Case Report

A Case of Flavor-Induced Lung Disease

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Abstract: Bronchiolitis obliterans, a rare inflammatory disorder of the small airways, has been associated with various infections, aspiration, toxic fume inhalation, drugs, transplants, and collagen vascular disorders. In May 2000, this condition was described in eight workers in a microwave popcorn plant in Missouri. Subsequent studies reported its association with exposure to volatile organic compounds used in butter flavoring. Diacetyl was found to be the most predominant of these compounds. We report a case of this rare but serious disease in a 41-year-old flavor industry worker who was initially diagnosed with occupational asthma.

Key Words: bronchiolitis obliterans, food flavorings, popcorn butter flavoring, diacetyl, fibrosing inflammatory disorder

Bronchiolitis obliterans (BO) is a relatively rare inflammatory and fibrosing disorder of the small airways. Common causes include infection, chronic aspiration, toxic fume inhalation, drugs, allograft transplants, and collagen vascular disorders.[1] Occupational causes are commonly attributed to exposure to high concentrations of noxious gases such as nitrogen dioxide, sulphur dioxide, phosgene, ammonia, and chlorine.[1]

In May 2000, eight cases of BO in former workers of a microwave popcorn industry were reported to the Missouri Department of Health and Senior Services.[2–4] Subsequent studies conducted by Missouri Department of Health and Senior Services in collaboration with the Centers for Disease Control[3,5] found an association between volatile organic compounds (VOCs) used in the butter flavoring industry and development of BO. Diacetyl (2,3-butanedione), a ketone with butter flavoring properties, was found to be the predominant VOC.[3–5] Subsequent animal studies[6,7] in rats and guinea pigs have demonstrated airway damage when exposed to a high concentration of butter flavoring compounds. We report a case of this rare but serious disease in a 41-year-old flavor industry worker who was initially diagnosed as a case of occupational asthma.

Case Report

A 41-year-old man presented with gradually progressive shortness of breath over the previous 6 to 8 years. He also complained of wheezing, severe nonproductive cough, and one episode of cough-induced syncope. He had no chronic medical illnesses and had never smoked. He had worked in the flavoring industry for almost 20 years. One of the items he prepared was microwave popcorn with butter flavoring. His respiratory symptoms began 7 years after he started working in the flavoring industry. He was initially diagnosed and treated for asthma and his symptoms improved. However, over the next 6 years his symptoms worsened significantly, as the production of butter flavorings simultaneously increased.

On physical examination, the patient was mildly tachypneic and had a barrel-shaped chest. Auscultation of his lungs revealed decreased breath sounds throughout and prolonged expiration with scattered expiratory wheezes. He was diagnosed with occupational asthma and was started on oral prednisone. He was also given weekly subcutaneous Omalizumab injections for 6 weeks without any improvement in his symptoms. Pulmonary func-

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Key Points

- Bronchiolitis obliterans is a rare inflammatory disorder of the small airways that causes severe irreversible damage to the lungs.
- Diacetyl used in popcorn butter flavoring and other flavorings used in the food industry are associated with the development of bronchiolitis obliterans.
- It is imperative to increase awareness about this entity among health care professionals, industry officials, and industry workers to limit exposures to such potentially lethal flavors.

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tion tests demonstrated fixed airflow limitation, which raised the concern for a diagnosis other than asthma. He was referred to a specialized tertiary care center where he underwent extensive workup.

The blood tests showed an elevation of C-reactive protein to 0.64 (normal less than 0.4) and of serum immunoglobulin E (IgE) to 303 (normal 1–100). The remaining blood tests were normal. High-resolution computed tomography (CT) scan of the chest showed bronchiectasis with widespread mosaic attenuation and airtrapping, suggesting severe obstructive lung disease consistent with BO.

Pulmonary function tests (Table) were significant for hyperinflation with severe airflow limitation and a decreased carbon monoxide diffusing capacity. There was borderline response to albuterol.

The patient was not sent for lung biopsy because his symptoms, pulmonary physiology, and high-resolution CT findings in the context of employment in the flavor industry were consistent with a diagnosis of BO. He also had a component of asthma. He was given a trial of oral prednisone 40 mg/d combined with methotrexate 12.5 mg/wk for 3 months, but there was no improvement in his symptoms or pulmonary function tests. He has currently been referred to a lung transplant center.

Discussion

BO is a relatively newly recognized occupational health hazard among microwave popcorn industry workers exposed to diacetyl and other VOCs used in butter flavoring. Recently, in addition to the initial Missouri reports, two more cases have been described in the flavor industry in California.[8] Also, for the first time, van Roov et al[9] described a cluster of cases in the flavor industry outside North America in a diacetyl production plant in the Netherlands.

Once established, BO is difficult to reverse.[1] It is imperative to limit any further exposure by complete removal from the workplace or inciting exposure. Patients can be given a trial of steroids or immunosuppressant therapy, such as methotrexate or cyclophosphamide.[1] The last resort is lung transplant. Of the nine cases initially described by Kreiss et al,[3] five had developed irreversible injury and were awaiting lung transplantation.

Primary prevention strategies to limit exposure to such chemicals can limit the devastating consequences of exposure to these chemicals. National Institute for Occupational Health and Safety has issued recommendations for the same, which include substitution, engineering controls, administrative controls, education, personal protective equipment, exposure, and serial monitoring of worker health.[8]

Table. Pulmonary function test

Lung function	Pre % predicted	Post % change
Forced vital capacity	65	1
Functional residual capacity	134	−8
Expiratory reserve volume	20	4
Residual volume	312	−9
Total lung capacity	117	−5
Residual volume/total lung capacity	266	
Forced vital capacity	58	10
Forced expiratory volume at 1 s	29	11
Forced expiratory volume at 1 s/forced vital capacity	49	1
Diffusing capacity of the lung for carbon monoxide	60	

Conclusion

Diacetyl used in popcorn butter flavoring and other flavorings used in the food industry are associated with the development of BO. Although the patient described in this case report was exposed to microwave popcorn butter flavoring, he was also exposed to innumerable other food flavors. It is difficult to attribute his illness to exposure to any particular flavor(s). Nevertheless, proper protective equipment, adequate ventilation, and early detection can prevent permanent damage in workers exposed to these flavorings.

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Please see Maureen R. Horton's editorial on page 466 of this issue.