Case Study

Cavitating BOOP Associated with Myeloperoxidase Deficiency in a Floor Cleaner with an Incidental Heavy Exposure to Benzalkonium Compounds

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Bronchiolitis Obliterans Organizing Pneumonia (BOOP) is an inflammatory lung disease simultaneously involving the terminal bronchioles and alveoli. BOOP is defined idiopathic in most patients, but it can also be secondary to several known causes (drugs, infections, organ transplantation, radiotherapy) or associated to tumours and haematologic malignancies, rheumatologic and connective tissue diseases, immunodeficiency syndromes, inflammatory bowel diseases and other systemic disorders¹⁾.

Rarely BOOP has been reported as related to occupational or environmental agents exposure. We describe a lady developing BOOP two weeks after she inhaled vapours of benzalkonium compounds, components of a cleaning agent a lot which was spilled on the floor.

Case History and Clinical Findings

A 46 yr old lady was hospitalized for severe dyspnea, cough and fever. Her medical history was negative for any disease. She had been working as cleaning lady in a shopping center. She said that two weeks before the hospitalization, she spilled on the floor a large amount of a cleaning agent which she was pouring into the container of a floor-polisher, inhaling its vapours. The components of this cleaning agent turned out to be benzalkonium compounds, a group of biocides with the general formula alkyl-dimethyl-benzyl-ammonium-chloride.

Her first symptoms upon the exposure were a dry cough and burning eyes which made her stop working immediately. In the afternoon (the spilling accident

occurred early in the morning) she felt much better so that she did not seek medical advice, but she had a discontinuous dry cough which became continuous after 4–5 d. She was given 15 d off work from the occupational physician, who arranged for her a spirometry and a methacoline test which resulted to be normal. Despite being home her dry cough did not improve and when she developed also dyspnea and fever, she was referred to hospital.

On physical examination she had a regular pulse rate, blood pressure of 130/80 and respiratory rate of 20 breaths/min. Tubular breathing and rales were heard in the lower region of the right lung.

A chest radiograph showed ground glass opacities of the right lower lobe. A CT scan performed at the same time showed an alveolar and interstitial infiltrate with multicavitary lesions in the posterior segment of the right lower lobe (figure).

The erythrocyte sedimentation rate (ESR) was 44 mm/h. All routine laboratory test results, including complete blood cell count, liver and kidney profile, serum proteins, and urine analysis were normal. The CBC count was normal but the cytometer used (Technicon Coulter), gave a plot indicative of neutrophils myeloperoxidase deficiency, confirmed by a cytochemical study of blood smears. Sputum examination and culture for microorganisms including acid fast bacilli, *Candida*, *Aspergillus* and other moulds were repeatedly negative. Serologic test results for *Aspergillus*, *Mycoplasma*, Cytomegalovirus, Adenovirus, Herpes viruses, Respiratory Syncytial virus and *Legionella* urine antigen were negative. Blood and urine culture findings were also negative. Antinuclear antibodies and antineutrophil cytoplasmic antibodies (ANCA) were negative. After performing a bronchoscopy with bronchial-alveolar lavage (BAL) and transbronchial biopsy, the patient started empirically treatment with IV piperacillin/tazobactam and clarythromycin with no clinical improvements. No bacteria, acid fast bacilli, or moulds were microscopically seen on bronchial secretions and culture findings of the BAL liquid were negative. The BAL showed an elevated cell recovery with 10% lymphocytes and 54% neutrophils. Histology of the transbronchial biopsy showed intraluminal organization and polypoid granulation tissue within small bronchioles and alveolar ducts; myxoid fibroblastic tissue and intrabronchiolar aggregates of mononuclear cells invading alveolar spaces. These findings were consistent for a diagnosis of BOOP.

The antibiotic empirical treatment was stopped and prednisone (50 mg/d) was started with prompt resolution of symptoms. The patient was discharged feeling well and a control CT scan revealed only minimal residual infiltrates. The dose of prednisone was slowly tapered within three months. At the sixth month of follow up she

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Figure. Chest CT scan performed in a lady who suffered severe dyspnea two weeks after she had inhaled vapours of benzalkonium chloride contained in a cleaning agent, spilled massively on the floor. In the posterior segment of the right lower lobe is evident an alveolar and interstitial infiltrate with multicavitary lesions.

was still asymptomatic and a chest radiograph was completely clear.

Discussion

In the reported case, the exposure to benzalkonium compounds had a clear causative role in the pathogenesis of this occupationally related BOOP. There was no evidence of other causes which could have determined the disease. Moreover the case did not qualify for the diagnosis of cryptogenic BOOP, both for the clinical presentation and course.

