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# Chlorine-induced extensive tracheobronchial necrosis concomitantly benzene-induced pancytopenia presented with severe pneumonia

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## ÖZET

*Ciddi pnömoni ile kendini gösteren kloramin inhalasyonuna bağlı yaygın trakeobronşiyal nekroz ve eş zamanlı benzen maruziyetine bağlı pansitopeni*

*Bu olgu sunumunda, evde kullanılan temizlik maddelerinin karıştırılması sonucu ortaya çıkan klorin gazı maruziyeti ile gelişen trakeobronşiyal nekrozlu 25 yaşındaki bir kadın olgu sunulmuştur. Olgu, temizliği takiben benzen içeren bir yapıştırıcı ile koltukları yapıştırmış ve böylece benzen maruziyeti de olaya eklenmiştir. Olgu, öyküsü, gecikmiş tanısı, bronkoskopik bulguları ve fatal gidişi ile ilginç bulunmuştur. Literatürde daha önce gösterilmemiş olan klorin gazına bağlı trakeobronşiyal nekrozun bronkoskopik ve patolojik görünümleri de sunulmuştur.*

**Anahtar Kelimeler:** *Havayolu hastalıkları, klorin maruziyeti, akciğer hasarı, solunum yetmezliği.*

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## SUMMARY

### *Chlorine-induced extensive tracheobronchial necrosis concomitantly benzene-induced pancytopenia presented with severe pneumonia*

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*We report a case of 25-year-old woman with severe tracheobronchial necrosis caused by chlorine released from a mixture household cleaning agents. She subsequently exposed benzene while she was fixing the seats with benzene containing gum. The case was found interesting with its history, delayed diagnosis, bronchoscopic features, and fatal outcome. We presented its bronchoscopic and pathological images which has not been shown in the literature up to date.*

**Key Words:** Airway disease, chlorine exposure, lung injury, respiratory failure.

Mixed domestic cleaning agents produce noxious gases such as chlorine or chloramine having hazardous effects to the airways. It has been commonly used by housewives without being aware of their dangers in the worldwide. The first reports about their effects were published in the 1960s (1,2). Although, these effects had been considered as transient in most instances, more serious cases which resulted respiratory failure have been seen in the past (3). After Brooks et al. had described reactive airways dysfunction syndrome (RADS), several reports of RADS following exposure irritant gases have been increasingly reported in the literature (4-7). In this report, we present a distinct case of a woman exposed to chlorine gas resulting severe tracheobronchial necrosis, not RADS; and concomitantly exposed to benzene resulting pancytopenia. To our knowledge, this is the first reported case provides bronchoscopic images.

## CASE REPORT

A 25-year-old woman was referred to our respiratory intensive care unit (RICU) because of severe dyspnea and tachypnea. Her complaints were begun with sore throat and fever 6 days before admission. She was examined by an ear-

nose-throat specialist at the local hospital and given penicillin orally for 4 days. Dyspnea and tachypnea were developed and progressed within the last 2 days. She admitted to the local hospital with severe respiratory distress, then she was sent to our RICU urgently. She mentioned that she had cleaned the poorly ventilated bathroom about 45 minute with a solution which she had produced by pouring 0.6 L of household hydrochloric acid (HCl) into 1 L sodium hypochlorite (NaOCl) containing bleach, and subsequently she fixed the seats with a benzene-containing gum 7 days before admission. And also she explained that she had been cleaned bathroom in such way at least once a month regularly, but the duration of exposure was longer on the last occasion. Her chest X-ray which was taken before 3 months due to breathlessness was normal. Clinical examination revealed an anxious but fully conscious woman in acute respiratory distress with tachypnea (45/min), tachycardia (134/min), hypertension (185/70 mmHg), rigorous inspiratuar retraction, and wheezing. Laboratory results were as follows: WBC 900/mm<sup>3</sup>, platelet count 72.000/ mm<sup>3</sup>, hemoglobin 6.6 g/dL, blood urea nitrogen (BUN): 62 g/dL, creatinine: 2.2 mg/dL; arterial blood gases: pH

