CASE REPORT

Occupational eosinophilic bronchitis in a foundry worker exposed to isocyanate and a baker exposed to flour

Fabio Di Stefano, Luca Di Giampaolo, Nicola Verna, Mario Di Gioacchino

Eosinophilic bronchitis without asthma may occur as a consequence of occupational exposure. The cases of a foundry worker and a baker who developed symptoms, respectively, due to exposure to isocyanate and flour, are reported. Cough was not associated with variable airflow obstruction or with airway hyper-responsiveness 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 used in addition to the objective monitoring of lung function for workers who have asthma-like symptoms in an occupational setting.

CASE REPORT 1

A 44-year-old male foundry worker, non-smoker, had been exposed to isocyanate for 10 years. In the previous 2 years he had developed a non-productive chronic cough without wheezing or dyspnoea. The cough worsened at work and waned during holidays. He was prescribed antitussive medication by his general practitioner who also prescribed inhaled fluticasone (500 µg daily) was started. He had a marked response to treatment and was asymptomatic after 1 month. While still receiving treatment and being followed up in our outpatient clinic, he took temporary leave from the bakery work so we discontinued his treatment and advised him to contact us if symptoms occurred and to come to our outpatient clinic before he started baking again. During this period he remained asymptomatic. Sputum induction was performed while asymptomatic, still exposed at work but taking inhaled steroids, and while asymptomatic, not exposed at work and after flour-specific bronchial challenge.

The flour bronchial challenge was performed, according to the European Respiratory Society guidelines in a worksite simulation with the patient’s own flour samples. The patient shook approximately 100 g of flour in an open bag for up to 30 min, with flour concentrations in air (measured by nephelometry, Grimm Technik GmbH & Co. KG, Ainring, Germany) ranging between 90 and 130 mg/m³. During the challenge he had a non-productive cough which persisted for several hours, but no changes in FEV₁ were measured during the 24 h observation period. After this period, sputum induction was performed before the methacholine challenge. The methacholine challenge was normal at a maximal dose-response curve (provocative dose inducing a 20% fall in FEV₁ >3200 µg). Table 1 shows the percentages of non-squamous epithelial cells in induced sputum.

CASE REPORT 2

A 41-year-old male baker, non-smoker, had been exposed to flour for 10 years. In the previous 2 years he had developed a non-productive chronic cough without wheezing or dyspnoea. The cough worsened at work and waned during holidays. He was prescribed antitussive medication by his general practitioner, with a poor response, and was not receiving any medication for asthma. Physical examination and a chest radiograph (prescribed by the general practitioner 2 months before) were normal. Peripheral blood count was normal. Table 2 shows the skin and blood tests for allergy, lung function, and asthma. We report the cases of a foundry worker and a baker who developed chronic cough as a consequence of occupational exposure to isocyanate and flour, respectively.

Abbreviations: FEV₁, forced expiratory volume in 1 s; MDI, methylene diphenyl isocyanate
induction was performed before methacholine challenge. The methacholine challenge was normal at a maximal dose–response curve (provocative dose inducing a 20% fall in FEV1 >3200 μg). Table 2 shows the percentages of non-squamous epithelial cells in induced sputum.

### DISCUSSION

Occupational exposure to isocyanate and flour was the cause of eosinophilic bronchitis in cases 1 and 2, respectively. The condition was characterised by work-related changes in sputum eosinophils that were significant and reproducible. Causative

### Table 1  Skin and blood tests for allergy, lung function and induced sputum of case 1

<table>
<thead>
<tr>
<th>Skin prick test</th>
<th>Common aeroallergens (Alk)*</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total serum IgE</td>
<td>Normal (&lt;10 kU/l)</td>
<td></td>
</tr>
<tr>
<td>Specific serum IgE</td>
<td>HDI, Negative (&lt;0.35 kU/l)</td>
<td></td>
</tr>
<tr>
<td>ImmunoCAP Pharmacia</td>
<td>TDI, Negative (&lt;0.35 kU/l)</td>
<td></td>
</tr>
<tr>
<td>FEV1</td>
<td>3.14 litres (92% predicted value)</td>
<td></td>
</tr>
<tr>
<td>FVC</td>
<td>4.1 litres (93% predicted value)</td>
<td></td>
</tr>
<tr>
<td>FEV1/FVC</td>
<td>75%</td>
<td></td>
</tr>
<tr>
<td>Peak expiratory flow rate$^\dagger$</td>
<td>Daily variability &lt;20%</td>
<td></td>
</tr>
<tr>
<td>PD20$^\ddagger$</td>
<td>&gt;3200 μg</td>
<td></td>
</tr>
</tbody>
</table>

<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 ($\times 10^6$/ml)</td>
<td>2.7</td>
<td>1.3</td>
<td>3.8</td>
</tr>
<tr>
<td>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>

FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity; HDI, hexamethylene diisocyanate; TDI, toluene diisocyanate.

