Case Report

A Case Report of Occupational Asthma due to Gluteraldehyde Exposure

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Abstract

Introduction: We report the first case of occupational asthma due to gluteraldehyde exposure in Singapore and also describe the use of a specific inhalational challenge (SIC) test in confirming the diagnosis. Clinical Picture: A 32-year-old laboratory technician presented with adult-onset asthma 2 years after daily exposure to gluteraldehyde which was used to sterilise the mouthpieces used for lung function testing. SIC testing showed a 25% drop in FEV_1 after exposure to gluteraldehyde but not after exposure to a control, thus confirming the diagnosis. Treatment: Alternative arrangements were made for sterilisation of the mouthpieces so that gluteraldehyde could be removed from the workplace. There was a marked improvement in her asthmatic control thereafter. Conclusions: This case illustrates the use of a SIC test in the diagnosis of occupational asthma. Gluteraldehyde is a known cause of occupational asthma and should be kept in mind when evaluating asthmatic patients in at-risk occupations. Effective ventilation and proper storage should be ensured to minimise exposure to gluteraldehyde where its use is necessary.

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Introduction

Worldwide, asthma is estimated to affect between 5% and 10% of the population and, among adults, 4% to 9% of these cases have been attributed to an occupational cause.[1,2] Yet, only 3 cases were reported and confirmed in Singapore in the year 2000 – an incidence of only 0.14/100,000 workers.[3,4] Part of this discrepancy is thought to be due to under-reporting; there is also a lack of awareness of this illness among healthcare professionals in Singapore, and hence failure to identify those suffering from the condition. We report here the first known case of gluteraldehyde-induced asthma in Singapore, and also describe the use of a specific inhalational challenge (SIC) in clinching the diagnosis.

Case Report

A 32-year-old Indian lady was referred to our occupational lung clinic for assessment of asthma. She had first noted episodic chest tightness associated with wheezing in 1999. The attacks initially occurred about twice a year, but increased in frequency over the next 2 years. By January 2001, she was experiencing attacks every other day. Her symptoms were relieved intermittently by short courses of prednisolone and she had courses of various inhaled corticosteroids. At the time of referral, she was taking inhaled beclomethasone (QVAR™) 400 mcg twice a day from her family doctor. Her symptoms were noted to improve considerably during 1 week of annual leave in August 2001, and also when she went on 2 months of maternity leave from November to December 2001.

She had been working as a technician in a pulmonary physiology laboratory since December 1997. Her daily duties included administration of methacholine for the methacholine bronchoprovocation challenge tests, and also included sterilisation of mouthpieces for spirometry. This was done by soaking the mouthpieces in 2.5% gluteraldehyde solution in a container in an enclosed room. The mouth pieces were soaked in a tray containing the gluteraldehyde solution for about 10 minutes per batch, with a total of at least 10 batches per day. She was

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exposed to the gluteraldehyde vapour whenever she opened the cover of the tray to place the mouthpieces in or to take them out.

Her background history was notable for concurrent allergic rhinitis which was treated with intranasal fluticasone. Her mother was also a known asthmatic. She had no past history of childhood asthma.

Physical examination was essentially unremarkable. There were no nasal polyps, and her lungs were clear with no crepitations or rhonchi. Her absolute eosinophil count was mildly elevated at 650/mm^3. Her chest radiograph was clear. Her lung function test results (on 12/6/2000) were as follows: Forced expiratory volume in one second (FEV_1) 2.44 L (92.7% predicted); forced vital capacity (FVC), 2.98 L (90.1% predicted); FEV_1/FVC ratio, 81.8. Methacholine bronchoprovocation challenge test at the same sitting was positive with a maximum 26% fall in FEV_1 from baseline.

Methods

The patient was asked to record her peak expiratory flow rate (using a Mini-Wright's peak flow meter) every 3 hourly during waking hours, each time charting the best of 3 efforts. She was also instructed to continue with her beclomethasone. Her daily maximum and minimum peak flow rates are charted in Figure 1.

SIC Test

The patient was instructed to stop the beclomethasone for 1 week while she was on medical leave, after which she was admitted for the SIC test. All bronchodilators were also stopped for 12 hours prior to the test.

On the first day of the test, she was exposed to methylated spirit which was transferred between 2 containers for 15 minutes in her room. Serial measurements of FEV_1 and peak expiratory flow rate (PEFR) were taken at baseline, at 15-minute intervals for 2 hours and then ½ hour intervals for the next 10 hours (i.e., for 12 hours post exposure). FEV_1 was measured at the bedside (autospiroAS600™, Minato, Japan). The methylated spirit functioned as a control.

The next day she was exposed to gluteraldehyde solution which was transferred between 2 containers for 15 minutes in a similar fashion to the methylated spirit. Serial measurements of PEFR and FEV_1 were again taken as described above.

Results

The patient's PEFR charting is shown in Figure 1. PEFR variability was noted to decrease significantly when she went on medical leave.

