Case Report

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Secondary organizing pneumonia following occupational acute nitrogen oxide poisoning: a case report

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Abstract

Secondary organizing pneumonia (SOP) is a nonspecific inflammatory response towards acute lung injuries caused by various diseases. However, organizing pneumonia (OP) secondary to occupational acute nitrogen oxide poisoning has been reported rarely. We report a 49-year-old man who suffered from nitrogen oxide poisoning after inhaling mixed gas at work. After pathological examination, he was diagnosed with OP. In the absence of other underlying factors causing OP, he was diagnosed with SOP owing to acute nitrogen oxide poisoning. After systematic treatment, the patient recovered and was discharged in better health. In patients with lung injury caused by acute nitrogen oxide poisoning, physicians should be alert to the risk of patients subsequently developing SOP, and timely diagnosis and treatment are essential for complete recovery.

Keywords

Case report, nitrogen oxide, organizing pneumonia, occupational exposure, poisoning, secondary

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Introduction

Organizing pneumonia (OP) is a pulmonary clinicopathological syndrome characterized by a reaction to noxious environmental or endogenous factors. The American Thoracic Society/European Respiratory Society[1] classified pneumonia with unknown causes as cryptogenic organizing pneumonia (COP) and that related to other diseases as secondary organizing pneumonia (SOP). Many diseases and factors are associated with SOP, such as infection,[2] drug reaction,[3] connective tissue disease,[4,5] cancer,[6] radiation therapy,[7] and organ transplantation.[8] However, to the best of our knowledge, there are no reports of SOP owing to occupational nitrogen oxide poisoning. Therefore, our report is of great significance for clinical diagnosis and treatment.

This report had two primary objectives. The first was to describe the clinical course of SOP caused by acute nitrogen oxide poisoning in detail to provide a reference for clinical diagnosis and treatment. The second was to emphasize the importance of safety awareness at work to prevent similar incidents.

Case presentation

The patient was a 49-year-old man whose job was to monitor the acid pickling shop of a machinery factory. On 10 May 2019, at 2:30 am, he mistakenly mixed sodium nitrite with industrial waste (the main component was hydrochloric acid) while cleaning the workshop, and inadvertently inhaled the mixed gas that was generated. The patient took no protective measures at that time and did not leave the toxic environment. As a result, he developed nausea, chest tightness, cough, lacrimation, and other symptoms. After 40 minutes, he left the toxic environment because of worsening symptoms. Two hours later, he developed a fever and went to the local health center, where he was advised to go to the hospital for treatment.

Upon admission, the patient's vital signs were as follows: blood pressure (BP), 138/80 mmHg; heart rate (HR), 90 beats/minute; respiratory rate (RR), 36 breaths/minute; body temperature (BT), 37.9°C; and oxygen saturation, 76%. The patient was conscious and irritable. A black powdery substance was observed under his fingernails. His breathing sounded normal in both lungs, and his heart rhythm was normal. His abdomen was flat and soft without any apparent abnormalities. Table 1 shows the laboratory findings on admission to the local health center. Computed tomography (CT) scans demonstrated diffuse lung disease, suggesting infection or injury, and abnormal changes in the right rib (Figure 1). Electrocardiography demonstrated sinus tachycardia, frequent premature ventricular contractions, and left atrial enlargement. He received non-invasive ventilation, glucocorticoids, and anti-infectives. However, the symptoms of chest tightness and shortness of breath gradually worsened, and oxygenation could not be maintained. Therefore, mechanical ventilation was initiated through endotracheal intubation and pressure-controlled ventilation with the following settings: pressure control, 18 cmH_2O; respiratory frequency, 15 times/min; positive end-expiratory pressure, 8 cmH_2O; fraction of inspired O_2, 50%; and oxygen saturation, 96%. He also received sedatives, organ protection therapy, and other treatments.

The patient was admitted to our hospital for further treatment on 14 May. Upon admission, his vital signs were as follows: BP, 155/80 mmHg; HR, 78 beats/minute; RR, 21 breaths/minute; and BT, 36.7°C. He was receiving assisted mechanical ventilation, and he was conscious. Physical examination showed normal-sized pupils briskly reacting to light. Some rhonchi and moist rales could be heard. His heart

Table 1. Local hospital laboratory findings on 10 May.

