Massive Fatal Hemoptysis Secondary to Invasive Aspergillosis in a Patient with COPD

To the Editor:

Invasive aspergillosis is recognized as a complication in patients with altered host defenses. This is commonly seen in patients with neoplastic disease, especially leukemia and lymphoma. The patients are immunocompromised both by the disease and by the treatment. 1-3

Hemoptysis has been frequent in the aspergilloma patient, but rarely has it been fatal. 4-6 Hemoptysis secondary to invasive aspergillosis or aspergillomas in patients with neoplastic disease is rare. 7-8 Borkin et al., however, have recently described massive, fatal hemoptysis in two patients with underlying neoplastic disease. We report massive, fatal hemoptysis in a patient with chronic obstructive pulmonary disease (COPD) to broaden the perspective of fatal hemoptysis secondary to invasive aspergillosis.

A 68-year-old black man with end-stage COPD was admitted with shortness of breath, fever, and general malaise. For the three days prior to admission, he had had fever to 39°C and cough productive of thick yellow sputum. There was no history of hemoptysis. On admission he was described as ill-appearing and in respiratory distress. The chest examination revealed wheezes in all lung fields and coarse rhonchi. The heart showed irregularly irregular rhythm, and a loud pulmonic component of the second heart sound. The abdomen was distended and tender and bowel sounds were present. The chest roentgenogram showed a small density in the left upper lobe and an infiltrate in the right lower lobe. The arterial blood gas analysis on room air showed PaO2 53, P(A-a)O2 45, Pco2 40, and pH 7.45. Further laboratory studies showed white blood cell count of 8400/µm ³ with a differential of 30 percent neutrophils, 49 percent bands, 1 percent eosinophils, 11 percent lymphocytes, 8 percent monocytes, and 1 percent metamyelocytes with a hemoglobin of 11.7 g/100 ml.

The patient was initially started on ampicillin, 1 g by intravenous infusion every four hours. He was also placed on intravenous aminophylline. Oral prednisone was continued at 25 mg per day as well as digoxin, 0.25 mg every day, and terbutaline, 2.5 mg three times per day.

Sputum culture was positive for Klebsiella pneumoniae and the patient was subsequently placed on tobramycin to which the organism was sensitive. Blood levels of tobramycin were routinely checked and found to be adequate.

By hospital day 34, the patient's chest roentgenogram showed right mid-lung and right lower lobe, as well as left lower lobe infiltrates. He continued to have a fever, and his sputum culture continued to grow Klebsiella pneumoniae and Serratia marcescens.

On hospital day 52, his temperature was normal, but his chest roentgenogram showed bilateral pleural effusions as well. On hospital day 55, the patient had mild hemoptysis. On day 56, the patient had fatal massive hemoptysis. Autopsy revealed invasive pulmonary aspergillosis with abscesses and infarcts (Aspergillus fumigatus was cultured from the lungs at autopsy) (Fig 1). In addition, the right lower lobe of the lung showed an 8 mm nodule of keratinizing, well differentiated, infiltrating squamous cell carcinoma.

Massive fatal hemoptysis due to invasive aspergillosis is rare. More importantly, in any compromised individual who has had bacterial pneumonia and who has received treatment without resolution on chest roentgenogram, an opportunistic infection must be suspected. 9 Any compromised patient, whether with neoplastic disease, immunocompromised, or as in the patient here described, end-stage COPD (on prednisone, localized malignancy found at autopsy) is a candidate for invasive aspergillosis. Thus, as pointed out by Borkin et al., massive fatal hemoptysis secondary to invasive aspergillosis is perhaps more common than realized. We would like to emphasize further that it may be found in a broader spectrum of disease states than previously reported, particularly in the host with altered immunity.

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REFERENCES

Endogenous Opiates, Pulmonary Edema, and Sleep Apnea Syndrome

To the Editor:

Chaudhary et al (Chest 1982; 82:122) reported pulmonary edema as a presenting feature of the sleep apnea syndrome. I would like to suggest that endogenous opiates might have a role in the patho-