Figure 2 shows the changes in FEV_1 during the SIC. There was a sustained 25% drop in her FEV_1 from a baseline value of 2.25 L to a nadir of 1.8 L. This drop started 2.5 hours after the gluteraldehyde challenge, lasted about 4 hours, and was associated with wheezing. No such drop was noted with methylated spirit, where the lowest value reached was 2.09 L (a 7% drop from baseline).

Follow-up

After the diagnosis of gluteraldehyde-induced asthma was made, the patient was put on extended medical leave. The offending solution was removed from the workplace and henceforth the mouthpieces were sent to the central sterilising services department for gas sterilisation. She returned to the workplace shortly after this and has been able to carry out her duties with no problems; her asthmatic symptoms are now much improved although she continues to require a low dose of maintenance inhaled corticosteroid.

Discussion

Occupational asthma has been defined as a disease characterised by variable airflow limitation and/or bronchial hyper responsiveness due to causes and conditions attributable to a particular working environment and not to

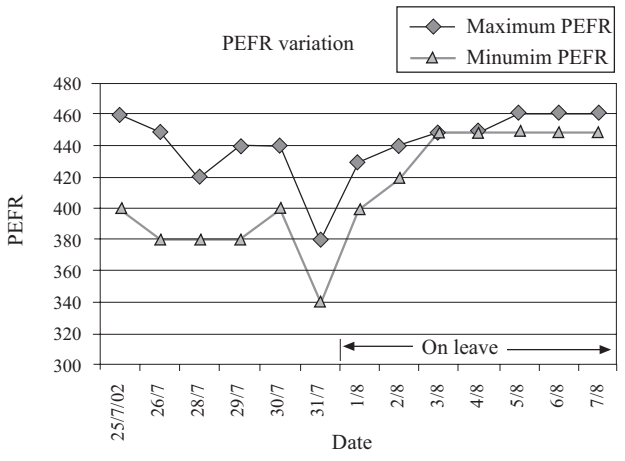

Fig. 1. PEFR monitoring.

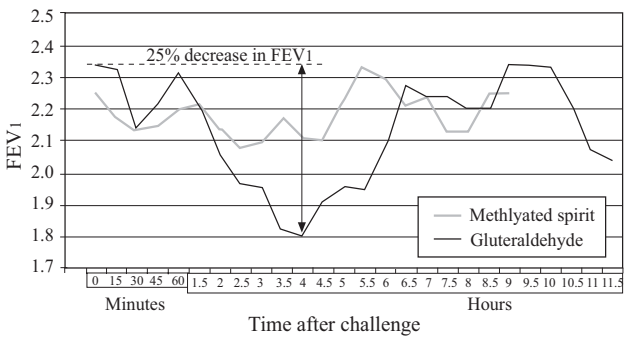

Fig. 2. Specific inhalational challenge.

stimuli encountered outside the workplace.[5] A diagnosis requires several conditions to be met:

1. a firm diagnosis of asthma
2. onset after entry into the workplace
3. association between symptoms of asthma and work
4. one or more of the following: work-related changes in FEV_1, peak flow or bronchial hyper reactivity or a positive SIC.[5]

This case illustrates the diagnostic evaluation of occupational asthma. The possibility of this diagnosis must first be kept in mind by the attending physician and a directed history taken. The diagnosis here was suggested by the classical history given by the patient: onset of symptoms after a lag time of exposure at the workplace (in this case, 14 months) and symptoms which improved noticeably when the patient was away from the workplace while on leave. A visit to her workplace revealed that she was exposed to gluteraldehyde. The diagnosis was further suggested by serial peak flow measurements which showed a marked reduction in her PEFR variability when she was outside the workplace.

The diagnosis in our patient was confirmed by a SIC. This is regarded as the gold standard for diagnosis of occupational asthma, but has seldom been performed outside a few specialised centres in Canada and Europe.[6]

The patient was taken off her usual inhaled corticosteroids for 1 week prior to the challenge. This is in line with the usual recommendations as inhaled steroids have been shown to attenuate both the early and late phase asthmatic reactions.[7] However, it must be borne in mind that the patient's asthma must be reasonably well controlled for a SIC to be carried out safely, and in cases where the asthma is moderate or severe, it may not be possible to stop the inhaled corticosteroids. Other medications such as long-acting β2-agonists should also be stopped at least 24 h prior to the test.

The initial step in the SIC is to expose the patient to a control, in this case to methylated spirit. This is necessary for 2 reasons: firstly, to ensure that the fluctuations in FEV_1 are <10%, indicating that the asthma is under reasonable control and that it is safe to proceed with the challenge test; and secondly, to verify that the reaction is not due to a non-specific irritant effect. The control substance is chosen according to the nature of the agent suspected of causing occupational asthma – for instance, lactose powder for SIC with agent in powder form (flour, drugs etc), diluent for SIC with isocyanates.[8] Methylated spirit was chosen in this case as it is a colourless solution which looks similar to gluteraldehyde, and could be administered in the same way. Also, it is known to be a non-specific airway irritant.

