Cough-variant asthma: a diagnostic dilemma in the occupational setting

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Background
Cough-variant asthma (Corrao’s syndrome) is defined as the presence of chronic non-productive cough in patients with bronchial hyperresponsiveness (BHR) and response to bronchodilator therapy. This variant of asthma may present a diagnostic problem in occupational medicine.

Aims
To describe additional evaluation of cough-variant asthma in a cyanoacrylate-exposed worker in whom standard diagnostic testing was negative.

Methods
A female beautician was evaluated for suspected occupational allergic rhinitis and asthma. A specific inhalation challenge test (SICT) was performed with cyanoacrylate glues used for applying artificial eyelashes and nails. Spirometry and peak expiratory flow (PEF) measurements were recorded hourly for 24 h; methacholine challenge testing was performed and nasal lavage (NL) samples were analysed for eosinophilia.

Results
After SICT, the patient developed sneezing, nasal airflow obstruction and cough. Declines in forced expiratory volume in 1 s and PEF were not observed. Eosinophil proportions in NL fluid increased markedly at 4 and 24 h after SICT. A significant increase in BHR also occurred 24 h after SICT.

Conclusions
Clinical symptoms, post-challenge BHR and increased NL eosinophil counts confirmed a positive response to SICT and validated the diagnosis of cough-variant occupational asthma. SICT may be useful in cases where history and clinical data suggest cough-variant asthma and spirometric indices are negative.

Key words
Beautician; Corrao’s syndrome; cough-variant asthma; inhalation challenge test; occupational asthma; sensitization to cyanoacrylates.

Introduction

In 1979, Corrao et al. [1] described six patients suffering from chronic cough without wheezing who had baseline normal lung function but evidence of bronchial hyperresponsiveness (BHR). Cases with cough, BHR and a good clinical response to bronchodilator therapy were recognized as a cough variant of asthma, also known as Corrao’s syndrome. Since then, the natural history of this asthma variant has been more completely described [2]. Traditional pulmonary function testing in the workplace, including serial peak expiratory flow (PEF) and forced expiratory volume in 1 s (FEV₁) monitoring, are considered standard diagnostic tools for occupational asthma (OA) [3]. However, false-negative results may occur in cough-variant OA.

A number of reports describing occupational sensitization to cyanoacrylates [4–6], in conjunction with their increasingly common use in beauty salons, underscores the importance of attention to the health hazards of these materials and recognition of associated disorders. In this report, we describe a case of cough-variant asthma in a female beautician reporting work-related respiratory symptoms linked to cyanoacrylates in glues used for application of artificial eyelashes and nails.

Case report

A 27-year-old non-smoking woman who had been working for 3 years as a self-employed beautician developed sneezing, nasal congestion and a persistent dry cough. Review of material safety data sheets identified the following materials in glues used for cosmetic procedures: ethyl 2-cyanoacrylate, alkoxy-2-cyanoacrylate, polymethyl methacrylate, carbon black and 1,2-dihydroxybenzene. The patient completed a detailed questionnaire on
medical history and relationship between symptoms and work exposure and a physical examination, a chest radiograph and skin prick testing (SPTs) to common allergens with commercial available extracts (Allergopharma, Germany and Stallergenes, France) were performed. Spirometric testing and methacholine inhalation challenge tests were performed using MasterScope PC spirometer equipment (Jaeger, USA). The patient underwent a single-blind, placebo-controlled and specific inhalation challenge test (SICT) with cyanoacrylates. The control challenge involved nebulizing 2 ml of 0.9% saline. Two days later, the patient applied cyanoacrylate glues to a glass surface for 120 min in a 6 m³ chamber. Nasal lavage (NL) samples were collected before the SICTs as well as 4 and 24 h afterwards. During the 24 h post-challenge period, hourly spirometry, PEF and peak nasal inspiratory flow (PNIF) measurements were monitored with 8 h allotted for a night’s rest. BHR was assessed in 24th hour after the specific challenge.

Ethical approval for the study was granted by the Bioethical Committee at the Nofer Institute of Occupational Medicine in Lodz (decision number 20/2011) and informed consent was obtained from the patient prior to the procedures.

