

Effectiveness of CT for Clinical Stratification of Occupational Lung Edema^a

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Abstract: We treated two occupational lung diseases in different situations during military training. The purpose of this study is to investigate the availability of CT scanning for the evaluation of inhalation pulmonary edema. Two soldiers suffered severe lung edema after using a spray for the daily maintenance of their firearms. Four soldiers suffered severe dyspnea after undertaking drills in a narrow zone where numerous smoke bombs had been used. We evaluated these patients from several aspects. CT scans of the chest of spray-induced patients revealed bilateral infiltration predominantly in the upper lung fields. The patients received steroid pulse treatment and gradually recovered. CT scans of the chest of smoke-induced patients revealed bilateral ground-glass attenuation with peripheral lung sparing. The patients gradually recovered with steroid therapy. In accordance with previous studies, CT scans of the chest in our patients demonstrated that the periphery of the lungs remained normal, except in cases of serious injury. When differential diagnosis is required, we consider that CT scans of the chest are particularly useful; CT findings are useful in determining the severity of lung injury as well as the diagnosis of inhalation pulmonary edema.

Key words: Spray, Smoke, Polytetrafluoroethylene, Zinc chloride, CT scan, Military, Occupational, Lung

Introduction

Occupational disease is caused by problematic actions and noxious agents that arise in the work environment. Safety measures and prophylactic education are undertaken for workers to ensure an awareness of the potential risk factors that may occur in the work environment. While

workers can take steps to minimize known risks, unforeseeable hazards will always remain. In a given work environment, ordinary products can represent a health hazard to workers.

Lung injuries that developed after using water-proofing spray were commonly reported in Japan from 1992 to 1994^{1,2}. The spray used in these incidents included water-repellent spray particles that contained polytetrafluoroethylene (PTFE) and/or fluororesin. Many similar cases were reported abroad^{3–6}. PTFE and fluororesin produce hazardous materials when heated and are known to cause lung injury^{7–11}.

Smoke flares are used by the police and armed forces in

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the course of active duty and during training. Civilians occasionally use smoke canisters in community fire-fighting exercises. The components of smoke canisters manufactured for military use are similar to those used in civilian products. In certain instances, smoke bombs can become life-threatening materials; smoke bombs are known to cause lung damage^{12–15}.

Soldiers can potentially develop lung edema in different situations during military training when using sprays that contain PTFE particles and when using smoke bombs. The clinical manifestations in these patients lead physicians to consider the development of an infectious disease. As the clinical course differs only slightly from that of infectious disease, the illness is difficult to diagnose. A final diagnosis is reached by consideration of the patient's history and the findings of a chest CT scan.

The purpose of the present study is to investigate the availability of CT scanning for evaluation of inhalation pulmonary edema with the aim of early diagnosis and assessment of severity.

Patients

Spray-induced cases

Twenty-nine male troops (22–34 yr of age) of the Ground Self-Defense Forces of Japan (JGSDF) were given the honor of being selected for a certain curriculum that was physically extremely tough. After quotidian training, the soldiers used rust-proofing sprays and dust-removal sprays for the daily maintenance of firearms in their barracks. Some of the rust-proofing sprays contained PTFE and/or fluororesin; the dust-removal sprays contained hydrofluorocarbon. All of the soldiers lodged in a single room within their barracks. The soldiers did not normally use kerosene heaters for indoor heating while maintaining their rifles in the barracks; however, kerosene heating was used on one very cold day in winter during which time which they cleaned their firearms in their room for a period of 5 h. That night, the soldiers slept in the same room in which they had maintained their rifles.

The following day (Day 1), most of the soldiers suffered from fever, cough, and dyspnea, and visited the army dispensary where the army surgeon considered their illness to be an infectious disease because of the clinical manifestation and the number of patients presenting simultaneously from the same barracks.

