



## Case report

## Chemical pneumonitis by prolonged hydrogen fluoride inhalation

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## ABSTRACT

Hydrogen Fluoride (HF) inhalation is one of the industrial accidents. It causes serious damage, although it is quickly recognized. Since hydrofluoric acid leaks are under surveillance by the alarm system, and low concentrations of gas also have a distinctive smell, most accidents occur from exposure in a short period to a large amount of HF. Thus, prolonged exposure to HF is exceedingly rare in a developed country. We report seven cases of chemical pneumonitis due to HF inhalation to share clinical course and prognosis.

## 1. Introduction

Hydrogen Fluoride (HF) is an extremely corrosive substance. It is used in many industrial branches such as brick cleaning, etching microchips in the semiconductor industry, leather tanning, aluminum production, fire extinguishers manufacturing [1,2]. It is a gas at room temperature, is usually supplied as a liquefied gas, and is also widely used in aqueous solutions [3]. The inhaled HF causes pneumonitis, and solution contact causes cutaneous injury. Skin burn is the most common type of HF-related accident [4]. When it contacts the skin, HF molecules quickly diffuse into tissues, release fluoride anion, result in a deep chemical burn. Toxic molecules bind to calcium, which can cause lethal hypocalcemia [1]. Inhalation injury occurs from exposure to HF gas or vapors arising from HF solutions.

According to the reported literature, inhalation injuries are mostly caused by unexpected major accidents [5–7]. In such an accident, the victim inhaled a large amount of gas in a short time; usually, fatal damage occurs [8]. People around disaster or accident are also exposed to the gas, but they are exposed to low concentrations due to physical distance. This type of accident is quickly recognized, so these victims are evacuated from the contaminated area immediately. Moreover, HF gas has a pungent odor and can be detected by smell at concentrations lower than the permissible exposure limit [1]. It helps a person to escape from a contaminated area in time before severe damage occurs. Therefore, it is rare to be exposed to HF for extended periods. While with the increasing use of HF in industry, low-dose inhalation possibly can still occur anytime and anywhere [9]. We report seven cases of chemical pneumonitis resulting from prolonged HF exposure to share clinical course and prognosis.

## 2. Case report

## 2.1. Circumstances of the cases

Seven construction workers who worked at the factory site that produces semiconductor etching gas visited the hospital sequentially. They all had worked to install additional HF gas storage tanks for five days. No manpower other than them was put in. The work site was an excavated ground surrounded by dirt. The site was outdoors without a monitoring system because it was a place rarely visited by people. However, gas storage tanks and connecting pipes were near the working area. They were not given a description of the potential hazard in advance. They wore hard hats, safety shoes, and gloves, but never had any respiratory protection, such as an N95 mask or gas mask. They worked there for 5 days in a row. They had confirmed that there were no abnormal results in their medical check-up before had been put into construction. However, after five days of work, case 1 complained of severe myalgia and shortness of breath. He was hospitalized with suspicion of hypersensitivity pneumonia. A week later, the others came to the hospital for accurate diagnosis and treatment, realizing that it was unusual for everyone who worked in the same place to suffer from similar symptoms. Two of them (cases 2, 3) were hospitalized for severe dyspnea, and case 4 ~ case 7 was on outpatient treatment. Factory officials denied HF gas leakage, but industrial accident experts determined the area was contaminated.

## 2.2. Presenting symptom

The average age of the patients was 54. Two people had high blood

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pressure, one person had diabetes mellitus, one was a hepatitis C virus carrier, and others had no personal past medical history. They were physically fit before work. While working for five days, all of them felt some irritant smells, but they did not think it is particularly dangerous. There was a mild sore throat ( $n = 5$ ) and a runny nose ( $n = 2$ ) while working for five days. After a first day job, they felt myalgia ( $n = 7$ ), and it gradually became worse. They thought it was a common cold symptom because it was winter. On the fifth day, everyone had difficulty breathing, and three of them felt dyspnea at rest. (case 1 ~ case 3). They complained of cough, myalgia, chilling, skin irritation, sore throat, dizziness, and headache. Some had red tints in their faces and hands. Laboratory findings showed leukocytosis, high ESR, and high CRP. Three people who were admitted showed saturation of 90%–92% on pulse oximetry. Chest X-ray was non-specific, but computer tomography (CT) showed diffuse patchy ground-glass opacities with or without centrilobular nodules (Fig. 1). Three of them underwent bronchoscopy showed no abnormal findings at their central airway. Pulmonary function test (PFT) showed decreased FVC, FEV1, and DLCO/VA. FEV1/FVC was normal. The symptoms and test results of the cases at presentation are shown in Table 1.