7.31; PaCO<sub>2</sub> 41 mmHg, PaO<sub>2</sub> 63 mmHg, HCO<sub>3</sub> 22 mEq/L. Bilateral pneumonic infiltration was seen on chest X-ray (Figure 1). Moxifloxacin was begun in case of atypical pneumonia, and systemic steroid was begun in case of inhalational injury. Noninvasive mechanical ventilation (NIMV) was applied with the full-face mask as a first-line intervention. However, the clinical situation was deteriorated, and she was intubated 20 minutes after NIMV trial. During the intubation, although oral and laryngeal structures were seem normal, tracheal narrowing which caused intubation difficulty was noticed. She was deeply sedated and paralyzed because of patient-ventilator interaction, and volume-controlled ventilation was begun. Toxic gas inhalation, pneumonia, myelodysplastic diseases, collagenosis, and vasculitis were considered in the differential diagnosis. Blood culture, urine and tracheal aspirate were obtained for microbiologic studies. Blood tests for collagenosis and atypical pneumonia, bone marrow aspiration for myelodyscrasia, and bronchoalveolar lavage (BAL) were planned. Fiberoptic bronchoscopy (FOB) performed so as to obtain BAL. Bronchoscopic appearance was as follows: trachea was seen as a rigid tube extremely hyperemic having hemorrhagic inflammation associated with white necrotic lines on the mucosal surface (Figure 2), the cartilage rings of trachea had been almost disappeared; main bronchial lumens were obstructed with yellowish hard materials. FOB could

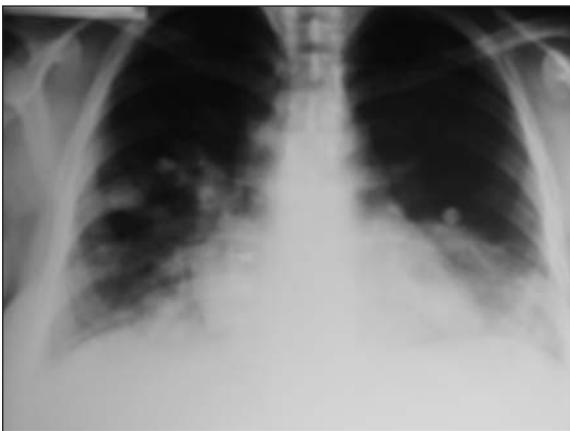


Figure 1. Bilateral pneumonic infiltration is seen on the chest X-ray.

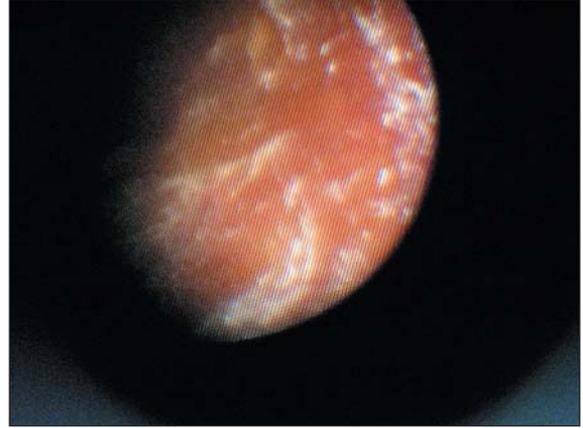


Figure 2. FOB revealed tracheobronchial mucosal injury.

not been advanced distally through the main bronchies, so BAL could not be performed. Bronchial biopsy demonstrated extensive tissue necrosis containing yellowish foreign bodies (Figure 3). Studies for hematologic malignancy, collagenosis, vasculitis, and microbiological cultures were all negative. A differential of white blood cell count was revealed that there was no neutrophil. Bone marrow aspiration was reported as a regenerative bone marrow without blastic features. Immunophenotypic research of the bone marrow was revealed that there was an increase in the myelomonocytic series (49%), and mature monocyte rate was found 1.6%. On the 2<sup>nd</sup> hospital day, FOB was performed again in order to evaluate if the obstructive materials co-

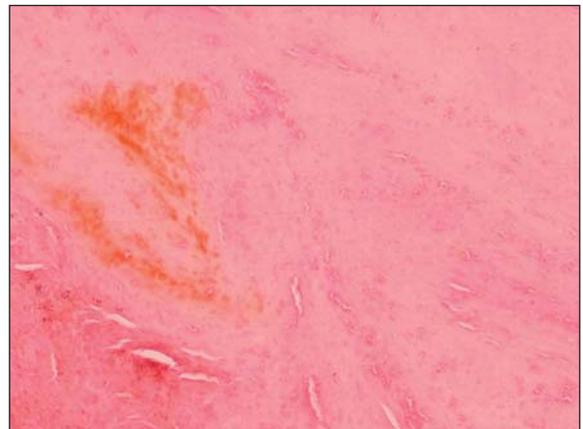
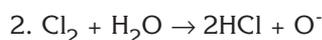
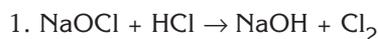


Figure 3. Extensive tissue necrosis and yellowish foreign bodies on the bronchial biopsy (Hematoxylin-eosin x100).

uld be removed or bronchial stenting was possible. However neither stenting nor extracting of these hard materials could be done. She died with severe acidosis, hypoxemia, and high fever on the 3<sup>rd</sup> day of admission. Autopsy was rejected by her family.