Two days later (Day 2), five soldiers were hospitalized because of their symptoms. The two personnel with the most severe illness and most abnormal chest radiographs are the subject of this study.

Smoke-induced cases

Nineteen male soldiers (20–29 yr of age) were selected to join a training course of the same type as the course being undertaken by the spray-induced cases. The soldiers were undertaking drills in a restricted area and many smoke canisters were used; there was little wind at the time. Most of the soldiers suffered from cough and dyspnea at that time; 4 d later, four personnel suffered from dyspnea on exertion.

They were hospitalized because their chest radiographs showed abnormalities.

These four soldiers are included as subjects in the present study.

Here, we investigate the correlation between the clinical course and the CT scans under taken of the chests.

To evaluate the severity of lung injury, CT scans (LightSpeed QX/i, HiSpeed FX/i, GE Yokogawa Medical Systems; Hino, Japan; Emotion6, Siemens; Erlangen, Germany) of the chest were performed for all patients. A blood chemical study was preformed in the dispensary of the army post on Day 1 to assess their inflammatory condition.

The blood chemical study was performed using an auto analyzer (Hitachi 7600-020; Hitachi; Ibaraki, Japan). To determine the degree of pulmonary functional impairment, a pulmonary function test was performed using a spirometer (Fudac-70; Fukuda Denshi; Chiba, Japan).

Clinical Course

Spray-induced cases

Both patients presented to the dispensary with fever, cough, and general fatigue on Day 1. Case 1 complained of headache. Both patients were hospitalized on Day 2 because they suffered from severe dyspnea. Chest examination revealed inspiratory coarse crackles and fine crackles over both lung fields that were more prominent in the upper lung fields. Their respiratory rate was elevated and their oxygen saturation depleted. The chest radiographs revealed bilateral consolidation shadows (Fig. 1). CT scans on admission demonstrated bilateral consolidation with peripheral lung sparing (Fig. 2). Initially, the patients had high fever and leukocytosis; the fever and white blood cell count quickly returned to normal (Table 1). High C-reactive protein (CRP) values were detected over a period of 7 d. Steroid pulse treatment (methylprednisolone 1,000 mg/d, from Day 3 to Day 5 or 6) was administered for both patients. Other supportive treatment was also given. Seven days after admission, their chest radiographs showed almost normal appearances (Figs. 1 B and D).

Smoke-induced cases

All patients presented to our hospital with fever, cough,

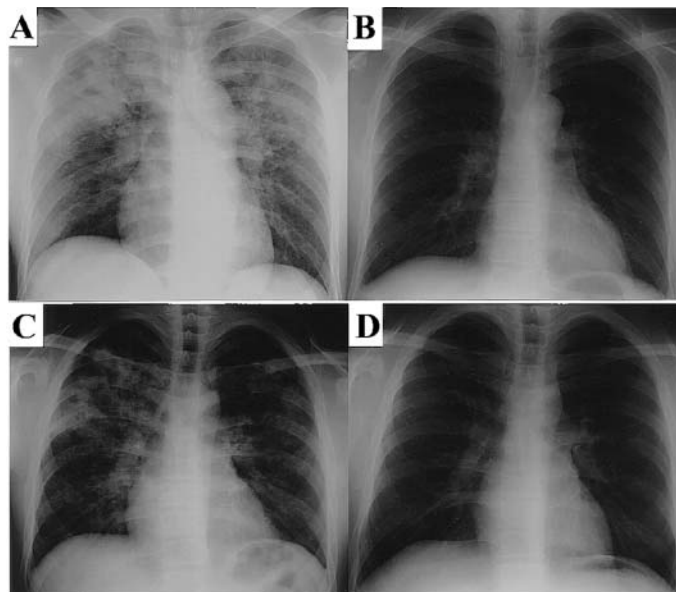


Fig. 1. Chest radiographs of spray-induced patients.