Questionnaire data indicated a strong positive association between the patient’s sneezing and cough and her

**Figure 1.** Hourly PEF (litre) and FEV₁ (litre) recording (upper panel) and peak nasal inspiratory flow (PNIF; l/min) (lower panel) before (0*) and after specific inhalation challenge test (SICT; with placebo and cyanoacrylate glues). *Measurement performed 15 min before SICT.

**Table 1.** Cytological analysis of NL samples collected before SICT and 4 and 24 h after SICT with placebo and with cyanoacrylate glues

<table>
<thead>
<tr>
<th>Time point</th>
<th>% of cells in NL</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Epithelial cells</td>
</tr>
<tr>
<td>Before SICT</td>
<td>2</td>
</tr>
<tr>
<td>4 h after SICT with placebo</td>
<td>12</td>
</tr>
<tr>
<td>24 h after SICT with placebo</td>
<td>8</td>
</tr>
<tr>
<td>4 h after SICT with cyanoacrylates</td>
<td>33</td>
</tr>
<tr>
<td>24 h after SICT with cyanoacrylates</td>
<td>9</td>
</tr>
</tbody>
</table>
presence in the work environment. She was symptom-free on weekends and holidays. A physical examination and chest X-ray did not reveal any abnormalities. SPTs to common allergens were negative. The baseline spirometry values were within normal predicted limits. Baseline inhalant methacholine challenge test showed borderline non-specific BHR (with marked provocative methacholine concentration PC_{20} = 8 mg/ml).

Placebo inhalation challenge testing produced no clinical or cytological changes. Spirometric measurements, PEF and PNIF values (Figure 1) and eosinophil counts in NL samples showed no significant changes (Table 1). Methacholine-induced BHR after the placebo-inhalant test did not increase (PC_{20} = 9.2 mg/ml).

One hour after the SICT with cyanoacrylate glues, the patient reported sneezing and nasal obstruction. Two hours later, a non-productive cough was noted. A dual-phase nasal reaction with a 35% fall in PNIF 4h after challenge and a 60% drop at 10h was observed (Figure 1, lower panel). Neither FEV1 nor PEF fell >15% during the 24h post-challenge (Figure 1, upper panel). An airways allergic reaction was demonstrated by the significant increase of eosinophilic cell counts in NL samples at 4 and 24h after the SICT (Table 1). BHR significantly increased with a PC_{20} = 0.9 mg/ml. We concluded that the combination of nasal symptoms and dry cough with increased BHR after exposure to cyanoacrylates established a diagnosis of occupational allergic rhinitis and cough-variant asthma.

Discussion

The increase in cyanoacrylate use in cosmetic procedures has increased hazards to workers’ health in the beauty industry. A 3-fold increased risk of OA development among beauticians who work with cyanoacrylates has been reported [6]. OA as well as eosinophilic inflammation and marked reduction in pulmonary function have been observed after exposure to cyanoacrylate [4–6]. To our knowledge, the current report is the first of cough-variant OA arising from cyanoacrylate exposure.

The principal limitation of our study was lack of analysis of airborne vapour distribution in the subject’s breathing zone while working. Moreover, although we were not able to obtain a sample of sputum from the patient for analysis, based on the involvement of both the upper and lower respiratory tracts [7], we can indirectly conclude on the basis of the NL sample analysis that the same inflammatory process is occurring in both.

Although the patient’s dry cough was related to the work environment, the presence of an occupational airways allergy was not irrefutable. Questionnaire data are considered as sensitive but not highly specific tools for detecting OA [8]. PEF shows reproducibility and sensitivity similar to well standardized FEV1, but is more dependent on subject effort [9]. Pulmonary function tests performed at the workplace may not be a sufficient diagnostic tool in occupational Corrao’s syndrome [3] because they may result in false-negative findings. A significant increase in post-SICT BHR provides evidence of positive clinical asthmatic response when changes in FEV1 are indeterminate [10].

In conclusion, inhalation challenge testing performed under controlled conditions is the most useful diagnostic test in the assessment of potential occupational cough-variant asthma. SICT may be advisable in cases where history and other clinical data indicate a likely relationship between cough and other respiratory symptoms and work exposures, when pulmonary function tests are negative.

Key points

- Widespread use of cyanoacrylates in cosmetic procedures has resulted in increased workplace health hazards among beauty industry workers.
- Specific inhalation challenge testing may be the only reliable method of diagnosing occupational cough-variant asthma.

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Conflicts of interest

None declared.

References