### 2.3. Treatment and follow up

Three people who had severe dyspnea were hospitalized. Oxygen supply, IV antibiotics, and bronchial dilators were applied. Case 1 was initially diagnosed as hypersensitive pneumonia, as we did not get any information about HF in the history taking. Systemic steroid therapy was performed for case 1. Case 2 and case 3 were diagnosed with HF induced pneumonitis on the day of hospitalization, received calcium carbonate, nebulized calcium, and systemic steroids. They were discharged on day hospital day 7. After the dyspnea was somewhat stabilized, all cases were consulted to several specialists. Along with respiratory medicine, neurology for headaches and dizziness, otolaryngology for dizziness and tinnitus, dermatology for skin irritation, and rehabilitation medicine for pulmonary rehabilitation, which was continued for three months. A few months later, psychiatric consultation for depression and anxiety was also needed.

Three months later, breathing difficulties were somewhat alleviated,

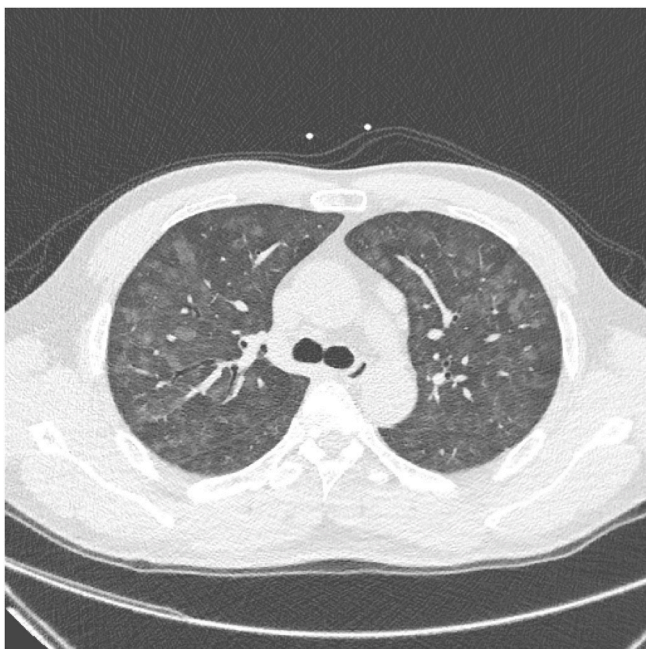


Fig. 1. A 49-year-old man (case 1). Diffuse patchy ground-glass opacities in both lungs of hydrogen fluoride-induced pneumonitis.

but continued at grade 2 modified Medical Research Council Dyspnea Scale (mMRC). Various tests such as Brain MRI, EEG, and vestibular function tests were performed, but there were no specific findings. PFT and chest CT findings have improved, but most cases have not experienced a full recovery. After 24 months, they were still showing various symptoms, and gradually depression and anxiety were developed. On the other hand, CT and PFT showed improvement. After 36 months, most of them still had dyspnea. Tinnitus, headache, insomnia, and skin problems were continued. The only symptoms of complete recovery were fever and chills. The severity of symptoms subjectively evaluated was recovered by 30% within one week, 40% within three months, and 30% of symptoms and subjective functional deterioration continued for 36 months (Table 2).

## 3. Discussion

### 3.1. Suspicion of diagnosis

In patients with interstitial pneumonia, history taking should be particularly detailed, and the possibility of chemical inhalation should be reconsidered as well as regular workers in chemical factories, the patient who exposed to the factory surroundings may have inhaled unnoticed chemicals. In this reported case, colleagues who worked at the same place visited together, and we could suspect chemical pneumonitis. (case 2 ~ case 7). If they visited different hospitals without contacting each other, they were likely diagnosed with HP or other ILD, as in case 1. Moreover, if chemical inhalation is suspected, clinicians should ask the industry officials for a possible unnoticed accident. In these cases, a small amount of HF was leaked outside of the factory building near the construction site. A factory official belatedly revealed it after the leak occurred, and the victims occurred.