Parameter	Laboratory result	Reference range
WBC ($\times 10^9$/L)	**25.42**	3.5–9.5
RBC ($\times 10^{12}$/L)	4.66	4.3–5.8
HGB (g/L)	145	130–175
NEUT%	**93.20**	40–75
LYM%	**3.40**	20–50
AST (IU/L)	**13**	15–59
ALT (IU/L)	34	21–72
Cr (μmol/L)	60.20	58–133
pH	7.35	7.35–7.45
pCO_2 (mmHg)	41	35–45
pO_2 (mmHg)	90	80–100
Glu (mmol/L)	**12.1**	3.9–6.1
Lac (mmol/L)	**2.1**	0.5–1.8

WBC, white blood cells; RBC, red blood cells; HGB, hemoglobin; NEU%%, neutrophil ratio; LYM%, lymphocyte ratio; AST, aspartate aminotransferase; ALT, alanine aminotransferase; Cr, serum creatinine; pCO_2, partial pressure of carbon dioxide; pO_2, partial pressure of oxygen; Glu, glucose; Lac, lactic acid. Values in bold in the table indicate out of reference range.

Table 2. Qilu emergency department laboratory findings on 14 May.

Parameter	Laboratory result	Reference range
WBC ($\times$ 10^9/L)	**15.33**	3.5–9.5
HGB (g/L)	132	130–175
NEUT%	**91.40**	40–75
LYM%	**3.50**	20–50
AST (IU/L)	**11**	15–59
ALT (IU/L)	33	21–72
Cr (μmol/L)	**55**	58–133
pH	7.44	7.35–7.45
pCO_2 (mmHg)	36	35–45
pO_2 (mmHg)	**76**	80–100
Na^+ (mmol/L)	**133**	135–145
K^+ (mmol/L)	3.7	3.5–5.5
Glu (mmol/L)	**7.7**	3.9–6.1
Lac (mmol/L)	1.6	0.5–1.8

WBC, white blood cells; HGB, hemoglobin; NEUT%, neutrophil ratio; LYM%, lymphocyte ratio; AST, aspartate aminotransferase; ALT, alanine aminotransferase; Cr, serum creatinine; pCO_2, partial pressure of carbon dioxide; pO_2, partial pressure of oxygen; Na^+, serum sodium; K^+, serum potassium; Glu, glucose; Lac, lactic acid. Values in bold in the table indicate out of reference range.

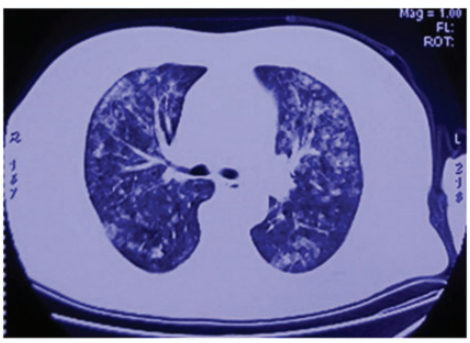

Figure 1. Computed tomography image showing diffuse lesions in both lungs.

rhythm was normal, his abdomen was flat and soft, and no abnormalities were apparent. He had no previous history of disease. We performed unobstructed urethral catheterization. Table 2 shows the laboratory findings on admission to the Qilu Hospital. The patient underwent electrocardiographic monitoring, anti-infection therapy, blood glucose control, maintenance electrolyte and acid-base balance therapy, nutritional support, and stomach, kidney, and liver protection. On 15 May, the patient's vital signs were stable, and respiration was smooth; therefore, we weaned him off the ventilator and administered persistent low-flow oxygen therapy. The next day, tracheal extubation was successfully performed. On 20 May, chest CT revealed pulmonary infection, local consolidation, bilateral pleural thickening, and mediastinal lymphadenopathy. Therefore, we administered 80 mg of methylprednisolone intravenously daily for 5 days.

Two weeks after admission (27 May), the patient's condition was relatively stable, and laboratory test results had improved (Table 3). Methylprednisolone was discontinued and replaced with oral prednisone, which was gradually reduced. He remained

Table 3. Dynamic changes in the Qilu headquarters laboratory findings.

Parameter	20 May	27 May	3 June	16 July	19 August	Reference range
WBC	**49.99**	**22.81**	**16.69**	**13.74**	**10.11**	3.5–9.5
NEUT%	**93.00**	**84.10**	**90.40**	71.30	63.80	40–75
LYM%	**1.00**	**10.30**	**4.50**	20.90	27.20	20–50
AST (IU/L)	**98**	20	33	28	38	15–59
ALT (IU/L)	**177**	**98**	**101**	31	62	21–72
Cr (μmol/L)	**57**	**43**	**48**	61	59	58–133
HS-CRP (mg/L)	**54.89**	**12.98**	–	**10.25**	–	0–8

WBC, white blood cells; NEUT%, neutrophil ratio; LYM%, lymphocyte ratio; AST, aspartate aminotransferase; ALT, alanine aminotransferase; Cr, serum creatinine; HS-CRP, high-sensitivity C-reactive protein. Values in bold in the table indicate out of reference range.

