq magnesium, and 188 mEq potassium. On Days 7 and 11, electrolyte replacement was reduced by 25%, but this immediately led to hypocalcemia. Only after stepwise reduction (1 mEq/h per day), magnesium and calcium infusion could be withdrawn on Days 13 and 14, respectively. In total, 860 mEq calcium, 736 mEq magnesium, and 1283 mEq potassium were intravenously infused. Surgical management included debridement and artificial skin coverage (Epigard®, Biovision, Ilmenau, Germany) on Day 2, and definitive skin grafting on Days 10 and 15 (scalp, both forearms). Wound dressings were performed daily; antibiotic prophylaxis (penicillin G + cefamandol), and supportive analgesia (continuous sufentanil, intermittent remifentanil) handled according to institutional guidelines. On Day 5, the patient developed clinical and laboratory signs of sepsis. Antibiotic therapy was empirically started with imipenem/cilastin plus vancomycin, and changed to imipenem/cilastin plus amikacin after microbiological identification of *Enterobacter cloacae* in all wound smears, catheter tips, and blood cultures. On Day 7, a significant deterioration in pulmonary function occurred (bilateral opacification in chest X-ray; PaO_2/FiO_2-quotient, 144), which could be adequately managed with short-term mechanical ventilation and intense respiratory physiotherapy. On Day 16, the patient was transferred to a low-dependency unit, and discharged from hospital 9 days later. He rapidly regained almost full range of motion, and 3 months after the accident, he was free of complaints with an aesthetically satisfactory result.

3. Discussion

3.1. Pathophysiology of HFA burns

HFA is a particularly dangerous acid because of its high electronegativity facilitating free tissue penetration [13]. This unique capability among acids results in a dual mechanism of injury: whereas, the hydrogen ion causes only mild caustic burn of the skin, major toxicity is mediated by the readily penetrating fluoride ion [2].

As HFA is only a weak acid (1000 times less dissociated than hydrochloric acid), dermal burns significantly depend on the concentration of HFA [14]. Therefore, skin symptoms after burns with concentrations <20% may be delayed up to 24 h. Twenty–fifty percent concentrated HFA exposure usually results in clinical symptoms after 1–8 h, whereas concentrations >50% induce immediate skin damage [1]. Common dermal signs are redness and edema, progressing to whitish discoloration and blistering. Grey areas indicate severely damaged tissue and may proceed to deep ulceration and skin necrosis [14]. If left untreated tissue destruction may continue and result in alkali-like liquefactive necrosis, tendosynovitis, and even osteolysis [15].

After tissue penetration, HFA continuously dissociates into hydrogen and fluoride ions. The highly reactive fluoride ions complex with calcium and magnesium in a variety of intra- and extra-cellular structures resulting in severe cellular dysfunction [16]. Fluoride is directly toxic to a number of cellular enzymes (e.g. key enzymes of glycolysis, phosphatase, cholinesterase) [17] and organs (central nervous system, heart, liver, kidney, and the pulmonary endothelium) [1,18,19].

In major HFA burns, significant absorption of fluoride ions into the systemic circulation occurs, where calcium and magnesium are bound to inactive fluoride complexes [3]. The consequent decrease in extracellular calcium and

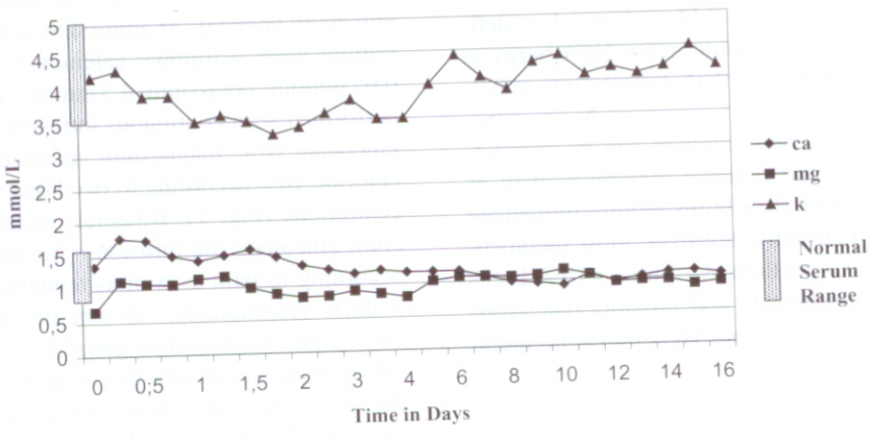

Fig. 1. Serum concentrations and infusion rates of ionized calcium (Ca^{++}), magnesium (Mg^{++}), and potassium (K^{+}).