The patient is then exposed to the suspected agent. We effected this by pouring the gluteraldehyde into a container in an enclosed room with the patient nearby; this simulated a level of exposure similar to that which she would have experienced in the workplace. We were unable to measure the exact ambient levels of gluteraldehyde either at the patient's workplace or during the challenge. However, the mode of exposure was similar to that at her workplace. Bronchoprovocation here was in any case due to the patient's having been sensitised to gluteraldehyde and not to a dose-specific irritant.

There is no established consensus as to the exact mode of administration, dose or length of exposure a patient needs to be exposed to for each SIC. This will vary according to the nature of the suspected aetiological agent and also according to the available facilities at the centre administering the SIC. The primary concern in every case would be to subject the patient to the minimum safe dose needed to stimulate bronchoprovocation without unnecessarily exposing others to the agent or stimulating an unnecessarily severe bronchoprovocation.[8]

SICs are considered positive when there is a sustained fall in FEV_1 of more than 20% from prechallenge value in the absence of significant (>10%) changes after exposure to a control product. The pattern of reaction may be approximately divided into 2 broad patterns: immediate reactions with onset 10 to 20 minutes after exposure and lasting 1 to 2 hours, and late reactions, which occur subsequent to this. Late reactions develop more slowly and progressively either 1 to 2 hours ("early late") or 4 to 8 hours (late) after exposure.[9] FEV_1 needs to be monitored till at least 8 hours post-exposure in order not to miss a late asthmatic reaction. In our patient's case, the maximal fall occurred at about 3 hours post-exposure, consistent with an "early-late" reaction.

False positive results (i.e., non-specific broncho-constriction due to an irritant effect) can occur and can be excluded by a control test. Only patients whose asthma is well controlled and in a stable state should be subjected to a SIC. False negative tests can also occur where the delivery of the inhalational challenge is faulty or where the dose of substance delivered is inadequate.

In clinical practice, it is not always easy to administer a SIC – there may be technical difficulties in obtaining and administering the suspected offending agent. The test is extensive and lengthy and generally needs to be done as an inpatient with close monitoring.

Indications for specific inhalational testing include the following:

1. A diagnosis of occupational asthma has to be made without delay.
2. Exposure to the workplace has been reported to induce severe asthmatic reactions.

3. The casual agent must be precisely identified in order to implement appropriate prevention strategies.
4. The suspected agent has not been reported to cause occupational asthma. If the patients has left the workplace and cannot or will not return to work on a trial basis, then specific inhalational testing may be the only means of proving the diagnosis.[5,8]

Occupational asthma is the most common occupational lung disease in Singapore; Kor et al[4] reported that the most common reported cause was isocyanates, followed by solder flux and welding fumes. The cases were diagnosed from history taking, factory visits, PEFR monitoring, positive non-specific bronchoprovocation testing and/or SIC.

Occupational asthma due to gluteraldehyde, although not common, is a well-established cause of occupational asthma. Gluteraldehyde is an aliphatic dialdehyde with a slightly acidic and powerful odour. It is commonly used for gas sterilisation of instruments, e.g. endoscopes, and is also used in X-ray film processing, as a fixative in electron microscopy and as a leather-tanning agent. Gluteraldehyde-induced asthma has previously been reported in endoscopy nurses, X-ray department staff and also in respiratory technologists.[10,11] In previous reports, the mean onset of asthma occurred after 4 years of exposure to gluteraldehyde[11] (our patient had 14 months exposure prior to her first presentation). In cases where SIC testing was used for diagnosis, the patients displayed late asthmatic reactions similar to that of our patient.[11] The type of allergic mechanism responsible for gluteraldehyde-induced asthma is not known; it is a low-molecular weight compound and specific IgE antibodies to it have not been demonstrated in affected subjects.

Many patients with occupational asthma continue to be symptomatic even after removal from exposure; early removal is associated with better prognosis. Continued exposure may lead to worsening symptoms and deterioration of lung function and has even been reported to cause death.[5] Studies have shown that patients who can be removed from exposure do have improved control of their asthma, but had significant loss of income. A balance must be stuck, therefore, between protection of the patient's health and causing financial hardship. In our patient's case, an alternative arrangement could fortunately be made, which allowed removal of the offending agent from the workplace and allowed the patient to continue in her current occupation.

Conclusion

Our case illustrates the principles of diagnosis and management of occupational asthma. The use of a SIC test to diagnose occupational asthma is described as well. Gluteraldehyde is a well-established cause of occupational asthma and should be kept in mind when evaluating asthmatic patients in appropriate occupations. Its use should be minimised and replaced by steam sterilisation where possible. In cases such as sterilisation of endoscopy instruments where there is no practical alternative, exposure should be minimised by providing effective ventilation, enclosed washing machines and the use of a ventilated cabinet for gluteraldehyde storage.[12]

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