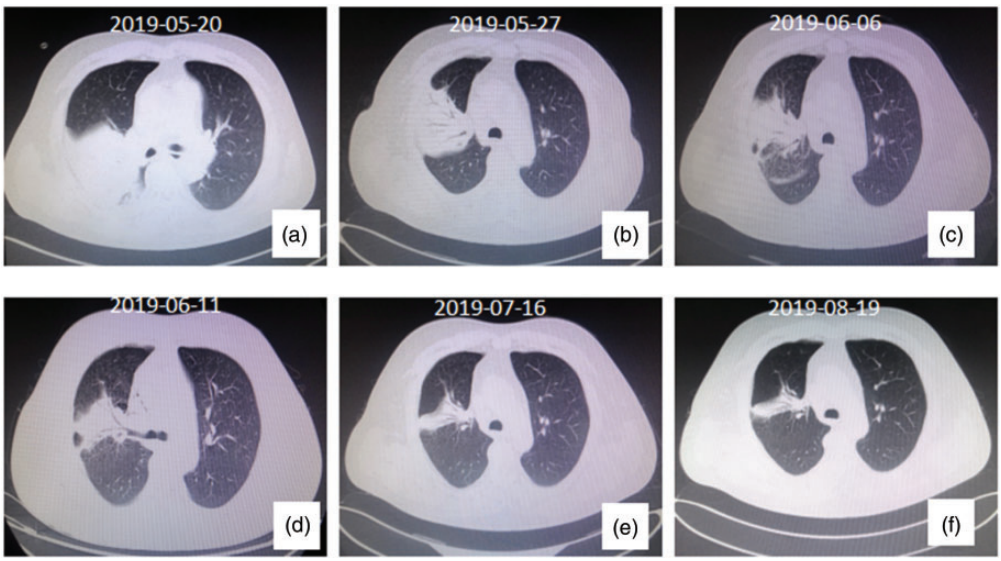

Figure 2. a–f: Dynamic changes in the patient's pulmonary computed tomography (CT) images from May to August 2019. The images show that the right lung consolidation decreased significantly

stable (laboratory findings are shown in Table 3), and biopsy of the right upper lung and examination of the exfoliated cells in bronchoalveolar lavage fluid (BALF) were performed on 3 June. The biopsy results from the right upper lung showed that acute and chronic inflammation of the lung tissue was accompanied by inflammatory granulation tissue, aggregated tissue cells were observed in the alveolar cavity, and some areas showed interstitial pneumonia (Figure 3). The results of the immunohistochemical analysis were as follows: alveolar epithelial cytokeratin (CK) (+), periodic acid-Schiff (PAS) (−), acid-resistant (−), and cluster of differentiation (CD)68 (+) (Figure 4). Biopsy of the posterior segment of the right upper lobe showed pulmonary fibrous connective tissue hyperplasia with extensive cell necrosis and chronic inflammation (Figure 5). Therefore, according to the

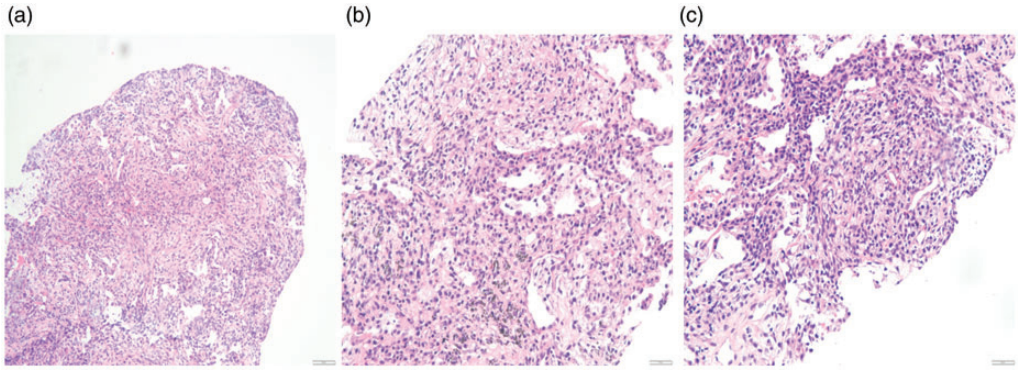

Figure 3. Aggregated tissue cells were observed in the alveolar cavity, and some areas showed necrotizing pneumonia (a: hematoxylin and eosin (HE), 10× magnification; b, c: HE, 20× magnification).

