

*Case Report*

# **Bronchiolitis Obliterans in a Civilian Survivor of a Chemical Warfare Attack**

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## **Abstract**

Bronchiolitis obliterans is an uncommon disease characterized by cough, exertional dyspnea, and fixed airflow limitation arising from exposure to noxious chemicals, infections, systemic disease, and hematopoietic cell or lung transplant. We report a case of bronchiolitis obliterans found in the U.S. several years after exposure to sulfur mustard gas during the Iraq war. Bronchiolitis obliterans is the main late pulmonary consequence of sulfur mustard exposure and has recently been studied in military personnel in Iran and U.S. military personnel who served in Iraq and Afghanistan. In the age of recent terror attacks and the use of chemical warfare abroad, our case highlights the need for a high index of clinical suspicion and a thorough exposure history in patients with unexplained dyspnea and fixed airways obstruction who may have been exposed to chemical warfare.

**Keywords:** bronchiolitis obliterans, sulfur mustard

## **Introduction**

Bronchiolitis Obliterans (BO) is an uncommon disease characterized by cough, exertional dyspnea, and fixed airflow limitation arising from exposure to noxious chemicals, infections, systemic disease, and hematopoietic cell or lung transplant [1]. Noxious chemical inhalational exposure such as sulfur mustard has been found to induce BO [2,3]. In fact, BO has been found to be the main late pulmonary consequence of sulfur mustard inhalational exposure in Iranian soldiers exposed to sulfur mustard in the 1984-1988 Iraq-Iran war [3]. BO has also been reported in U.S. military personnel who were deployed to Iraq and Afghanistan [2]. Here we report a case of BO in a civilian survivor several years after exposure to sulfur mustard gas.

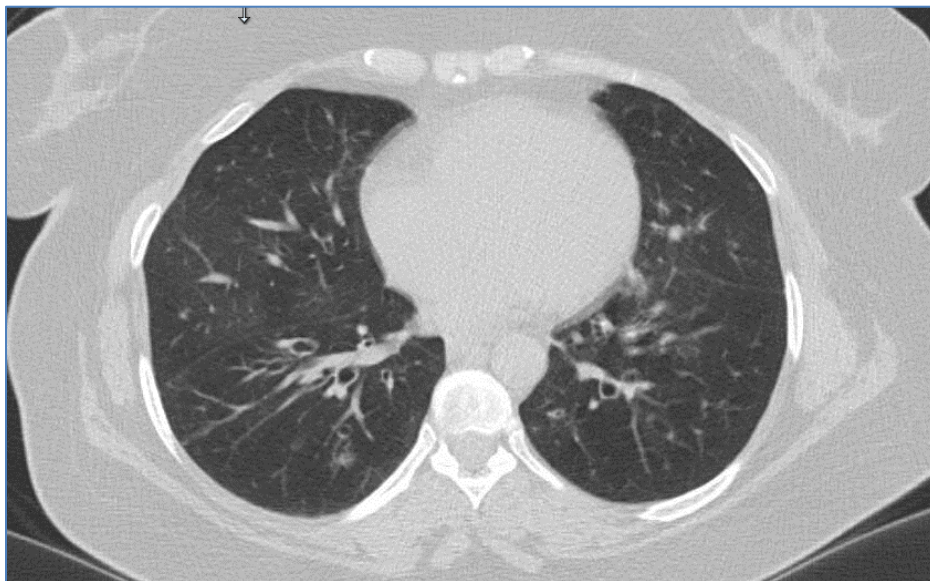
## **Case Report**

A 37-year-old Kurdish female was seen in our clinic for evaluation of chronic shortness of breath. She lived in the Northern part of Iraq until about 20 years ago. In 1988 while residing in Kurdistan, she was exposed to chemical warfare where she describes bombs were dropped and the sky was filled with smoke. This was followed by several days of difficulty with blurred vision, eye pain, tearing, cough, and dyspnea. Since the event she has been

