

Correspondence

High Exposure to Passive Tobacco Smoking and the Development of Asthma in an Adult Patient Who Had Never Smoked

To the Editor:

A 50-year-old white woman, a professor of medicine, who had never smoked, was referred to our outpatient clinic with bronchial asthma symptoms. Her illness began in October 2007 with a bad, dry, nonproductive cough occurring during the day and night with wheezing and shortness of breath. Her cough increased with exercise and when she was exposed to asthma triggers and allergy-causing substances, like dust or strong fragrances, or when she was in cold air. Her cough was so severe that she could not sleep. The above symptoms systematically increased over the subsequent 2 years. Until she was referred to our clinic, she was not treated with any medications. She had no family history of asthma, and before that time (October 2007), she had no symptoms of rhinitis or asthma. The patient was never diagnosed with any other chronic illness.

She described that her symptoms strictly followed her 5-week stay in prison (she was under arrest) when she was assigned to a smoking cell (size about 250 sq ft) with five other women actively smoking day and night in the cell. At the time of the visit (January 2010), chest examination revealed wheezes. A spirometry test revealed a 4% increase in Tiffeneau ratio and 16% increase in maximal expiratory flow at 25% of forced vital capacity (MEF 25) after inhalation of 400 µg of salbutamol (obstruction in small airways); FE_{NO} 91.8 ppb. Body plethysmography revealed increases in the values of residual volume (RV), intrathoracic gas volume (ITGV), RV% TLC and ITGV% TLC, and decreases in the values of VC and TLC. The skin prick tests with a set of allergens were positive to seasonal allergens: grass pollen (*Dactylis glomerata* and *Lolium perenne*) and trees (birch and alder). Other mechanisms of bronchoconstriction were excluded (including infection). X-rays were negative. She was diagnosed with atopic asthma and was treated with high doses of budesonide, salbutamol, and cetirizine. This treatment was effective.

Cigarette smoke is a highly complex mixture, and many of its components are known carcinogens and mutagens. Cigarette smoke has been linked to a variety of chronic lung disorders and is a major cause of lung cancer. Acute exposure to cigarette smoke is related to airway and systemic inflammation and oxidative stress. Although symptoms improve after the cessation of smoking, the oxidant and protease burden in the airways continues for months (1).

Asthma, on the other hand, is caused by the interaction of genetic susceptibility and exposure to various environmental factors. Longitudinal studies have described smoking as a risk factor for developing asthma (2–5). The case we present suggests that asthma and atopy can be developed by high exposure to environmental tobacco smoke (under conditions that usually do not occur in real life) even in later stages of life. The results from the Meyers and colleagues (6) study revealed that the influence of susceptibility genes for asthma might not be apparent unless there is the appropriate exposure to environmental stimuli, such as passive exposure to cigarette smoke. In addition, evidence for a significant gene–environment (passive tobacco smoke exposure) interaction has been observed in a genetic linkage study by Colilla and colleagues (7). Tobacco seems to influence innate immunity predisposing to

Th2-associated respiratory diseases and increasing the risk for IgE-mediated sensitization. Some epidemiological and laboratory studies categorize smoke as a risk factor for the development of asthma and suggest that exposure to cigarette smoke and other inhalation insults shifts the Th1:Th2 balance toward a Th2 response (8–12). Also endotoxin, one of the most potent inflammatory agents, is offered in huge amounts (more than hundred times compared with nonsmoking environment) by exposure to tobacco smoke (13). These high levels of endotoxin could contribute to an elevated IgE and the subsequent development of atopic diseases and asthma. The present case may explain new asthma diagnoses in adult patients who never smoked but experienced high exposure to passive tobacco smoke. The effects of such exposure are not surprising. On the other hand, this case is casuistic because of the environmental setting, which has features of a medical experiment. Such conditions have never been and will not be designed due to ethical reasons. Tobacco smoking provokes a strong immunological imbalance to those exposed, and the innate immunity is impaired by tobacco exposure. As a consequence, typical allergic diseases such as atopy and asthma could initiate or aggravate preexisting conditions or both. Therefore, this report should be useful for the identification of asthma susceptibility genes. Periodic examinations should be performed in patients exposed to secondary smoke to monitor lung damage with special attention to early symptoms of lung cancer.

