OCCUPATIONAL EOSINOPHILIC BRONCHITIS IN A FOUNDRY WORKER EXPOSED TO ISOCYANATE AND A BAKER EXPOSED TO FLOUR

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Abstract

Eosinophilic bronchitis without asthma may occur as a consequence of occupational exposures. We report the case of a foundry worker and a baker who developed symptoms respectively due to isocyanate and flour exposure. Cough was not associated with variable airflow obstruction nor with airway hyperresponsiveness and was responsive to inhaled corticosteroids. The eosinophilia detectable in their sputum was causally related to the occupational exposure in the workplace. The examination of induced sputum should be complementary to the objective monitoring of lung function for workers who complain asthma-like symptoms in an occupational setting.

**Key words:** eosinophilic bronchitis, isocyanate, flour
Eosinophilic bronchitis is a condition presenting with chronic cough and characterized by sputum eosinophilia (> 3% of non squamous epithelial cells), but unlike asthma there is no evidence of variable airflow obstruction and airways hyperresponsiveness (1,2). Exposure to certain occupational allergens or sensitizers, such as natural rubber latex (3), acrylates (4), mushroom spores (5) and an epoxy resin hardener (6), have been reported to cause eosinophilic bronchitis without asthma. We report the case of a foundry worker and a baker who developed chronic cough as a consequence of occupational exposure respectively to isocyanate and flour.

Case report 1

A 44 years old man working in a foundry for eight years. He used to smoke 10 cigarettes daily and had no history of atopy and asthma. He described his job as making cores and from the safety data sheet he gave us, we realized that he was exposed to MDI. He had never complained of respiratory symptoms since the last six months, when he started suffering a non productive chronic cough without wheezing or dyspnea. The cough worsened at work and improved on week-ends off work or holidays. Physical examination, chest radiography, peripheral blood count were normal. Skin and blood test for allergy, lung function and cellularity of sputum induced after the work shift are shown in table 1. Sputum induction was performed as described by Pin et al. (7) within 6 hours the last exposure at work and the sample examined as described by Pavord et al. (8). Due to his cough, the worker was relocated by the foundry occupational physician to a new job in the foundry stores where he was not exposed to isocyanate. His cough improved and after a month he was completely asymptomatic. Sputum induction was performed while asymptomatic and after specific bronchial challenge with isocyanate. Specific inhalation challenge with MDI was carried out in a 10 m³ dynamic chamber. A MDI atmosphere was generated in the chamber by passing dry air trough MDI contained in a flask and injected into the ultrafiltered air stream in the chamber through a Venturi effect. Isocyanate concentration was continuously monitored with an MDA device (Iso-Check). On the day of the challenge, he was exposed to MDI up to a maximum concentration of 20 ppm for 30
minutes. After the isocyanate challenge he started to have non productive persisting cough, but no changes in FEV1 occurred during the 24 hours observing period. After this period, sputum induction was performed before methacoline challenge. The methacoline challenge was normal at a maximal dose response curve (PD 20 > 3200 ug). Induced sputum percentages of non squamous epithelial cells are shown in table 1.

Case report 2

A 41 year old male baker, non smoker, exposed to flour for 10 years. In the last 2 years he had a non productive cronic cough without wheezing or dyspnea. The cough worsened at work and waned off during holidays. He was prescribed by his general practitioner antitussive medication with a poor response and was not receiving any medication for asthma. Physical examination and a chest radiography (prescribed by the general practitioner 2 months before) were normal. Peripheral blood count was normal. Skin and blood test for allergy, lung function and cellularity of sputum induced after the work shift are shown in table 2. Sputum induction as described by Pin et al. (7), was performed in the morning after his night shift and the sample was processed as described by Pavord et al. (8). As he had complained occasionally of headache and heartburn, we performed also a sinus radiography as well as a 24-hour gastric Ph monitoring, which were normal then excluding post nasal drip and atypical symptoms of gastroaesophageal reflux. He continued to work in the family bakery and so we decided to start treatment with inhaled fluticasone (500 ug daily). He had a markedly response to therapy and after a month of treatment he was asymptomatic. After a while, the patient still on treatment and followed up in our outpatient clinic, took a temporary leave from the bakery work. Therefore we decided to stop treatment, advising him to contact us if symptoms would have occurred and to come to our outpatient clinic before he would have started again to bake. During this period he remained asymptomatic. Sputum induction was performed while asymptomatic still exposed at work but on inhaled steroids, while asymptomatic not exposed at work and after flour specific bronchial challenge.
The flour bronchial challenge, accordingly to the European Respiratory Society guidelines (9), was performed in a worksite simulation with the patient’s own flour samples. The patient shook approximately 100g of flour in an open bag for up to 30 minutes with air concentration (measured with nephelometry, Grimm Technik) ranging between 90 and 130 mg/m³. During the challenge he had non productive cough persisting several hours later, but no changes in FEV1 were measured during the 24 hours observing period. After this period, sputum induction was performed before methacoline challenge. The methacoline challenge was normal at a maximal dose response curve (PD 20 > 3200 ug). Induced sputum percentages of non squamous epithelial cells are shown in table 2.