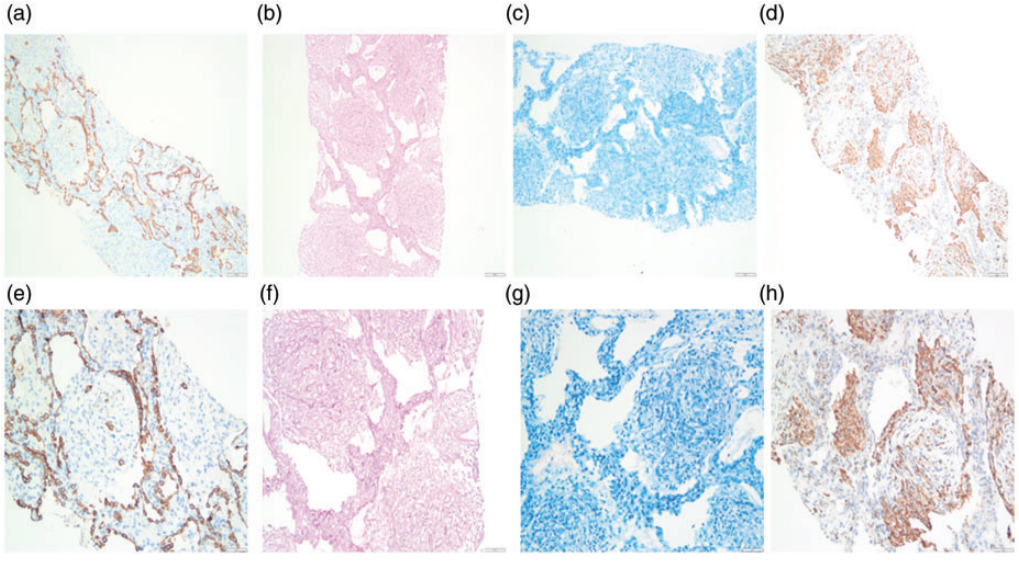

Figure 4. Immunohistochemistry of lung epithelial cells. a, e: cytokeratin (CK) (+); b, f: periodic acid-Schiff (PAS) (−); c, g: acid-resistant (−); d, h: cluster of differentiation (CD)68 (+); (a–d: 100× magnification; e–h: 200× magnification).

results of the histopathological examination, we diagnosed SOP. The analysis of the exfoliated cells in BALF revealed neutrophils (25%), lymphocytes (5%), and alveolar macrophages (70%), which further confirmed our diagnosis. Pulmonary CT on 3 June showed an obvious reduction in the right lung consolidation (Figure 2), and the patient was discharged on 16 June. He was followed-up for 2 months after discharge, and has not relapsed to date (Figure 2 and Table 3).

Discussion

Sodium nitrite is an inorganic salt formed by nitrite ions and sodium ions. It liquifies easily and is highly soluble in water and liquid

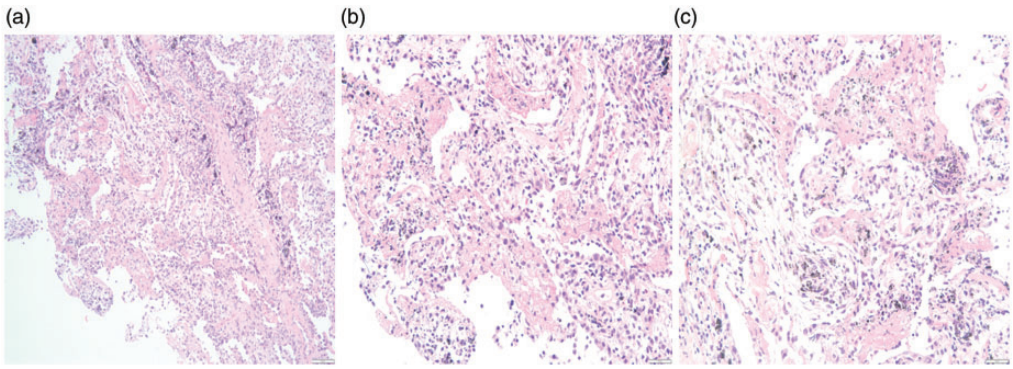

Figure 5. Biopsy results of the posterior segment of the right upper lobe. The photomicrographs show pulmonary fibrous connective tissue hyperplasia with extensive cell necrosis and chronic inflammation; (a: hematoxylin and eosin (HE), 10× magnification: b–c: HE, 20× magnification)