Author Disclosure: None of the authors has a financial relationship with a commercial entity that has an interest in the subject of this manuscript.

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Compromised T-Cell Immunity and Virus-like Structure in a Patient with Pulmonary Hypertension

To the Editor:

HIV infection is widely recognized as one of the causes for the pathogenesis of pulmonary arterial hypertension (PAH) (1, 2). In a previous study of HIV-related pulmonary hypertension, the authors pointed out that the pathogenesis of HIV-PAH is believed to be associated with viral proteins such as Nef, Tat, and gp120 (3). HIV-1 Nef protein, perhaps in conjunction with persistent immune dysregulation, contributes to the development of pulmonary vasculature remodeling by inducing secretion of inflammatory cytokines (4). However, whether other types of viruses, especially those that cannot be routinely identified in clinical practice, can also play an important role in the pathogenesis of PAH has not been investigated until now. At the same time, there has been little direct evidence of the pathogens' action during the pathogenic process of PAH. Therefore, we report a case of a previously healthy 11-year-old girl in whom PAH was diagnosed 3 months after an upper respiratory tract infection caused by an undetermined virus. Thirteen months after diagnosis of PAH, the girl died of right heart failure. Blood tests revealed the increase of D-dimer, which indicated the possibility of embolism in this patient. Immunophenotyping showed that function of T-cell immunity was compromised with the decreased cell count of CD3 (50.7% decrease, normal value 60–85%) and CD8 (17.8% decrease, normal value 18.5–42.1%) but with a normal cell count of CD4 (29.0%, normal value 24.5–48.8%). In addition, we found the same phenomenon in the other 6 of 8 (75%) patients with chronic thromboembolic pulmonary hypertension when performing T-cell immunity testing in 30 patients with pulmonary embolism with or without PAH. Meanwhile, enveloped mulberry-like structures were detected in the cytoplasm of T lymphocytes, accompanied by budding and proliferation under electron microscopy observation. The size of these structures is similar to virus. The dynamic process of adhering to and departing from T lymphocytes for these structures was in line with the process of virus pullulation and release to and from T cells (Figure 1). Thus, we supposed that the compromised T cell-mediated immunity function is associated with the infection of these viruslike structures with the exclusion of other causes clinically in this patient.

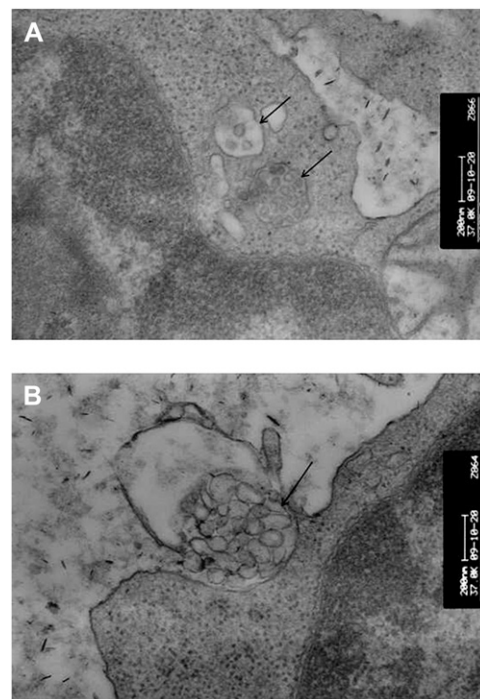


Figure 1. (A) Round structures with intact capsules and different densities of granules in the cytoplasm of T cells (arrow). (B) Mulberry-like pathogenic microorganisms penetrated through the T-cell membrane and pullulated (arrow).

We previously showed that T-cell immunity function-associated genes were down-regulated in patients with pulmonary embolism by means of gene profiling analyses (5). Therefore, we hypothesize that not only HIV infection but also other types of viral infections might lead to pulmonary hypertension through deteriorating host T-cell immunity function and ensuing events. This special case offers a clinical clue for studies of the etiology of pulmonary hypertension and needs to be further verified.

Author Disclosure: None of the authors has a financial relationship with a commercial entity that has an interest in the subject of this manuscript.

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