Chest radiographs of Case 1 on Day 2 (A) and Day 8 (B). Chest radiographs of Case 2 on Day 2 (C) and Day 8 (D). Bilateral infiltration was seen in the upper lung fields of both patients on Day 2 (A and C). Chest radiograph of Case 1 shows areas of faint ground-glass opacity on Day 8 (B).

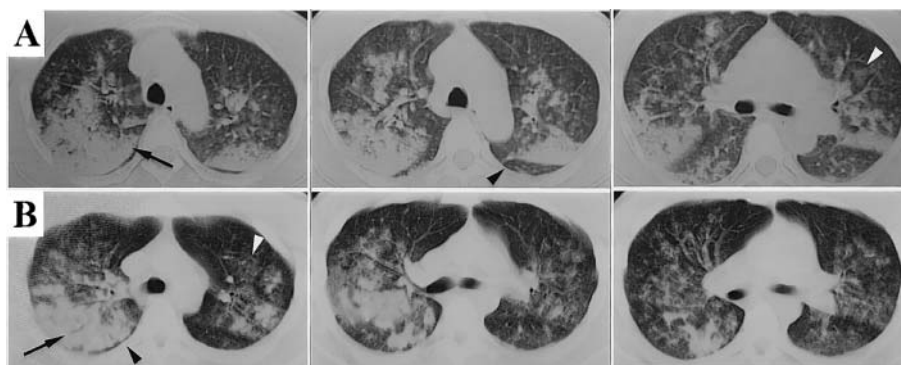


Fig. 2. CT scan of the chest of spray-induced patients on admission (Day 2).

CT scans of both patients shows ground-glass opacity areas (white arrowheads) and airspace consolidation (arrow). Black arrowheads indicate spared peripheral lung (A: Case 1; B: Case 2).

and dyspnea on exertion (Day 4). Case 4 presented with expiratory wheeze in both lung fields. The chest radiographs revealed areas of faint ground-glass opacity in the upper lung fields (Fig. 3). The patients received 30 mg of prednisolone once daily for 8 d, starting on Day 4. In addition, Case 4 received steroid inhalation therapy (50 μ g of fluticasone propionate twice daily for 8 d starting on Day 4). The patients presented with normal body temperature and white blood cell count on admission (Day 4). High CRP values were detected in these patients for 6 d.

Seven days later, subtle abnormal shadows were detected on the chest radiographs. CT scans of the chest revealed areas of faint ground-glass opacity (Fig. 4); their reduced diffusing capacity was sustained.

CT Scans Evaluation and Pulmonary Function Test

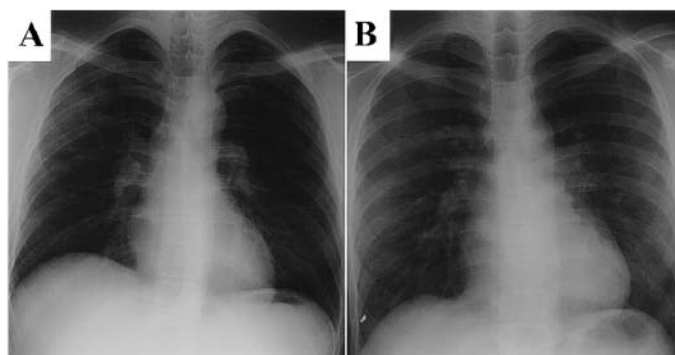
Spray-induced cases

The chest radiographs revealed diffuse consolidation, particularly in the upper lung field (Figs. 1 A and C). The