magnesium concentrations can transiently be buffered by protein-bound and osseous stores, but finally results in severe hypocalcemia and hypomagnesemia. While hypocalcemia has been traditionally considered the primary cause of HFA toxicity [20], it is highly reasonable that hypomagnesemia [21,22], cardiodepressant and vasodilating effects of fluoride, and a fluoride-mediated increase in pulmonary vascular resistance, significantly contribute to toxic effects of HFA [23,24].

Hypocalcemia may develop in (1) >1% burn with >50% HFA, (2) >5% burn with HFA at any concentration, [3] inhalation or ingestion of HFA at any concentration [1,19,25].

Further electrolyte imbalances have been reported to include hyperkalemia and hyponatremia resulting from massive cell destruction [1–3]. Development of acidosis is common and additionally aggravates electrolyte imbalance [26].

Severe electrolyte imbalance leads to ventricular arrhythmias; particularly ventricular fibrillation and *torsades de points* have been reported to be the primary cause of death in patients with HFA burns [5–7,8,22]. Common clinical signs of hypocalcemia or hypomagnesiemia, e.g. neurological, respiratory, or cardiovascular symptoms, are typically absent, leaving a prolonged QT-interval as the most sensitive clinical indicator of electrolyte imbalance [1].

3.2. Emergency treatment

Primary measures in major HFA burns include immediate rescue, removal of contaminated clothing, and irrigation with copious amounts of waters [13,27]. Water lavage should begin immediately and prior to transport to a health care facility. Although time of hydrotherapy is well disputed, it is suggested to rinse contaminated skin for at least 20 min [1]. Use of calcium gel, calcium tablets, or neutralizing agents (e.g. sodium bicarbonate) has been proposed immediately after the accident [1,10,28]. Since none of these agents is of proven value, water remains the primary and most important emergency treatment to minimize tissue penetration and systemic sequelae from HFA [29].

When caring for patients with HFA burns, all emergency and hospital personnel must take extreme caution not to contaminate themselves. The use of standard surgical gloves are recommended as *minimum* protection [20]. Disposable gloves should never be worn without double gloving because of the potential for pinholes, and subsequent secondary HFA exposure [30].

3.3. Electrolyte therapy

In major HFA burns, intravenous replacement of divalent cations is the mainstay of critical care management. The primary aim of this electrolyte therapy is not to ameliorate local tissue destruction or pain, but to buffer lethal systemic effects of fluoride ions. In minor HFA burns, calcium and magnesium infusion may be withheld until a drop in serum concentrations occurs [25,31]. However, in major HFA burns, intravenous electrolyte replacement must not await results of laboratory analysis and has to be started empirically, because the decrease in calcium and magnesium is much more rapid and lethal electrolyte imbalance very likely [1]. If hypocalcemia and/or hypomagnesemia have once developed adequate restoration of electrolyte deficiency is extremely difficult [7]. Although the decrease in serum calcium and magnesium concentrations occurs within a short time, it is unlikely that this alone reflects total body deficiency, but probably significantly underestimates calcium and magnesium loss in major HFA burns [7].

The first-line electrolyte for intravenous replacement has traditionally been calcium [1,20]. Aside from magnesium, calcium is the only cation that can inactivate fluoride ions [2]. In major HFA burns, calcium therapy should be started with slow intravenous bolus injection. Twenty milliliters of calcium gluconate 10% may also be added to the first liter of fluids [32]. Further calcium should be infused continuously and titrated according to 2 h monitored serum electrolyte levels in order to prevent over- or underdosing.

Magnesium is equal to calcium in its capacity to bind fluoride ions [16], but has so far not been recommended for treatment of major HFA burns [20]. Magnesium is as effective as calcium for topical, subcutaneous, or intravenous treatment of HFA burns in animals [21,33,34]. In our case report, magnesium infusion, together with calcium, was considered a lifesaving measure to prevent ventricular fibrillation and death.