### 3.2. Toxic level and exposure limit

According to the Emergency Response Planning Guides (ERPG) documents from the American Industrial Hygiene Association (AIHA), concentrations below two ppm of HF, which is ERPG-1, are low-level one-hour exposure limits that do not cause minor non-symptom health problems and may not be perceived by smell. The concentration of below 20 ppm (ERPA-2) is a concentration that requires immediate mitigations, such as leaving the place or wearing protective gear, since severe symptoms occur when exposed for more than an hour [10]. If the human body is exposed to HF gas less than three ppm for more than 8 hours, symptoms of irritation to the neck or eyes occurs, even if no serious harm occurs [3]. If the body is exposed to a concentration of 4.1 ppm for more than 6 h, irritations to the face and eyes occur, and if exposed for more than ten days, erythema occurs on the skin [10]. Besides, inhalation-induced toxicity can occur immediately, but after 12–36 hours [11,12]. Based on these references, it is estimated that these patients were exposed to 3–5 ppm of HF for more than 40 hours. On the first day, patients were aware of some odor in the workplace, but no physical problems occurred within the first three to 4 h. After they worked for 8 h and they had a mild sore throat and febrile sense. After two days of work, the symptoms of the three patients became a little worse. After about five days of work, they gradually suffered from dyspnea and systemic pain, and erythema occurred in their faces and hands. The symptoms worsened over time. The symptoms were the worst in 48 hours after work, which means that low concentration exposure can cause cumulative effects, and low concentration exposure can also have delayed toxicity.

### 3.3. Multiple symptoms

Symptoms of HF acid inhalation in these cases can be divided into three categories: respiratory, systemic, and neurological symptoms. The main respiratory symptoms were dyspnea. Cough and sputum were

**Table 1**  
The symptoms and test results of the cases at presentation.

		Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	
Age		48	61	50	45	57	61	55	
Sex		male	male	male	male	male	male	male	
past medical history		no	HTN 5yr dyslipidemia 5 yr	no	no	HTN 15yr dyslipidemia 1yr ex-smoker	DM	HCV early LC child A	
Symptoms & Sign	fever/chilling	100%	+	+	+	+	+	+	
	myalgia	100%	+	+	+	+	+	+	
	dyspnea	100%	mMRC4	mMRC4	MRC2	mMRC2	mMRC4	mMRC3	MMRC3
	Skin	57%	redness desquamation	redness pruritus			pruritus, desquamation		desquamation
	headache	100%	+	+		+	+	+	
	insomnia	57%		+	+	+	+		
	sore throat	71%	+	+		+	+	+	
	voice change	43%		+			+	+	
	runny nose	29%				+		+	
	cough	57%		+	+	+		+	
sputum	43%		+		+		+		
lung sound	29%	decreased			decreased				
laboratory findings	WBC	15.6	11.4	8.2	6.1	14.60	11.50	8.9	
	Hemoglobin	14.8	15.6	13.4	14.4	10.8	14.0	15.9	
	Platelet	312	331	332	224	354	193	114	
	CRP	12	3.3			6.6	10.9	0.1	
	Calcium		8.69	8.5	8.9	8.4	9.1	8.9	
	Phosphate		1.71	4.2	3.4	3.31	3.7	2.6	
	ESR	43	33			58	60	11	
	BNP		41			395.4			
	procalcitonin		<0.02			0.291			
	Creatinine	0.91	0.81	0.82	1.01	0.84	1.18	0.86	
Radiologic findings	Chest X-ray	14%	no active lesion	no active lesion	no active lesion	patchy GGO	no active lesion	no active lesion	
	CT GGO	100%	diffuse patchy	diffuse patchy	patchy	diffuse patchy	diffuse patchy	patchy	
	CT nodules	43%	centrilobular nodules	centrilobular nodules		centrilobular nodules			
	affected lung lobes		entire lung	both upper lungs	entire lung	entire lung	entire lung	both upper lungs	
other findings			subsegmental atelectasis both lower lung		subpleural nodule right lower lung		subsegmental atelectasis both lower lung		
pulmonary function test	FVC, %	89	101	104	110	91	92	87	
	FEV1, %	96	88	106	106	102	97	98	
	FEV1/FVC, %	81	70	89	78	80	84	90	
	DLCO, %	69	96	82	56	50	84	82	
	DLCO/VA, %	75	93	82	61	74	82	82	