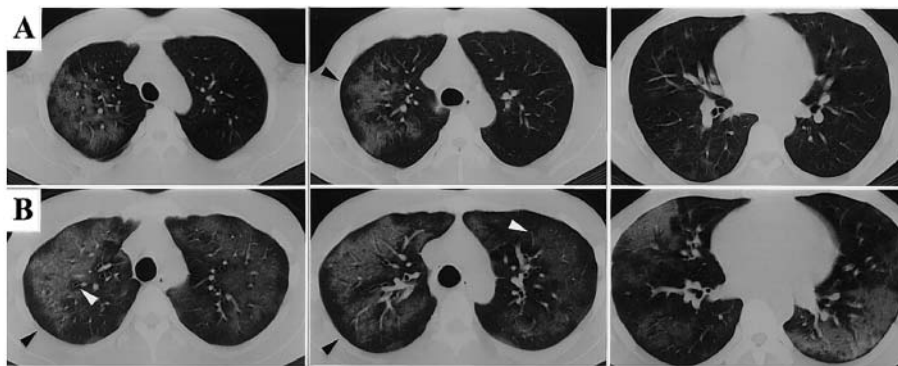
Table 1. Temperature, white blood cell (WBC), and C-reactive protein (CRP) values in spray-induced patients

	age	body temperature (°C)		WBC (/μl)		CRP (mg/dl)		
		Day 1	Day 3	Day 1	Day 2	Day 1	Day 7	Day 8
Case 1	33	<u>39.2</u>	36.2	<u>16,300</u>	5,400	<u>≥7.0</u>	<u>25</u>	<u>1.6</u>
Case 2	28	<u>39.0</u>	36.6	<u>15,800</u>	7,200	<u>3.7</u>	<u>12.6</u>	<u>0.7</u>

Underlined values indicate out of normal range; Day 2 means two days after Exposure Day.

**Fig. 3. Chest radiographs of smoke-induced patients.**

Chest radiographs of Case 3 (A) and Case 4 (B) on Day 4. Areas of ground-glass opacity were detected in the right upper lung fields of Case 3 (A). Bilateral areas of faint ground-glass opacity were detected in Case 4 (B).

**Fig. 4. CT scan of the chest of smoke-induced patients on admission (Day 4).**

CT scans of both patients show ground-glass opacity areas (white arrowheads). Black arrowheads indicate spared peripheral lung (A: Case 3; B: Case 4).

chest radiographs indicated near-normal findings on Day 8 except for sustained areas of faint ground-glass opacity in the right upper lung fields of Case 1. A CT scan of the chest on Day 2 demonstrated bilateral consolidation with peripheral lung sparing (Fig. 2). Several areas of ground-glass opacity were detected in the CT scan on Day 8.

The pulmonary function test was not performed on spray-induced patients because of the severity of illness on admission. Pulmonary function tests at the time of discharge revealed normal pulmonary function except for reduced diffusing capacity in Case 1. Results for the pulmonary function test performed seven days later were better than

Table 2. Pulmonary function test values in smoke-induced patients

	age	DLCO		FEV _{1.0}		VC (Litter)		FEV _{1.0} /FVC Ratio, %	
		Day 4	Day 11	Day 4	Day 11	Day 4	Day 11	Day 4	Day 11
		Case 3	27	<u>62.2</u>	84.1	<u>63.5</u>	90.9	<u>3.89</u>	4.70
Case 4	25	<u>40.2</u>	<u>61.0</u>	<u>46.2</u>	84.8	<u>2.11</u>	<u>3.69</u>	96.2	98.4
Case 5	24	<u>31.1</u>	<u>52.7</u>	<u>29.0</u>	72.1	<u>1.45</u>	<u>3.03</u>	80.0	95
Case 6	28	<u>52.1</u>	<u>68.4</u>	<u>29.2</u>	82.7	<u>2.64</u>	<u>3.70</u>	<u>50.0</u>	93.8

*Data are presented as % of predicted value unless otherwise indicated. DLCO = single-breath diffusing capacity for carbon monoxide; VC = vital capacity; FVC = forced vital capacity; Day 4 means four days after exposure day; Underlined value indicate out of normal range.

those at time of discharge.