Large quantities of calcium and magnesium may be needed to bind systemically absorbed fluoride ions. In our patient, 860 mEq calcium and 736 mEq magnesium were intravenously infused during the intensive care unit stay. Although hypercalcemia has been reported as an adverse side effect of calcium therapy in minor HFA burns [25], electrolyte overdosing in major HFA appears low for several reasons: First, most of the patients are healthy workers without significant premorbities [4]. Particularly with intact renal function, excess calcium and magnesium will be excreted with the urine. Second, as calcium counteracts effects of the antidiuretic hormone on renal collecting ducts, polyuria results additionally preventing a significant increase in calcium and magnesium levels [35]. Third, frequent serum electrolyte monitoring should facilitate calcium and magnesium dosing.

Hyperkalemia has been reported to be a severe systemic complication of major HFA burns [36]. In our case report, hyperkalemia did not occur, but continuous potassium infusion was even necessary to keep serum levels within normal range (Fig. 1). Abundant calcium treatment and calcium-induced polyuria could have significantly contributed to this unexpected finding.

So far, no data exists on duration of fluoride toxicity during calcium and magnesium therapy in HFA burns. Considering a half life time of hydrogen fluoride between 12 and 24 h, it seems reasonable to attempt a reduction

in intravenous electrolyte replacement after cardiovascular stabilization and decrease of pain, usually after 48–72 h. However, such an attempt, if performed too vigorously, can lead to hypocalcemia. As high dosage calcium and magnesium infusion may result in upregulation of renal electrolyte secretion and thus induce a new electrolyte equilibrium, calcium and magnesium replacement must be withdrawn in small steps. Reductions of continuous infusion by 1 mEq/h per day proved to be safe in our patient.

3.4. Fluid and hemodynamic therapy

Replacement of calcium-induced polyuria represents the most important aim of fluid therapy in major HFA burns. In our patient, polyuria led to renal fluid loss of up to 18 liters/d, what could be effectively managed by using a fluid control system that safely prevented hypovolemia.

Another effect of polyuria is increased renal elimination of fluoride ions [37]. Further improved fluoride excretion has been reported after alkalization of the urine with sodium bicarbonate [38]. Acute hemodialysis, using a fluoride free, low potassium, and slightly elevated calcium concentrated dialysate, has also been used in patients with severe systemic HFA toxicity [39,40]. The decision to institute hemodialysis or high volume hemofiltration should be based on the condition of the patient and effectiveness of primary therapeutic steps.

Postmortem myocardial infarction and increases in myocardial enzymes after HFA burns have repeatedly been reported in case reports and animal studies [1,18,41]. Also in our patient, a troponin I increase could be detected (intensive care unit Day 2, 2.7 mg/l). Therefore, myocardial enzymes should be included into standard laboratory monitoring of patients with HFA burns [18].

Multiple pulmonary emboli may be further hemodynamic complications associated with major HFA burns [19]. For this reason, and because calcium therapy also increases thromboembolic risk [35], a continuous heparin infusion was instituted in our patient.

3.5. Pain management

One characteristic clinical feature of HFA exposure to the skin is pain out of proportion to appearance of the dermal injury [1]. Typical severe, throbbing pain is suggested to result from immobilisation of calcium ions in extracellular spaces, thus causing nerve depolarisation by extracellular shifting of potassium ions [42]. Analogous to dermal symptoms, pain after HFA burn may be delayed depending on the concentration of HFA exposed [1].

As pain in HFA burns is causally related to the activity of fluoride ions, relief of pain is an important guide to and individual parameter of the effectiveness of local therapy. Thus, it is necessary to treat HFA pain by intense topical and regional therapy, and not only with local anaesthetics or potent morphine derivatives [43,44]. Interestingly, our patient could clearly differentiate between pain from the HFA burn and other types of pain.

3.6. Surgery

In most major HFA burns, the role of surgery is to debride wounds, open blisters, and excise necrotic tissue in order to ensure effective topical treatment [27,43,45]. Early aggressive surgery with primary excision of necrotic skin areas has been recommended as an emergency measure to prevent deep tissue destruction and systemic absorption of fluoride ions [46,47]. In extensive HFA burns, like in our patient, such a procedure carries a high risk for complications (e.g. bleeding and infection). Nonetheless, in certain cases when small parts of the skin have been burnt by highly concentrated HFA or in refractory cases, immediate surgical excision of the contaminated tissue can be lifesaving and must be considered the most important therapeutic measure [1,20,46].

