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Occupational asthma due to inhalation of aerosolized lipophilic coating materials

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Abstract

We present a case of onset of severe asthma in a 59 year old patient who worked in an aerospace plant. He was noted to have wheezing on exam and obstruction on PFTs. Review of his occupational history revealed exposure to lipophilic industrial compounds. We outline the radiographic and histologic findings that were found in the patient, and discuss occupational asthma due to inhalation of lipophilic compounds.

Introduction

A 58 year-old non-smoker presented to the pulmonary clinic with complaints of cough and wheezing. Four years prior to presentation, he noted episodes of productive cough, wheezing and shortness of breath. He was seen at an outside hospital, and underwent CT imaging which showed diffuse bronchial thickening. A bronchoscopy at that time showed diffusely erythematous airways. Endobronchial biopsies were obtained and described as showing chronic inflammation suggesting a diagnosis of chronic aspiration. However, a video fluoroscopic swallow evaluation showed no evidence of aspiration. Over the next two years, his symptoms worsened, progressing to dyspnea with minimal exertion. His symptoms improved with oral steroids, but quickly returned upon discontinuation. In the year prior to presentation at our clinic, he had become steroid-dependent.

He had no previous history of lung disease and had no pets or inhalational exposures at home. He worked in an aerospace plant for over thirty years, assembling cardboard boxes in a poorly ventilated room. His episodes of shortness of breath and dyspnea improved when he was away from work, and remained stable when he returned to work while still on oral steroids, but quickly worsened once the steroids were tapered.

On examination, he was alert but dyspneic with minimal exertion. His vital signs were notable for a heart rate of 78 beats per minute, BP of 161/88 mmHg, temperature of 37° C and oxygen saturation of 97% on room air. Peak Flow measurement was 450 L/min. His

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lung exam was notable for diffuse polyphonic wheezes. The remainder of his examination was normal.

Results

His initial labs were notable for a normal hemoglobin, white blood cell count (9100 mm^{-3}) and differential without peripheral eosinophilia (4%). His metabolic panel was unremarkable. Aspergillus specific antibodies and sputum cultures were negative. A repeat bronchoscopy with lavage was performed. BAL fluid analysis was notable for eosinophilia (47%). A repeat CT again demonstrated diffuse airway thickening (Figure 1A).

We obtained the endobronchial biopsy and cytopathology slides from his previous bronchoscopy for review. These biopsies showed bronchial walls with thickened basement membranes (Figure 2C) as well as mucostasis and alveolated lung tissue with lipid droplets along alveolar walls and within alveoli (Figure 2A, B). The droplets varied somewhat in size. Nuclear compression by the droplets was apparent. Adjacent foamy macrophages were noted. Review of the Oil Red O stain performed on bronchoalveolar lavage specimen showed lipid laden macrophages (Figure 2D).

Given the histologic findings, we sought to determine the nature of his occupational lung disease. His exposures included saw dust from wood milled from trees in the southeastern United States, starch based adhesives and a resin emulsion. Industrial resin emulsions are compounds with lipophilic properties used in various industrial applications including as glue for cardboard boxes. On further questioning, he revealed that the boxes that he worked with were often freshly glued and that he would often note fine aerosolized particulate matter in his work area. Based on this history and his histologic findings, we concluded that his symptoms, radiologic and histologic findings were due to occupational asthma from inhalation of a lipophilic industrial compound used in the construction of cardboard boxes, and that the alveolar lipid droplets and Oil Red O stain positivity were due to deposition of the workplace antigen in the alveolar walls and uptake by alveolar macrophages, respectively.

He was tapered off his steroids, and removed from his work environment. PFTs were obtained after steroid discontinuation but before abstinence from work exposure as well as three months after cessation of work exposure, and significant improvements were noted (Table 1). His lung exam and chest radiography (Figure 1B) returned to normal, his peak flow measurement increased to 650 L/min and he felt significantly improved.

Discussion

We suspected that our patient's occupational asthma was due to inhalation of aerosolized industrial resin. Indeed, workplace resins originating from pine-resin containing glue (similar to our patient's exposure)(6, 7) as well as colophony(8), a pine resin mixture found in a variety of materials including string instrument rosin and soldering paste, have been reported to elicit asthmatic responses to challenge, but the radiographic, BAL and histologic changes associated with these exposures have, to our knowledge, not been fully characterized in cases of suspected exposure.

Our review of possible exposures at the workplace did not reveal any documented exposure to isocyanates, formaldehyde or irritant gases. Specifically, there was no documented exposure to cyanoacrylates (super glue). Because our patient was exposed to wood dust in addition to the other chemicals, it is possible that another wood dust component could be contributing to his occupational symptoms. It is also possible that a non-listed agent (i.e. < 1% concentration) could have contributed to our patient's symptoms. It is also possible that other additives in the glue (in addition to pine resin) could have contributed to his occupational asthma. Furthermore, though clinical and radiographic improvement with cessation of work is consistent with occupational asthma, we did not perform provocation testing to confirm the diagnosis due to the severity of symptoms when the patient was symptomatic. Although on-the-job peak flow measurements were not able to be performed, office peak flow measurements during a period when the patient presented to clinic from work as well as following a period away from work show significant improvement which, taken together with the radiographic improvements and the pathology found on initial biopsy, are suggestive of bronchial hyperresponsiveness due to a lipophilic workplace antigen. That said, it is possible that another exposure not found in our investigation could have contributed to his asthma. Though lipid-laden macrophages are typically seen in conditions of aspiration of lipid, such as aspiration or lipoid pneumonia, they can also be present in conditions where lipid is either introduced inhalationally (as in this case) or generated within the alveolar macrophages (i.e. due to induction of cellular phospholipid production by off-target effects of amphiphilic drugs(9)).

In summary, we present a case of a non-smoker who presented with wheezing, bronchial thickening on imaging, mild airways obstruction on PFT's, BAL eosinophilia and evidence of vacuolation and lipid-laden macrophages on pathology. History and investigation of his occupational history revealed exposure to aerosolized resins that likely precipitated airways inflammation and hyperreactivity.

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Figure 1. Representative slices of CT images performed **A)** before and **B)** after work absence. Areas of bronchial thickening (arrows) are seen at baseline.

Figure 2.

A) Portion of bronchial wall with thickened basement membrane and lipid vacuoles (black arrow) (inset shows mucostasis) (H&E, x100) **B)** alveolated lung tissue with focal mucostasis and lipid vacuoles (black arrows) along airspaces and within alveolar walls and adjacent foamy macrophages (H&E, x400), **C)** high power of thickened basement membrane (black arrow) (H&E, x400), **D)** intracytoplasmic lipid droplets on bronchoalveolar lavage fluid (oil red O stain, x600)

Table 1

Spirometry values before and after work absence

	Baseline (%Pred)	After work absence (% Pred)
FEV1	3.69 (88%)	4.69 (114%)
FVC	4.94 (94%)	5.81 (112%)
FEV1/FVC	67%	81%
DLCO	34.1 (108%)	38.1 (122%)