Smoke-induced cases

Chest radiographs of the smoke-induced cases demonstrated mild infiltrative shadows (Fig. 3). The CT chest scans revealed bilateral areas of ground-glass opacity with peripheral lung sparing (Figs. 4 A and B). Figure 5 shows a representative time course of the CT chest scan findings for Case 4.

Pulmonary function test results for the smoke-induced patients are summarized in Table 2. Before treatment, pulmonary function tests showed restrictive ventilatory defect, obstructive impairment, and reduced diffusing capacity. Seven days later, the reduced diffusing capacity and restrictive ventilatory defect were sustained in three patients (Table 2).

Discussion

As many patients in Japan suffered lung injury caused by water-proofing spray during the period from 1992 to 1994^{1,2)}, the Ministry of Health and Welfare produced guidelines for the manufacture of waterproof spray in 1998. According to the guidelines, a high concentration of spray particles of less than 10 μm in diameter causes lung injury; consequently, spray manufacturers reduced the concentration of spray particles of less than 10 μm in diameter. The patients in the current study were exposed to rust-proofing sprays rather than water-proofing sprays, but these sprays contain fine PTFE particles.

We consider that manufacturers lowered the concentration of particles smaller than 10 μm ; however, our patients developed pulmonary disorders when using sprays that were manufactured after the announcement was made. The cases in the present study demonstrate that sprays containing PTFE particles are still harmful, depending on the environment of use.

There are few reports of pulmonary disorders resulting from the use of sprays that contain PTFE particles (anticorrosion sprays and lubrication spray) compared to the number of case reports that focus on waterproof spray. Previous studies have found that smoking and indoor heating are responsible for the development of lung injury following the use of waterproof sprays⁷⁻¹⁰⁾. Lit cigarettes or heaters can induce pyrolysis of PTFE particles, and pyrolytic products of PTFE and other fluororesins can cause lung injury such as the so-called 'polymer fume fever'^{3-8, 10, 16)}.

Polymer fume fever usually occurs as a flu-like, self-limited illness with minor pulmonary symptoms¹⁷⁾; however, the clinical presentations of polymer fume fever vary. The severity of the illness depends on the specific conditions of exposure. Our patients (Case 1 and Case 2) were heavily exposed when working at a low position close to the sprays for long hours. A previous case report stated that multiple attacks of polymer fume fever led to pulmonary fibrosis, with patients showing a reduced diffusing capacity⁹⁾.

We consider the etiology of spray-induced cases to be the pyrolytic product of PTFE and fluororesin. A previous case report relates the case of a woman who began to complain of cough and dyspnea 5 h after inhalation of a waterproofing spray¹⁰⁾. The period of latency between exposure and the development of dyspnea varies from almost no delay to several hours or more⁷⁻¹¹⁾. Our patients began to complain of dyspnea more than 12 h after exposure to the spray. Such a time lag before the appearance of symptoms makes diagnosis of inhaled pulmonary edema difficult. Furthermore, transitional leukocytosis was revealed in the laboratory analysis, and this finding made the differential diagnosis from infectious diseases more difficult.

Previous studies of the CT chest scans of inhalation pulmonary edema demonstrated diffuse ground-glass opacities predominantly in the upper lung fields^{8, 10, 11)}. The periphery of the lungs was reported to be normal except in