Analogous to conventional burn injuries, definitive skin grafting should be performed as early as possible to improve healing and reduce the risk of infection [48].

3.7. Topical and regional therapy

Topical and regional therapy is the mainstay of treatment in minor HFA burns, but also plays a pivotal role to minimise local tissue destruction in major HFA burns. However, it has only little influence on reversal of systemic toxicity of fluoride ions. In the patient presented, aggressive early topical and regional therapy seems to have substantially contributed to good wound healing requiring skin grafting only in minor parts of previously burnt skin areas.

3.7.1. Topical therapy

Several different agents have been studied and proposed for topical treatment of HFA burns (Table 2). Each of these agents aims at inactivation of free fluoride ions by promoting formation to insoluble fluoride salts. The principal limitation of all topical agents is their inability to adequately penetrate the skin and inactivate fluoride ions in deep tissue layers [27]. A recent experimental study could show that transcutaneous delivery of calcium was significantly enhanced by iontophoresis [49].

Because of its high effectiveness and low toxicity, calcium gel 2.5% has become the most widely used agent [12]. Treatment is much more effective, if applied within 3 h after HFA exposure [50]. Unfortunately, calcium gel is not immediately available in all hospitals. Therefore, if urgently required, a 2.5% calcium gluconate gel may be made by mixing K-Y® jelly with calcium gluconate powder or injection preparations (Table 3) [20].

3.7.2. Subcutaneous infiltration

Subcutaneous infiltration represents an important supplementary local therapy to gel application. It is highly

Table 2
Topical treatment of hydrofluoric acid burns

Agent	Effectiveness	Side effects	Comments
Calcium gel 2.5% [51]	Very good	None	Primarily used agent [1]
Calcium carbonate gel [52]	Very good	Stain, especially in colored patients [53]	Large quantities required for treatment [54]
Calcium acetate [55]	Good	Experimental data only	Experimental data only
Benzalkonium chloride [56] (Zephiran®)	Very good	Discomfort because iced solutions required	Very useful in mild burns, of less value in deeper burns [45,57]
Magnesium compounds [58]	Good	None	Only few clinical experience, poor tissue penetration [59]
Benzethonium chloride [57] (Hyamine®)	Very good	Discomfort because iced solutions required	Very useful in mild burns, of less value in deeper burns [45,57]
DMSO [60] (dimethylsulphoxide)	Good	High local toxicity [61,62]	Given together with calcium gel, considered obsolete by some authors [51]
Hexafluorine [63]	Good	Not known due to lacking experience	For emergency rinsing of skin or eye burns

effective and mostly applied to HFA burns of the head, neck, or trunk, whereas it may cause pressure necrosis when applied to distal extremities, such as fingers or toes [1,20]. The recommended dosage is 0.5 ml of 5% calcium gluconate per cm^2 [20]. Although the binding capacity of calcium chloride would be greater, it must not be used because of its irritating and corrosive effects on organic tissues [3,64]. Subcutaneous magnesium injections are equal to or even more effective than calcium gluconate in minimizing duration, depth, and progression of dermal HFA burns [65].

Two different techniques have been proposed for subcutaneous infiltration. In small area burns, infiltration can be performed with thin needles (27- or 30-gauge) by multiple subcutaneous injections beneath the involved skin. In more extensive burns, longer needles, e.g. thin spinal needles, can be used. After placement under the wound, the needle is slowly withdrawn and the calcium solution injected continuously [45]. Multiple injections may increase the risk of wound infection; use of antibiotic creams has been proposed [66].

3.7.3. Intra-arterial and -venous calcium infusion

Intraarterial infusion is a highly effective method to regionally inactivate fluoride ions in HFA burns [67–69]. It is recommended in digital burns and major HFA burns involving extremities. Depending on burn localization, either the radial, ulnar, brachial, or axillary artery (or femoral artery in the lower extremities) is catheterized and 2% calcium gluconate infused [70]. In the original protocol, 50 ml of 4% calcium gluconate solution were infused over four hours; this cycle was repeated at 12 h intervals until pain had disappeared [71]. In our patient, a modified approach with continuous infusion of 2% calcium gluconate was chosen, because of improved titration to pain and tenderness. Typically, heat sensation in the extremity occurred as a sign of overdosing intraarterial calcium infusion.