BOOP related to chemicals exposure occurring in the environment or workplace is reported rarely. In 22 textile airbrush workers BOOP was caused by the spraying of respirable aerosol, containing the textile printing dye used in their workshops²⁾. A worker developed BOOP after inhalation of powdery dust of a growth of *Penicillium janthinellum* mold on the top of a discarded orange juice container³⁾. Smoke inhalation BOOP was reported in a patient who was in a house fire and had erythema nodosum⁴⁾. To the best of our knowledge, benzalkonium compounds have never been described as causative of BOOP, while they are recognized as causing occupational asthma^{5, 6)}.

Benzalkonium compounds may cause allergic contact dermatitis, due to a delayed type hypersensitivity reaction, mediated largely by previously sensitised lymphocytes, that determine inflammation and oedema in the skin⁷⁻⁹⁾.

Although BOOP may present with a variety of radiologic patterns (patchy alveolar infiltrates, diffuse interstitial infiltrates, solitary opacities resembling tumours), this case showing cavitary infiltrates was very unusual. There are only few descriptions of cavitary infiltrates concerning the cryptogenic form of BOOP¹⁰⁾ or the form associated with disorders such as essential mixed cryoglobulinemia¹¹⁾ and lymphoma¹²⁾.

This patient was incidentally diagnosed a deficiency of myeloperoxidase, the most common inherited disorders of neutrophils¹³⁾. Myeloperoxidase is the principal component of azurophilic neutrophil granules and catalyzes the formation of hypochlorous acid. Despite the ability of hypochlorous acid to kill microorganisms, deficiency of myeloperoxidase is not generally associated with disease, except if it coexists in patients with diabetes mellitus who are then susceptible to disseminated candidiasis¹³⁾. BOOP has never been associated with defects in the innate immunity such as the formation of neutrophil granules, while it is well known the form associated with variable immunodeficiency syndrome¹⁴⁾, the most common primary immunodeficiency due to defects in lymphocytes. Further observations are necessary to establish if this defect in the formation of neutrophil granules was a casual finding in the reported case of BOOP, or was a concomitant cause together with the incidental heavy exposure to benzalkonium compounds.

The benzalkonium compounds, as well as the other biocides which are components of several cleaning agents, represent a health hazard for cleaners. These chemicals have protein denaturing properties and could create neoantigens from human proteins inducing sensitisation, or start in the distal airways an inflammatory process whose mechanisms are still not completely understood.

References

- 1) GR Epler: Bronchiolitis Obliterans Organizing Pneumonia. *Arch Intern Med* 161, 158–164 (2001)
- 2) P Camus, B Nemery. A novel cause for bronchiolitis obliterans organizing pneumonia : exposure to paint aerosols in textile workshops. *Eur Respir J* 11, 259–262 (1998)
- 3) C Bates, RC Read and AH Morice: A malicious mould. *Lancet* 349, 1598 (1997)
- 4) S Srivastava, R Haddad, G Kleinman and CA Manthous: Erythema nodosum after smoke inhalation induced bronchiolitis obliterans organizing pneumonia. *Crit Care Med* 27, 1214–1216 (1999)
- 5) RD Ponder and BB Wray: A case report: sensitivity to benzalkonium chloride. *J Asthma* 30, 229–231 (1993)
- 6) PS Burge and MN Richardson: Occupational asthma due to indirect exposure to lauryl dimethyl benzyl ammonium chloride used in a floor cleaner. *Thorax* 49, 842–843 (1994)
- 7) S Bendix: Benzalkonium chloride. *Contact Dermatitis* 35, 264–265 (1996)
- 8) L Kanerva, R Jolanki and T Estlander: Occupational allergic contact dermatitis from benzalkonium chloride. *Contact Dermatitis* 42, 357–358 (2000)
- 9) HJ Park, HA Kang, JY Lee and HO Kim: Allergic contact dermatitis from benzalkonium chloride in an antifungal solution. *Contact Dermatitis* 42, 306–307 (2000)
- 10) M Haro, M Vizcaya, A Texido, J Brune, P Bright and S Dame: Idiopathic bronchiolitis obliterans organizing pneumonia with multiple cavitary lung nodules. *Eur Respir J* 8, 1975–1977 (1995)
- 11) LH Zackrison and P Kats: Bronchiolitis obliterans organizing pneumonia associated with essential mixed cryoglobulinemia. *Arthritis Rheum* 36, 1627–1630 (1993)
- 12) R Safadi, N Berkman, YS Haviv, G Clunie, R Loire and M Burke: Primary non-Hodgkin's lymphoma of the lung presenting as bronchiolitis obliterans organizing pneumonia. *Leuk Lymphoma* 28, 209–213 (1997)
- 13) JA Lekstrom-Himes and JI Gallin: Immunodeficiency diseases caused by defects in phagocytes. *N Engl J Med* 343, 1703–1714 (2000)
- 14) J Kaufman and R Komorowski: Bronchiolitis obliterans organizing pneumonia in common variable immunodeficiency syndrome. *Chest* 100, 552–553 (1991)