



Case report

Indirect formaldehyde exposure and the appearance of respiratory symptoms

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ABSTRACT

This 70 year-old female patient, previously described as having undergone a toxicant-associated steatohepatitis during her childhood, now represents the core of a follow-up case report. After an apparent complete recovery at 13 years of age, she developed a paroxysmal dry cough, predominantly nocturnal, starting at age 24, during her first pregnancy. A seasonal recurrence was observed and bouts of cough have been resurgent at every subsequent winter. Several diagnoses, including asthma, gastro-esophageal reflux, and chronic pertussis have been suggested, as well as a sequel of her severe scoliosis, but the consequent treatments were of no avail. Moreover, repeated lung function tests have remained normal ever since. We presently propose a possible explanation for the puzzle.

1. Introduction

The patient is portrayed as having suffered on two occasions, as a child, from a toxicant-associated steatohepatitis, benzene-related [1]. After a clinically silent period, except for symptoms of the scoliosis, she reappears, at the age of 24, during her first pregnancy, and for the main part of every subsequent winter seasons, with paroxysmal cough. The cough is dry and more prominent at night [2–5]. The proposed diagnoses could not be substantiated, and the therapeutic modalities offered were not effective.

2. Case presentation

The childhood medical history is reported in the prior case report [1]. Of note, the child presented at age 6 and again at age 13 with a most probable benzene-associated steatohepatitis, consequent to an indirect mild chronic- and a severe acute direct exposure to benzene, with or without the addition of volatile organic compounds (VOC). Following glucocorticoid therapy, the child recovered [1].

In the present report, we meet the patient again, now aged 24 years, and pregnant for the first time. She discloses, at this point, a new complaint, a paroxysmal, nocturnal, dry cough. The symptom persisted for the whole of the winter, and was unresponsive to the various modes

of therapy. The various treatments were meant to respond to the different causes suggested by the numerous professionals that she consulted. Included, are asthma and variants, psychogenic cough, gastro-esophageal reflux, scoliosis-related cough, and also chronic pertussis.

None of the exams performed to confirm any of the diagnoses, was supportive. Thus, a CT scan of the chest, among a few, showed no pathological findings. Two separated lung function tests were within normal limits (Table 1). Several therapeutic trials for asthma were inconclusive. A PCR, performed for *Bordetella pertussis*, was negative. Moreover, the treatments advocated accordingly appeared irrelevant.

Among the many winters highlighted by the bouts of coughing, the patient did display evidence of infrequent to rare fits of laryngospasm, often highly stressful, but which resolved spontaneously within 1–3 minutes [6].

The patient was thoroughly examined on four instances by specialists in Allergy who, regularly, affirmed that hers, was not an allergic disorder; that, even though she described in full details, specific allergies, like to Diazepam® or Halothane®, as well as diffuse drug sensitivities, these were not accounted for.

Because of a mild to moderate degree of snoring, without apparent apnea, the patient was submitted to a study at a sleep laboratory. The results were interpreted as a moderate degree of obstructive sleep apnea syndrome, restricted to the supine position. However, for an obscure

Abbreviations: VOC, volatile organic compounds; PCR, polymerase chain reaction; HLA, human leukocyte antigen.

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Table 1
Lung functions tests carried out on two widely separate days.

Date, hour	Saturation	FVC% PRD	FEV1% PRD	%FEV1/ FVC	FEF 25–75% PRD
10/01/19 11:12	98	79	83	82	92
29/11/18 14:13	97	85	81	75	69

reason, neither the patient nor her physicians have addressed these results to any degree.

2.1. A role for the patient's husband

In the first case report, an idiosyncratic effect regarding the patient HLA and the level of a given cytochrome P450 isoenzyme, may have determined the degree of the benzene intoxication. Thus, it is not excluded that the patient displayed an exquisite sensitivity to several chemicals [1].

The subject was married to a medical student who soon became a pathologist. He pursued his career for nearly 40 years, during which he was exposed to non-toxic levels of formalin, as well as of VOCs [7].

Is it likely, that the patient's husband managed, on a daily basis, to carry back home, a significant amount of formalin, and/or of the VOC? These chemicals could have been transported on his hair, skin and clothes and they might have found their way to the patient's airways, subsequently evoking the respiratory symptoms (recurrent indirect exposure to chemicals).

A scenario might be reproduced with certain variations. Once conveyed on the patient's father clothes, hair and skin, the chemical was identified as benzene vapors [1]. Several years later, formalin and VOCs are being transferred via similar surface sites, except, this time, by the patient's husband.

The subject's hypersensitivity may originate in an idiosyncrasy. It is also expressed by a known sensitivity to Diazepam® and Halothane®, but is also affected in an indeterminate manner, by several other medications and chemicals. On the other hand, sensitivity to chemicals, as it relates to patients with prior hepatic damage and who suffer from back pain, should not be totally excluded.

If, indeed, an association obtains, between the indirect exposure to formaldehyde/VOC and the paroxysmal cough, a lapse of several years, without further exposure, might cause a significant reduction in the cough, or even its arrest.

3. Conclusions

The two portions of our saga show parallel features. It seems that, at widely distinct epochs of her life, the subject performed precisely the same choreography, except for exchanging partners, on the one hand and replacing the accessories, on the other hand. In both situations, she was hurt, and we cannot clarify, whether the sensitivity which was

displayed in each episode, was causative or circumstantial.

3.1. Limitations

Presently, the case report seems highly conjectural. However, the patient's husband has been retired for the last four years and has given up, almost entirely any contact with the Pathology Department. Even if, so far, no significant changes have occurred in the patient's symptoms, and damage to the lungs has not developed (based on CT scan and two separate lung function tests), a notable resolution of the cough may be expected within a few additional years. Such an evolution may very well confirm a cause-and-effect association between formalin vapor and the recurrent cough.

Patient consent

Informed consent was obtained from the patient.

Authors' contribution and authorship

DB – Conceptualization; formal analysis; methodology; resources; supervision; writing – draft; review and editing.

Y-BB – Data curation; investigation; project administration; software; validation; visualization; writing - review and editing.

Declaration of competing interest

None.

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The authors declare 'No conflict of evidence exists'.

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