Table 3
Preparation of calcium gluconate gel 2.5% [20]

75 ml K-Y® Jelly plus 25 ml Calcium Gluconate 10%; or
100 ml K-Y® Jelly plus 2.5 mg Calcium Gluconate Powder

Intravenous regional calcium gluconate infusion based on Bier's method has recently been demonstrated to be as effective as intraarterial infusion [72,73]. In the critical care setting, intravenous regional calcium infusion seems to be inferior to intraarterial infusion, at least for practical reasons.

3.7.4. Regional therapy for HFA inhalation

HFA is very volatile (boiling point of 100% HFA, 19.5 °C/67.1 °F; 75% HFA, 56 °C/132.8 °F; 60% HFA, 89 °C/192.2 °F) [2]. Therefore, inhalation injury must be assumed in all of the following states: (1) burns involving HFA concentrations of >50%, (2) burns involving head or neck, (3) burns involving >5% of the body surface area, (4) HFA soaked clothing, or delay in removing contaminated clothes, and (5) HFA burns occurring in confined spaces [20]. Any inhalation, irrespective of HFA concentration, carries a high risk of systemic toxicity [74,75].

HFA fumes may directly cause laryngospasm, laryngeal edema, bronchospasm, purulent tracheobronchitis, and/or acute hemorrhagic pulmonary edema with acute respiratory distress syndrome [2]. Development of respiratory symptoms may be delayed for several hours up to 2 days [76]. Deterioration of pulmonary function in our patient on Day 7 might have also been a delayed consequence of HFA toxicity, as he was at high risk to develop inhalation injury. Nevertheless, sepsis-related pulmonary dysfunction seems to be a more likely explanation for respiratory distress.

The first-line therapy of HFA inhalation injury is 100% oxygen [1]. Recently, application of nebulized 3% calcium gluconate has been reported [32,57,77,78]. Prophylactic antibiotic therapy or glucocorticoid therapy are of unproven value and not indicated [2].

3.7.5. Regional therapy for HFA ingestion

Ingestion of HFA is rare, but carries a high risk for lethal electrolyte complications due to extensive systemic absorp-

Table 4
Overview of regional treatment approaches for HFA burns using calcium gluconate

Indication	Mode	Concentration (%)	Comments
Cutaneous HFA burn	Topical skin application	10	Application with soaked gauzes directly placed on wounds
HFA burn extremities	Intraarterial infusion	2	Continuous infusion titrated to clinical signs (pain, tenderness), or 50 ml over 4 h, 12 h until relief of pain
HFA burn extremities	Bier's method	2	Effective, but unpractical in critically ill patients with major HFA burns
HFA burn trunk, neck, or head	Subcutaneous infiltration	5	0.5 ml/m^2 skin burnt
HFA ingestion	Gastric lavage	10	Consider also magnesium lavage
HFA inhalation	Inhalation	3	Nebulize calcium gluconate plus 100% oxygen
HFA burn eyes	Topical eye application	1	Eye drops or topical with soaked gauzes

tion of fluoride ions and its frequent association with inhalation injury [1,79].

HFA ingestions may result in necrotic lesions of the mouth, throat, esophagus, hemorrhagic gastritis, pancreatitis [80], and/or secondary *viscus* perforation. Clinical symptoms involve nausea, vomiting, and severe oral, esophageal, or abdominal pain (Table 4) [1,20,66].

For emergency therapy, stimulation of vomiting is not recommended, since further oral, esophageal, or pulmonary injury may occur [1]. The patient should be encouraged to drink either water or preferably milk which has been shown to precipitate fluoride ions in vitro [81,82]. Further regional therapy includes calcium tablets, and gastric lavage with 10% calcium gluconate or magnesium gluconide, if time since ingestion was brief [27,83,84]. The patient must be repeatedly examined for local complications, such as gastric or bowel perforation.

4. Conclusion

In the treatment of major HFA burns, high dose replacement of calcium and magnesium, as well as adequate fluid therapy make up the mainstay of critical care therapy. Electrolyte therapy must not await laboratory results, but has to be instituted on an empirical basis. In healthy patients with intact renal function, electrolyte overdosing appears to be unlikely. In addition to systemic therapy for prevention of lethal cardiac complications, topical and regional therapies, including application of gels, subcutaneous infiltration, and intraarterial infusion of calcium, as well as specific therapy of HFA inhalation or ingestion, are important parts in the critical care management of major HFA burns.

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