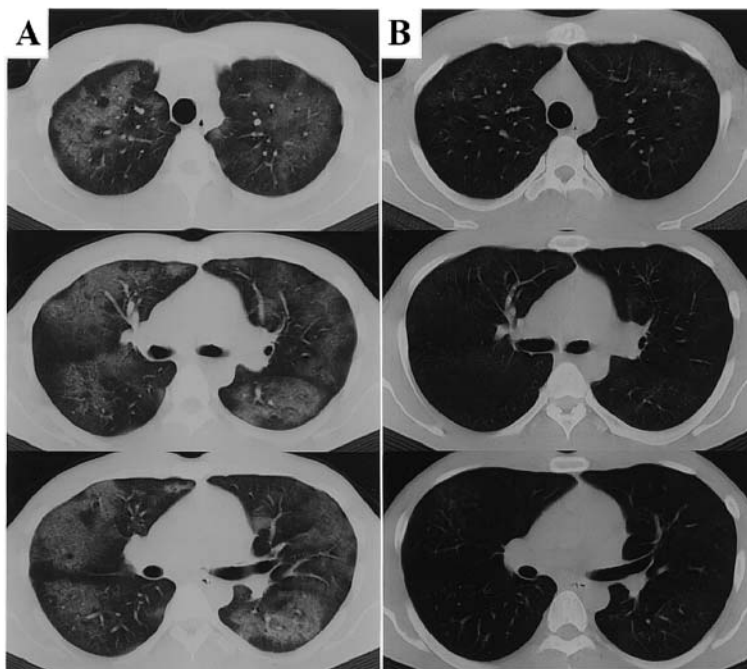


Fig. 5. CT scan of the chest of Case 4.

Chest CT scan of Case 4 on Day 4 (A) and Day 10 (B) at approximately the same anatomical level. Bilateral areas of ground-glass opacity were observed on Day 4. Areas of ground-glass opacity were reduced in the CT scan obtained on Day 10. Several areas of faint ground-glass opacity persisted (B). Square measure of lung fields on Day 10 is greater than that measured on Day 4.

the seriously ill cases^{7, 13, 14}). These findings are the same as those in the cases of the present study. The severity of symptoms appears to be related to the extent of infiltration apparent on the CT chest scan. The CT chest findings were useful not only for the diagnosis of pulmonary edema but also for determining the severity of lung injury.

In smoke-induced cases other than the former case, we were able to estimate etiology relatively easily; however, we were surprised that the soldiers endured their symptoms 4 d before seeking medical attention. We consider that the soldiers believed their training results would be adversely affected by requesting a checkup.

The smoke canisters used by our patients contained hexachlorethane and zinc oxide. Smoke bombs produce a large quantity of zinc chloride as a hot vapor during combustion¹²). Toxicities from exposure to zinc chloride smoke are caused primarily by inhalation of hydrated zinc chloride vapor; the vapor affects the mucous membranes, and the victims go on to develop lung edema. Until now, we considered that zinc chloride caused lung edema, as in previously reported cases¹²⁻¹⁵). In severe cases, some victims progressed to adult respiratory distress syndrome (ARDS)^{14, 18}).

In the literature, bilateral areas of ground-glass opacities are observed on the CT scans of all patients exposed to smoke bombs, and some patients demonstrated bilateral areas of patchy airspace consolidation¹³). All the patients in the present study exhibited bilateral areas of ground-glass opacities in their chest CT scans; however, areas of patchy airspace consolidation were not observed in our patients. The peripheral areas of lungs remained normal in our cases (Fig. 4). These differences in CT findings may reflect the severity of their illness.

The findings of the CT chest scans in the current study correlate well with the clinical course and pulmonary function test values (Fig. 5 and Table 2). All smoke-induced patients presented with restrictive ventilatory defect on Day 4. The CT chest scans may retrospectively indicate restrictive ventilatory defect by square measure of the lung fields.

Initial high fever, leukocytosis, and chest radiographs caused us difficulties in diagnosing the patients, particularly in the spray-induced cases. Because of their symptoms and its epidemic pattern, we first thought their illness to be an infectious disease.

We believe it is important to consider the possibility of

inhalation pulmonary edema when patients complain of fever, cough, and dyspnea, and when consolidation shadows are visible on the chest radiograph.

When differential diagnosis is required, we consider CT scans of the chest to be particularly useful. In addition, the findings of chest CT scans are useful not only for the diagnosis of inhalation pulmonary edema but also for determining the severity of lung injury.