Discussion

The occupational exposure to isocyanate and flour was the cause of eosinophilic bronchitis respectively in this foundry worker and baker, who were characterized by work related changes in sputum eosinophils significant and reproducible. The causative agents of eosinophilic bronchitis in the workplace have rarely been ascertained. At present, eosinophil bronchitis can be causally related to occupational agents only in the patients described by us and in two other published case reports (3,4). Challenge exposure to latex gloves in a nurse (3) and acrylates in the other worker (4) resulted in a marked increase in sputum eosinophilia in the absence of airflow obstruction and bronchial hyperresponsiveness. In a cross-sectional health survey conducted in a mushroom farm (5), eosinophilic bronchitis was among the causes of chronic cough in such an environment, but a causal relationship between a specific occupational agent exposure and the sputum eosinophilia was not reproducibly demonstrated with specific occupational bronchial challenge.

It is not known why these patients do not have airway hyperresponsiveness despite the eosinophilic bronchial inflammation, nor whether they may progress to typical occupational asthma. There is a recent prospective follow up study of patients with eosinophilic bronchitis not related to occupational exposure, showing that the recurrence of disease, after an initial remission obtained with inhaled corticosteroids, was associated in some of them with the development of asthma or
chronic airflow obstruction (10). Several hypotheses have been formulated trying to explain the eosinophilic bronchitis inflammatory response, which does not cause bronchial hyperresponsiveness (11). The missing link between airway inflammation and airway hyperresponsiveness probably should be investigated on the intricate relationships among inflammatory cells (eosinophils, lymphocytes, neutrophils), resident cells (mast cells, epithelial cells, macrophages), inflammatory mediators, cytokines as well as the neuropeptides (substance P, neurokinin A, calcitonin gene related peptide, etc) secreted by the bronchial sensory nerves and bronchial smooth muscle cells. Although eosinophilic bronchitis does not meet the current definition of asthma, deserves to be regarded as an occupationally induced condition when work related changes in sputum eosinophils are significant and reproducible. The examination of induced sputum should be part of the diagnostic algorithm for workers who complain asthma-like symptoms in an occupational setting. It is a further diagnostic tool complementary to the objective monitoring of lung function during periods at work and away from work, as well as before and after specific bronchial challenges with occupational agents.
**Skin prick test**
Common aeroallergens (Alk)* negative
Total serum IgE normal (10 KU/L)
Specific serum IgE (ImmunoCAP Pharmacia)  
HDI negative (<0.35 KU/L)  
MDI negative (<0.35 KU/L)  
TDI negative (<0.35 KU/L)

FEV1 3.14 L (92% predicted value)
FVC 4.1 L (93% predicted value)
FEV1/FVC 75%
Peak expiratory flow rate # daily variability <20%
PD20 ## > 3200 ug

<table>
<thead>
<tr>
<th>Induced sputum</th>
<th>after the work shift</th>
<th>while asymptomatic (not exposed at work)</th>
<th>after isocyanate bronchial challenge</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cell count (x10⁶/mL)</td>
<td>2.7</td>
<td>1.3</td>
<td>3.8</td>
</tr>
<tr>
<td>% of non squamous epithelial cells</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neutrophils</td>
<td>38%</td>
<td>35%</td>
<td>25%</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>35%</td>
<td>0%</td>
<td>60%</td>
</tr>
<tr>
<td>Macrophages</td>
<td>27%</td>
<td>65%</td>
<td>15%</td>
</tr>
</tbody>
</table>

**Table 1.** Skin and blood test for allergy, lung function and induced sputum of foundry worker. *(House dust mites, pollens, cat and dog dander, molds as Alternaria alternata, Aspergillus fumigatus and Cladosporium herbarum). # Peak expiratory flows measured six times daily for 4 weeks without significant changes at work or away from work. ## Methacoline challenge performed soon after the work shift (approximately 3 hours after) at a maximal dose response curve.
Skin prick test
Common aeroallergens (Alk)* negative
Baking allergens (Alk)
Wheat flour positive **
Rye flour negative
Oat flour negative
Corn flour negative
Soy flour negative
Total IgE increased (190 KU/L)
Specific serum IgE (ImmunoCAP Pharmacia)
Wheat positive (16 KUA/L)
Alfa-amylase negative (<0.35 KUA/L)
FEV1 3.49 L (106% predicted value)
FVC 4.62 L (110% predicted value)
FEV1/FVC 78%
Peak expiratory flow rate # daily variability <20%
PD20 ## > 3200 ug

<table>
<thead>
<tr>
<th>Induced sputum</th>
<th>after the work shift</th>
<th>while asymptomatic (still exposed at work but on inhaled steroids)</th>
<th>while asymptomatic (not exposed at work)</th>
<th>after flour bronchial challenge</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cell count (x10⁶/mL)</td>
<td>1.0</td>
<td>0.4</td>
<td>0.6</td>
<td>2.3</td>
</tr>
<tr>
<td>% of non squamous epithelial cells</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neutrophils</td>
<td>8%</td>
<td>6%</td>
<td>5%</td>
<td>4%</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>40%</td>
<td>2%</td>
<td>0%</td>
<td>54%</td>
</tr>
<tr>
<td>Macrophages</td>
<td>52%</td>
<td>92%</td>
<td>95%</td>
<td>42%</td>
</tr>
</tbody>
</table>

Table 2. Skin and blood test for allergy, lung function and induced sputum of baker.
*(House dust mites, pollens, cat and dog dander, molds as Alternaria alternata, Aspergillus fumigatus and Cladosporium herbarum). **Skin prick test positivity a wheal diameter of 5 mm, more than one half of that of histamine control. # Peak expiratory flows measured six times daily for 4 weeks without significant changes at work or away from work. ## Methacoline challenge performed soon after the work shift (in the morning after the night shift) at a maximal dose response curve.
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4: 87-91

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