*House dust mites, pollens, cat and dog dander, moulds such as Alternaria alternata, Aspergillus fumigatus and Cladosporium herbarum.

$^\dagger$Peak expiratory flows measured six times daily for 4 weeks without significant changes at work or away from work.

$^\ddagger$Methacholine challenge performed soon after the work shift (approximately 3 h after) at a maximal dose–response curve.

### Table 2  Skin and blood tests for allergy, lung function and induced sputum of case 2

<table>
<thead>
<tr>
<th>Skin prick test</th>
<th>Common aeroallergens (Alk)*</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baking allergens (Alk)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wheat flour</td>
<td>Positive $^\ddagger$</td>
<td></td>
</tr>
<tr>
<td>Rye flour</td>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>Oat flour</td>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>Corn flour</td>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>Soy flour</td>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>Total IgE</td>
<td>Increased (190 kU/l)</td>
<td></td>
</tr>
<tr>
<td>Specific serum IgE</td>
<td>(ImmunoCAP Pharmacia)</td>
<td></td>
</tr>
<tr>
<td>Wheat $\alpha$-Amylase</td>
<td>Positive (16 kU/l)</td>
<td></td>
</tr>
<tr>
<td>FEV1</td>
<td>3.49 litres (106% predicted value)</td>
<td></td>
</tr>
<tr>
<td>FVC</td>
<td>4.62 litres (110% predicted value)</td>
<td></td>
</tr>
<tr>
<td>FEV1/FVC</td>
<td>78%</td>
<td></td>
</tr>
<tr>
<td>Peak expiratory flow rate$^\dagger$</td>
<td>Daily variability &lt;20%</td>
<td></td>
</tr>
<tr>
<td>PD20$^\ddagger$</td>
<td>&gt;3200 μg</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Induced sputum</th>
<th>After the work shift</th>
<th>While asymptomatic (still exposed at work)</th>
<th>While asymptomatic (not exposed at work)</th>
<th>After flour bronchial challenge</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cell count ($\times 10^6$/ml)</td>
<td>1.0</td>
<td>0.4</td>
<td>0.6</td>
<td>2.3</td>
</tr>
<tr>
<td>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>

FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity; HDI, hexamethylene diisocyanate; PD20, provocative dose inducing a 20% fall in FEV1;

*House dust mites, pollens, cat and dog dander, moulds such as Alternaria alternata, Aspergillus fumigatus and Cladosporium herbarum.

$^\ddagger$Skin prick test positivity: a weal diameter of 5 mm, more than one half of that of the histamine control.

$^\ddagger$Peak expiratory flows measured six times daily for 4 weeks without significant changes at work or away from work.

$^\ddagger$Methacholine challenge performed soon after the work shift (in the morning after the night shift) at a maximal dose–response curve.
agents of eosinophilic bronchitis in the workplace have rarely
been established. To date, eosinophil bronchitis has been
causally related to occupational agents only in the two patients
described here and in two other published case reports.1,4
Challenge exposure to latex gloves in a nurse3 and acrylates
in a worker4 resulted in a marked increase in sputum
eosinophilia in the absence of airflow obstruction and bronchial
hyper-responsiveness. In a cross-sectional health survey con-
ducted on a mushroom farm,5 eosinophilic bronchitis was
among the causes of chronic cough but a causal relationship
between exposure to a specific occupational agent and sputum
eosinophilia was not reproducibly demonstrated with specific
occupational bronchial challenge.

It is not known why these patients do not have airway hyper-
responsiveness despite the eosinophilic bronchial inflamma-
tion, nor whether they will progress to typical occupational
asthma. A recent prospective follow-up study of patients with
eosinophilic bronchitis not related to occupational exposure
showed that recurrence of the disease, after an initial remission
obtained with inhaled corticosteroids, was associated in some
cases with the development of asthma or chronic airflow
obstruction.10 Several hypotheses have been proposed to explain
the eosinophilic bronchitis inflammatory response which does
not cause bronchial hyper-responsiveness.15 To examine the
missing link between airway inflammation and airway hyper-
responsiveness, the intricate relationships between inflamma-
tory cells (eosinophils, lymphocytes, neutrophils), resident cells
(mast cells, epithelial cells, macrophages), inflammatory
mediators, cytokines and neuropeptides (substance P, neuro-
kinin A, calcitonin gene-related peptide) secreted by the
bronchial sensory nerves and bronchial smooth muscle cells
need to be sustained. Although eosinophilic bronchitis does not
meet the current definition of asthma, it should 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 have asthma-like
symptoms in an occupational setting. It is a further diagnostic
tool which complements 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.

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