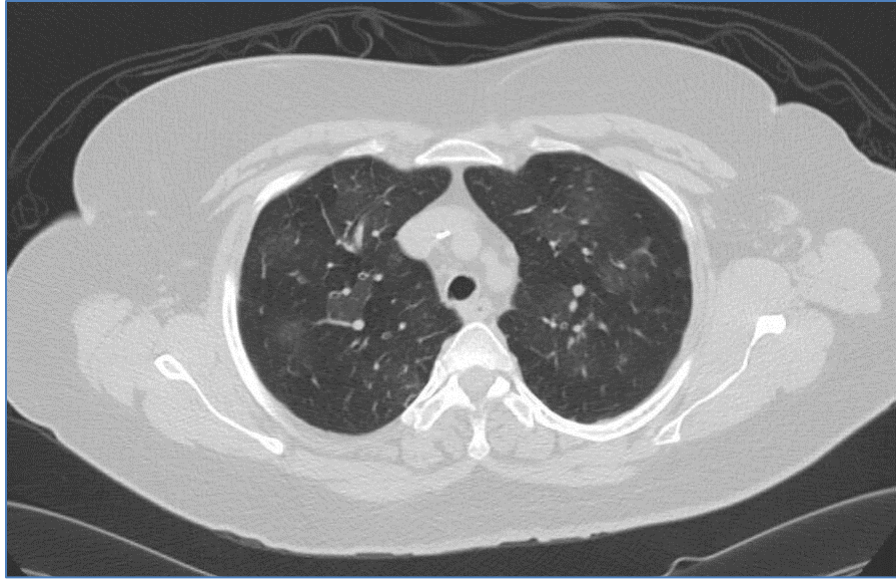
living with daily eye pain, cough, dyspnea, hoarse voice, and sputum production. Her cough and dyspnea have been worsening over the last few years limiting her ability to perform activities of daily living. She had been on antibiotics several times as well as several prednisone “bursts”, including long term steroid use with no improvement in her symptoms and a steroid induced 30-pound weight gain. The patient reports that her brother and mother who were also in Iraq at the time of the bombing have similar respiratory issues, but she has not been in contact with them recently. She denies any tobacco use and has not had any second-hand exposure to tobacco. She denies any other significant occupational or environmental exposure. She has not travelled outside of the U.S. recently. She does not drink alcohol or use illicit drugs.

Her blood pressure was 136/84, pulse was 104 beats/min, respiratory rate was 16, body mass index was 30.64 kg/m<sup>2</sup>, and her oxygen saturation was 92% on room air. Her examination was notable for a hoarse sounding, almost inaudible voice as well as mild bilateral lower lung field inspiratory crackles. Initial laboratory findings including results of a complete blood count and comprehensive metabolic panel were normal. Blood, urine, and sputum cultures were negative. Tests for HIV antibody, cryptococcal antigen, strongyloides antigen, aspergillus antigen, micropolyspora faeni antibody, and thermoactinomyces vulgaris were negative. Serologic testing for rheumatologic diseases were negative including rheumatoid factor, smith antibody, RNP antibody, SS-A and SS-B antibody, ANCA, anti-myeloperoxidase antibody, anti-proteinase 3 antibody, anti-scleroderma antibody, antinuclear antibody, and immunoglobulin IgE. Immunoglobulin testing for IgG, IgA, and IgM were all within normal limits. Allergy testing was negative for any specific pathogens.

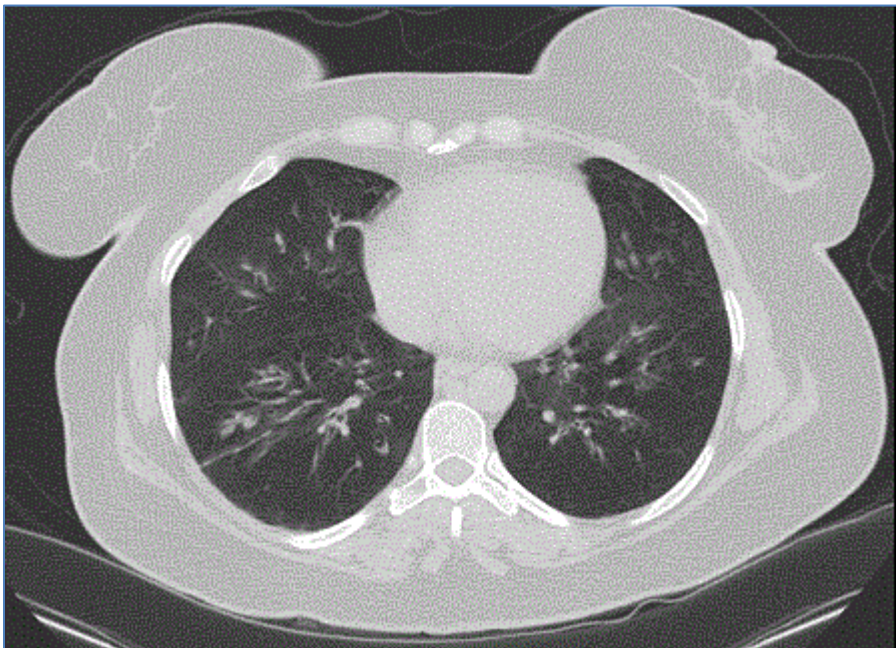
A chest CT scan revealed direct evidence of bronchial wall thickening and bronchiectasis, worse in the lower (Figure 1). There was heterogeneous mosaic attenuation throughout the lung parenchyma. (Figure 2). At 1 year follow up, her chest CT revealed redemonstration of cylindrical bronchiectasis which had progressed since the prior study, with multifocal mucous plugging and mosaic lung attenuation which was consistent with constrictive bronchiolitis (Figure 3). Pulmonary function testing revealed a severe obstructive pattern with no airflow reversibility (Table 1). Her six-minute walk test was notable for decreased exercised tolerance (434 meters) and desaturation to 87% on room air.