**Table 2**  
Changes in lung volume and diffusing capacity and subjective health condition scores over time.

pulmonary function test	time	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
FVC, %	0 M	89	101	104	110	91	92	87
	3 M	89	89	92	106	93		79
	12 M	105	78	82	97	95	71	82
	36 M	97	66	89	78	75	73	82
FEV1, %	0 M	96	88	106	106	102	97	98
	3 M	97	88	96	103	105		90
	12 M	114	83	90	99	109	79	93
	36 M	98	73	97	81	81	81	90
DLCO/VA, %	0 M	75	93	82	61	74	82	82
	6 M	110	97	115	84	98	97	101
	36 M	109	96	116	90	97	108	109
Degree of subjective symptoms, %	3 M	50	40	50	60	60	60	60
	12 M	60	50	60	70	70	60	60
	36 M	70	50	75	80	80	70	60

frequent, but not too severe. A small amount of inhaled HF causes irritation only in the upper airway, but a moderate amount may cause chemical pneumonitis, and a large amount appears to cause acute respiratory distress syndrome [13,14]. It appears that inhaled HF acid diffuses into the cells of the tissue and penetrates deeply, combines with calcium to cause electrolytic abnormalities, and gives off toxic effects while circulating throughout the body, causing systemic symptoms [8,

15]. It is thought that inflammation of the lung and systemic circulation of HF causes systemic symptoms such as myalgia, chilling, and febrile sensation. Moreover, HF acid spread to the nervous system seems to cause neurologic symptoms such as dizziness, tinnitus, and headache. Symptoms of residents exposed to mass leakage of HF in Gumi, South Korea, also showed respiratory, systemic, and nervous symptoms, as shown in this case series [16].

### 3.4. Laboratory and radiologic finding

The initial lab findings caused by prolonged low concentration HF inhalation were a non-specific elevation of inflammatory markers. There were no other unusual findings on a laboratory test. High concentration exposure, such as high dose Inhalation and skin burn, results in an imbalance in electrolytes [12]. We found low concentration HF pneumonitis shows only elevated WBC counts, ESR, and CRP. The chest X-ray was normal for everybody but clearly showed the patchy or diffuse ground-glass opacity on CT. Therefore, we recommend that a CT should be performed if a chemical inhalation is suspected. The bronchoscopy findings were normal. Inhalation of HF appears to damage the distal airway and alveoli. Since it is not a thermal injury but a chemical injury by low-concentration toxic ion, and the large airway, which is lined with mucus and has a relatively small contact surface for its ventilation amount, does not appear to have severe damage. In the previous literature, diffusion capacity was reduced in HF inhalation [13]. In these cases, DLCO/VA was also reduced, but FEV1/FVC was normal. It is thought that edema of the interstitium by chemical burn resulting in a defect in gas diffusion.

### 3.5. Treatment and prognosis

Prolonged low-concentration exposure also causes severe symptoms via accumulation effects. In severe cases of dyspnea, the patient needs to be closely monitored, oxygen supply, antibiotic treatment, and calcium nebulizer are known to be helpful [17]. Calcium nebulizer was not implemented for case 1 and was only implemented for case 2 and case 3. However, all of them experience the improvement of dyspnea in 7 days after hospitalization. Patients who were not hospitalized were prescribed oral antibiotics, inhaled bronchial dilator, calcium carbonate, and other medication for symptom control. After three months of follow-up tests, the CT and PFT recovered to almost normal range. In the tests examined after three years, the PFT did not deteriorate, and no sequelae were seen at CT. We assume that the drugs administered in a practical way relieved the symptoms to some extent, and there were no side effects caused by the drugs. Similar treatments were carried out in other previous literature [18,19]. Thus, we recommend best-supportive treatment for low dose HF inhalation pneumonitis.

After three years, headaches, dizziness, and tinnitus persisted. Although there were some improvements in symptoms and test results, dyspnea of mMRC 2 grade was still observed. Previous reports also showed that the symptoms related to HF inhalation last more than several months [7,17,20]. It is indicating that chronic symptoms persist despite radiological improvement. Since several symptoms persisted in patients but did not worsen, it is unlikely that the chronic inflammatory reaction will persist. We believe that symptoms persist as a result of the sequelae from early inflammatory organ damage.

## 4. Conclusion

Prolonged exposure to HF is rare. Clinicians need to be more careful because this situation occurs when the patient is not aware of the leak, and it is difficult to think of HF as the cause of the disease. After an accurate diagnosis, calcium administration and supportive treatment should be performed. HF pneumonitis showed chronic symptoms for more than three years, even if radiologic findings were improved.

### Submission declaration and verification

The work described has not been published previously and is not under consideration for publication elsewhere. Its publication is approved by all authors.

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## Consent

Informed consent was obtained from the patient before submission for publication.

## Declaration of competing interest

None.

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