ammonia. Its aqueous solution is alkaline with a pH of approximately 9. Sodium nitrite can act as a rust inhibitor by forming a dense oxide film with the metal to protect the metal from corrosion. Because of its low cost and good rust-prevention effects, sodium nitrate is widely used in industry and construction. Hydrochloric acid is an aqueous solution of hydrogen chloride gas, which is a monobasic inorganic strong acid commonly used in pickling steel, metal refining, household cleaning, food additives, and leather processing. Concentrated hydrochloric acid is volatile, especially at high temperatures, and it easily corrodes equipment and pollutes the environment. Therefore, hydrochloric acid used for pickling steel is mostly dilute hydrochloric acid, and the concentration generally does not exceed 15%. Nitrite ions react with dilute hydrochloric acid to form nitrous acid, which is a weak acid that is unstable, and easily decomposed and disproportionated to form nitric oxide and nitrogen dioxide. Nitric oxide and nitrogen dioxide weakly stimulate the upper respiratory tract. In the early stage of inhalation, patients may experience mild eye and upper respiratory tract irritation, such as dry cough and pharyngeal discomfort. When entering the lower respiratory tract and alveoli, these gases can form nitric acid and nitrous acid with water, which have strong stimulatory and corrosive effects on alveolar epithelial cells and capillary walls, causing enhanced capillary permeability; this can cause pulmonary edema in severe cases. In addition, nitrous acid combines with alkaline substances in lung tissue to form nitrite, which can convert hemoglobin into methemoglobin, causing erythrocyte oxygen-carrying disorder.[9] After an incubation period of a few hours or more, progressive respiratory distress syndrome occurs, and severely poisoned patients may have liver, kidney, and nervous system damage.

The pathogenesis of SOP is not completely understood. Some scholars consider that alveolar epithelial cells and microvascular endothelial cells are damaged by various factors that initiate the body's repair mechanism, promoting alveolar macrophages to produce abundant proinflammatory cytokines and chemokines, including interleukin 1 beta (IL-1β), IL-6, IL-8, tumor necrosis factor-alpha (TNF-α), and CC chemokine ligand 18.[10] At the same time, macrophage and lymphocyte activation enhances the Th1 response, which further promotes the growth of granulation tissue and infiltration of chronic inflammatory cells into the pulmonary

interstitium.[11] In a study by Major et al.,[12] BALF analysis in patients with SOP showed abnormal changes in the ratio of macrophages and lymphocytes, and a significant increase in the proportion of neutrophils, eosinophils, and mast cells. In our patient, the BALF analysis showed a significant increase in the proportion of neutrophils and a significant decrease in the proportion of macrophages, which is consistent with the results of the cited previous studies.

It has been reported that most SOP cases have elevated C-reactive protein (CRP) concentrations.[13] Studies have shown that elevated CRP in patients with SOP may be secondary to known diseases,[14] but the reason for this increase is not yet clear. The laboratory results of the patient in this study were also accompanied by an elevated CRP concentration. The patient experienced sustained acute lung injury after inhaling a large amount of toxic gas, and the lung lesions improved after administering glucocorticoids and infection control. Combined with the toxicological mechanism, SOP pathogenesis, laboratory examination, imaging findings, and biopsy pathology, we confirmed SOP caused by acute nitrogen oxide poisoning. For such patients, early active intervention and the treatment of pulmonary edema are key to successful treatment. In the early stage of poisoning, timely removal from the toxic substances, using glucocorticoids early and sufficiently, correcting hypoxemia and methemoglobinemia, and controlling pulmonary infection are essential. Furthermore, early diagnosis, early treatment, rational application of glucocorticoid therapy, and avoidance of glucocorticoid-related adverse events are also important factors affecting patients' prognosis.[15]

The cause of the accident in this report was mainly the patient's error and limited safety awareness. After inhaling the irritating gas, the patient did not leave the environment quickly and did not take protective measures. Therefore, for employees at risk of occupational exposure, companies should strengthen safety education and improve their awareness of emergencies. In addition, stricter operating rules and regulations should be introduced and implemented. The relevant departments should also methodically eliminate the hidden dangers of accidents, standardize the process of industrial waste treatment, and implement emergency plans.

Ethics statement

This report was approved by the ethics committee of the Shandong University Qilu Hospital (Approval number KYLL-2019-296). We thank our patient for providing verbal consent and agreeing to the publication of this case report.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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