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References

- 1) Ishizawa J, Tsujikawa A, Kuroki Y, Ohashi N, Endou Y, Iwamoto C, Goto K, Shintani S (1994) Acute poisoning after inhalation of waterproofing spray (second report). *Jpn Med J* **3680**, 49–52.
- 2) Ishizawa J, Tsujikawa A, Kuroki Y, Ohashi N, Endou Y, Iwamoto C, (1994) Acute poisoning after inhalation of waterproofing spray. *Jpn Med J* **3638**, 47–50.
- 3) Albrecht WN, Bryant CJ (1987) Polymer-fume fever associated with smoking and use of a mold-release spray containing polytetrafluoroethylene. *J Occup Med* **29**, 817–9.
- 4) Delgado JH, Waksman JC (2004) Polymer fume fever-like syndrome due to hairspray inhalation. *Vet Hum Toxicol* **46**, 266–7.
- 5) Shusterman D, Neal E (1986) Prolonged fever associated with inhalation of multiple pyrolysis products. *Ann Emerg Med* **15**, 831–3.
- 6) Silver MJ, Young DK (1993) Acute noncardiogenic pulmonary edema due to polymer fume fever. *Cleve Clin J Med* **60**, 479–82.
- 7) Jinn Y, Akizuki N, Ohkouchi M, Inase N, Ichioka M, Marumo F (1998) Acute lung injury after inhalation of water-proofing spray while smoking a cigarette. *Respiration* **65**, 486–8.
- 8) Tagawa A, Ikehara K, Tsuburai T, Nishiyama H, Miyazawa N, Hashiba T, Suzuki M, Suzuki S, Ishigatsubo Y (2003) Acute lung injury caused by inhalation of waterproofing spray. *Nihon Kogyoku Gakkai Zasshi* **41**, 123–6.
- 9) Williams N, Atkinson W, Patchefsky AS (1974) Polymer-fume fever: not so benign. *J Occup Med* **16**, 519–22.
- 10) Tanino M, Kamishima K, Miyamoto H, Miyamoto K, Kawakami Y (1999) Acute respiratory failure caused by inhalation of waterproofing spray fumes. *Nihon Kogyoku Gakkai Zasshi* **37**, 983–6.
- 11) Ota H, Koge K, Tanaka H, Akaishi T, Kikuchi K (2000) Acute respiratory failure due to inhalation of aerosol water proof agent. *Nihon Kogyoku Gakkai Zasshi* **38**, 485–9.
- 12) Holmes PS (1999) Pneumomediastinum associated with inhalation of white smoke. *Mil Med* **164**, 751–2.
- 13) Hsu HH, Tzao C, Chang WC, Wu CP, Tung HJ, Chen CY, Perng WC (2005) Zinc chloride (smoke bomb) inhalation lung injury: clinical presentations, high-resolution CT findings, and pulmonary function test results. *Chest* **127**, 2064–71.
- 14) Pettila V, Takkunen O, Tukiainen P (2000) Zinc chloride smoke inhalation: a rare cause of severe acute respiratory distress syndrome. *Intensive Care Med* **26**, 215–7.
- 15) Matarese SL, Matthews JI (1986) Zinc chloride (smoke bomb) inhalational lung injury. *Chest* **89**, 308–9.
- 16) Son M, Maruyama E, Shindo Y, Suganuma N, Sato S, Ogawa M (2006) A case of polymer fume fever with interstitial pneumonia caused by inhalation of polytetrafluoroethylene (Teflon). *Chudoku Kenkyu* **19**, 279–82.
- 17) Shusterman DJ (1993) Polymer fume fever and other fluorocarbon pyrolysis-related syndromes. *Occup Med* **8**, 519–31.
- 18) Hjortso E, Qvist J, Bud MI, Thomsen JL, Andersen JB, Wiberg-Jorgensen F, Jensen NK, Jones R, Reid LM, Zapol WM (1988) ARDS after accidental inhalation of zinc chloride smoke. *Intensive Care Med* **14**, 17–24.