FIGURE 1. Microscopic section of lung, hyphal forms and tissue invasion (methenamine-silver stain, original magnification × 250).
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 genesis of the pulmonary edema in this patient. Indeed, endorphins are released in stress situations and they can adversely affect physiologic systems, such as respiration and circulation. In the human fetus at term, plasma levels of beta-endorphins and beta-LPH are inversely correlated with arterial pH and Po2, suggesting that hypoxia and secondary acidosis may be important stimuli controlling the release of these peptides. Recently, Bar-Or et al. reported a dramatic clinical improvement after naloxone therapy in a patient with high-altitude pulmonary edema. The finding of a high plasma beta-endorphin concentration in this patient suggested that endorphins may play a role in this disorder. Development of pulmonary edema in animals by selective cerebral perfusion with the hypoxic blood as observed by Moot et al. might be explained in part by endorphinergic mechanisms. Interestingly, endogenous opioids might also play a role in the pathogenesis of apnea.1

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To the Editor:

The suggestion that endogenous opiates might play a major role in the pathogenesis of non-cardiac pulmonary edema occurring as a result of obstructive sleep apnea is an intriguing one. If severe hypoxemia is associated with the release of endogenous opiates, as suggested by Chernick et al., Dr. Smits' hypothesis is certainly quite reasonable. It is well known that overdoses of exogenous opiates may result in noncardiac pulmonary edema in some patients. Noncardiac pulmonary edema appears to be quite uncommon in patients with sleep apnea, and if the mechanism by which exogenous and endogenous opiates produce pulmonary edema is similar, one would almost have to postulate endogenous opiate "poisoning" in those patients who develop it. Since alternative mechanisms for the development of pulmonary edema in such patients seem quite plausible, it may be that multiple factors are involved. We agree with Dr. Smits, however, that the role of endogenous opiates in the development of pulmonary edema in the patient we described2 and, indeed, in the pathogenesis of sleep apnea syndrome, deserves careful investigation.

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REFERENCES


Occupational Asthma and Rhinitis Caused by Urea Formaldehyde?

To the Editor:

I am writing to comment on an article by D. W. Cockcroft et al. (Chest 1982; 82:49). I offer the following comments.

The conclusion that the authors documented, i.e., the occurrence of occupational asthma caused by (CUF), is not compatible with the data presented. However, they did document that CUF particle board dust caused asthma in both of their patients. The difference between these two conclusions is crucial! CUF particle board contains a number of known as well as industrially secret chemicals, each of which may be a cause of occupational asthmas. Since the exact chemical/allergy exposure of the work environment of the patients in this study was never precisely defined, since each of the potential triggers was not evaluated to determine their relationship to the initiation of asthma, and especially since urea formaldehyde per se was never evaluated in this study, it is difficult to understand how the authors could possibly conclude the urea formaldehyde was the cause of asthma in either patient.

Occupational asthma has extensive health, social, economic, political, legal, ethical, and moral dimensions. Physicians engaged in the assessment of patients with occupational asthma have an obligation to define precisely the initiating and triggering stimuli following the tenets of the scientific method. Included in this obligation is the responsibility to refrain from publishing conclusions which are not in fact supported by data lest one invite misconception, misuse and abuse of findings.

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To the Editor:

We are pleased to have the opportunity to reply to the important points raised in Dr. Boggs' letter. There appears to be confusion in interpretation, particularly concerning the terms "urea formaldehyde" and "urea formaldehyde resin." Asthma was provoked by particle board sawdust allegedly containing only wood particles, a low concentration (<1 percent) of an inert paraffin-like wax, and 6 percent urea formaldehyde resin bonding agent. Absence of asthma following exposure to the natural sawdust suggests the urea formaldehyde resin was responsible. The title of our paper, the discussion, and the conclusion ("it is likely that some component of the urea formaldehyde resin system was responsible . . . . . . this could not be proved"), were carefully worded to embrace this hypothesis.

The precise composition of the various urea formaldehyde resin systems remains an industrial secret. We have been told that the bonding agent used in this particle board consists of seven components: urea, formaldehyde, an inorganic ammonium (NH4+) salt which is the major acid catalyst, two other "common" organic salts, a "trace" of low molecular weight amine, and water as a solvent. The asthma in our carpenters may have been due to an individual component, a reaction product, or a breakdown product of this polymer resin system. For example, the reaction of formaldehyde with ammonia produces hexamethylene tetramine, which is a documented cause of occupational asthma. Many other reaction products and breakdown products may be involved. As was clearly stated, the exact chemical(s) responsible for the asthma could not be identified.

The simple resin system used as a particle board bonding agent uses different reactants than the more complex urea formaldehyde foam insulation resin. Consequently, the findings in our carpenters may not be applied to those exposed to urea formaldehyde foam.

In conclusion, we believe the urea formaldehyde resin system used to bond this particular particle board was responsible for asthma in our two carpenters. We emphasize again that any