**Figure 1:** Bronchial wall thickening and cylindrical bronchiectasis



**Figure 2:** Ground glass opacities with heterogenous mosaic attenuation



**Figure 3:** Bronchiectasis with mucoid impaction

Bronchoscopy findings included erythematous and friable airways with mucoid secretions found throughout the tracheobronchial tree. Bronchoalveolar lavage returned positive for *pseudomonas aeruginosa* resistant to ciprofloxacin. She was treated in the hospital with intravenous piperacillin-tazobactam and inhaled tobramycin for 8 days. After discharge she did not report any improvement in her symptoms.

Treatment has included high doses of prednisone (1mg/kg of body weight) for 6 weeks followed by a prolonged taper. She did not notice any respiratory benefit from the steroids and suffered a 30-pound weight gain. She was also placed on chronic azithromycin 250 mg three times weekly treatment, montelukast, acclidinium bromide,

fluticasone-salmeterol, as needed ipratropium-albuterol, and 2L home oxygen supplementation. She has had multiple hospitalizations for her dyspnea and recurrent pseudomonas infections. She has participated in pulmonary rehabilitation and has been referred for lung transplant.

**Table 1:** Pulmonary Function Testing

Pulmonary Function Test	
FVC-Pre	1.20
FVC-%Pred-Pre	37
FEV <sub>1</sub> /FVC-Pre	48
FEV <sub>1</sub> -%Pred-Pre	21
FEV <sub>1</sub> -Pre	0.58
TLCpleth-%Pred-Pre	117
TLCpleth-Pre	5.24
DLCOcor-%Pred-Pre	77
DLCOunc-Pre	17.54

## Discussion

Sulfur mustard (SM) gas was used as a chemical warfare agent in the Iran-Iraq war (1981-1989) which can cause severe chemical injuries involving the skin, eyes, and lungs [4,5]. Studies have shown that bronchiolitis obliterans is the main late pulmonary consequence of SM exposure [3]. However, BO is an uncommon disease in otherwise healthy young adults and is often missed. As pointed out by Ghanei et al. in some situations the patient may not recall or have been aware of low dose exposures to SM [6]. Therefore, diagnosis requires a high clinical suspicion and a very detailed exposure history, especially in the setting of terror attacks [6].

Bronchiectasis is a major finding in our patient causing much of her morbidity and recurrent symptoms. In a study of 21 Iranian soldiers who developed progressive hypoxemia and bronchiectasis as a result of severe inhalational exposure to sulfur mustard gas, early bronchoscopy revealed hemorrhagic inflammation of the tracheobronchial tree with severe erosions [7]. Initial damage of the tracheobronchial tree likely leads to depression of the local defense mechanisms and development of recurrent infections contributing to the development of bronchiectasis. Bronchoalveolar lavage in patients with SMBO have shown increases in the number of inflammatory cells, higher neutrophil count, decreased numbers of macrophages, and increased levels of transforming growth factor  $\beta$  [7-9]. These alterations in bronchoalveolar lavage fluid suggest an initial inflammatory process followed by impaired airway remodelling and chronic inflammation which results in bronchiectasis and bronchiolitis obliterans.

To our knowledge, this is only the second case of a U.S. civilian diagnosed with BO related to SM exposure reported in the U.S. Prior research has focused on Iranians who were exposed to SM and U.S. military personnel returning to the U.S. who were deployed to the Middle East [2-6,10-12]. Clinical BO related to SM exposure has been characterized by productive cough, difficult expectoration, and chronic dyspnea [3]. Hemoptysis, wheezing, and bilateral early inspiratory crackles have also frequently been reported [3]. Most patients with sulfur mustard-induced BO (SMBO) have fixed airways obstruction, however biopsy-confirmed case series have shown that spirometry can be normal, restrictive, obstructive, or mixed [2-6]. Finally, high-resolution computerized tomography (HRCT) of the chest with inspiration and suspended expiration has been shown to be a useful diagnostic tool. Patients with SMBO have findings of air-trapping, bronchiectasis, mosaic parenchymal attenuation, and bronchial wall thickening on HRCT [3,4,11,13]. Our patient had all of the clinical symptoms, pulmonary function testing, and HRCT findings

consistent with SMBO. In many cases that lack the typical spirometry abnormalities and HRCT findings, biopsy is often necessary to confirm the diagnosis.

In the age of recent terror attacks and the use of chemical warfare abroad, our case highlights the need for a high index of clinical suspicion and a thorough exposure history in patients with unexplained dyspnea and fixed airways obstruction who may have been exposed to chemical warfare.

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