## DISCUSSION

Mixing solutions of sodium hypochlorite and hydrochloric acid produces chlorine (Cl<sub>2</sub>) fumes. On contact with mucosal surface, chlorine gas reacts with water vapour, and creates hydrochloric acid (HCL) and nascent oxygen (O<sup>·</sup>) as shown in the following equations:



HCl has a highly irritant effect for airway epithelium depending on the concentration of inhaled gas as well as the duration of exposure. The clinical situation varies from mild and transient cough to severe respiratory failure. Although cases with similar concentration of exposure had been reported, our patient had exposed longer duration than the cases previously reported (3). This might explain the severity of tracheobronchial injury. Another cause of the severity might be the delayed diagnosis due to her unawareness of the breathing noxious gases. Several authors reported that chemical irritation of the respiratory tract may cause airway obstruction, inflammation, epithelial desquamation, sensory nerve impulses, and other nonspecific responses. Repeated exposures might cause an attenuation of these responses, especially airway reactivity (8). The phenomenon of attenuation has been well described for ozone, and has also been demonstrated for other chemical agents (9-11). In our case, repetitive exposure of chlorine gas presumably led her more tolerant, and she didn't pay attention her symptoms related to inhaling the noxious gas while she was cleaning the bathroom. And also, she didn't suspect of the cleaning agents when her complaints began.

Histopathologic findings are differed from mild epithelial desquamation to severe tissue necrosis (5,12,13). Postmortem descriptions revealed

that severe alveolar damage associated with destroyed or denuded airway epithelium and loss of mucociliary function (14). Serial measurements of spirometry and bronchial responsiveness combined with histological evaluation were performed by Lemi re and co-workers in a subject who abruptly exposed chlorine gas (6). They reported that epithelial regeneration had started about 2 months after the initial event, and functional integrity didn't necessarily mean histological integrity. In the present case, bronchoscopic biopsy revealed extensive coagulation necrosis which proved exposure of toxic gas in high concentration and long duration.

Although exposure for chlorine gas or hydrochloric acid aspiration cause most commonly RADS, different injury patterns are possible. Rubin et al. presented an unusual case of a man exposed to HCl resulting in tracheobronchial multiple strictures requiring airway stenting for treatment (15). In our patient, extensive airway obstruction with hard materials was seen bronchoscopically, however it couldn't be possible to extract them as well as to perform airway stenting. Because of tracheobronchial necrosis was proven pathologically, RADS was not suspected in this case.

Another distinct feature of this patient is inhalation of benzene containing glue after chlorine exposure. Benzene is a well known industrial and environmental pollutant as having hematotoxicity at high concentrations. It inhibits the incorporation of <sup>59</sup>Fe into developing erythrocytes in a dose-dependent manner and inhibition becomes maximal 48 hours after the administration of a single dose of benzene (16). The myelotoxic effect of benzene is believed due to the combine effects of its metabolites (e.g. hydroquinons, p-benzo-quinone, 1,2,4 benzenetriol). Benzene inhalation was thought to be responsible for the hematological changes in our patient. Presumably, benzene absorbed easily into the blood from injured lung tissue, and even it inhaled with lower concentration might have reached higher concentration in the blood. This mechanism can explain pancytopenia in our case. But, we don't know if there was a role of

benzene inhalation on the tracheobronchial injury. Although Gosepath and co-workers stated that high concentrations of benzene might cause an inflammatory responses in respiratory epithelial cell, there are no reported cases with airway injury resulting from benzene inhalation (17). It is possible that exposure to chlorine gas associated with co-exposure to benzene extended epithelial injury. Because of repetitive exposure to chlorine gas in our patient, benzene concentrations might have been easily reached to the toxic levels and more irritant to the previously injured epithelium. Histopathologically, yellowish foreign bodies were seen in extensive coagulation necrosis. We couldn't explain what the contents of these bodies are. However we suggested that they might be produced from the interaction benzene with chlorine gas or from the interaction benzene with the necrotic tissues.

In conclusion, chlorine gas was considered as the major cause of tracheobronchial necrosis, and benzene was considered as the cause of pancytopenia in this patient. This case presented as having an interesting history with delayed diagnosis, intoxication more than one agent, and FOB findings.

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