Fatal Pulmonary Aspergillosis Following a Farm Accident

To the Editor:

We read with interest the recent report by Lake and associates that short-course corticosteroid therapy may be the only risk factor for developing disseminated aspergillosis. We recently cared for a previously healthy immunocompetent man with no known lung disease who developed fatal pulmonary aspergillosis after a two-week course of corticosteroids. Unique to this case was antecedent trauma involving farm equipment.

Case Report

A 70-year-old farmer caught his right sleeve in the drive shaft of a manure spreader, trapping him against the machine for 15 minutes. This incident occurred on December 12, 1982. He was hospitalized for three days, for treatment of a brachial plexus injury with dexamethasone [Decadron] 6 mg qid. Over the next two weeks, the Decadron was tapered to 1 mg tid. A chest radiograph on December 12 showed normal findings. On December 31, he was re-hospitalized for treatment of a three-day bout of chest pain and cough. White blood cell count (WBC) was 20,500 with 97 percent neutrophils. Amlacin and ticarcillin were started. Sputum cultures showed Pseudomonas aeruginosa. On transfer to our hospital on January 6, the WBC count was 6,900 with 94 percent neutrophils. Chest radiograph showed bilateral fluffy infiltrates with bilateral nodulation, some of which were cavitated with focal consolidation in the right upper lobe, lingula, and right lower lobe. Antibiotics and corticosteroids were discontinued upon transfer. Fiberoptic bronchoscopy with biopsy of the right upper lobe revealed hyphae consistent with Aspergillus within alveoli and in necrotic tissue. Pathologic findings were not consistent with bacterial pneumonia. Aspergillus fumigatus was cultured from bronchial brushings. Despite amphotericin B therapy, the patient expired 24 days later secondary to respiratory insufficiency. A post-mortem examination was not performed.

Aspergillus fumigatus is an indigenous inhabitant of compost and as a thermophile, grows well in manure. Although controversy exists concerning occupational predisposition to aspergillosis, we postulate that the prolonged entrapment in the manure spreader exposed our patient to a large inoculum of Aspergillus conidia and was the initiating event in the development of disease. Subsequent corticosteroid therapy rendered him immunocompetent and resulted in overwhelming invasive disease.

We would suggest an addendum to the editorial comments that a diagnosis of invasive aspergillosis be considered not only as a consequence of acquired immunodeficiency syndrome, but also in the farm worker who presents with an unusual pulmonary infiltrate and history of prolonged exposure to manure.

References


To the Editor:

The recent editorial by Dr. Strieder (Chest 1983; 83:4-5) may be misleading. The author suggests that invasive aspergillosis may be seen with increasing frequency in young adults with acquired immunologic abnormalities involving the T-cell. While an increased number of other types of fungal infections may occur when the cell-mediated immune system is altered, this is probably not applicable to Aspergillus infection. In fact, it is not the T-cell, as Dr. Strieder asserts, but the neutrophil (or monocyte) which is primarily responsible for normal host defense against Aspergillus species.

Invasive aspergillosis is 20 times more frequent in acute leukemia than in lymphoma or transplant patients, the latter maladies involving T-cell dysfunction. Cohen et al have demonstrated that patients with chronic granulomatous disease who have normal immunoglobulins and intact cell-mediated immunity have pulmonary and osseous aspergillosis as their most common fungal infection. These patients have a neutrophil defect in generation of superoxide-free radicals which inhibits microbial killing once the organism is phagocytized. Further, it is recognized that the risk of invasive aspergillosis may be the greatest in neutropenic patients, and their survival is most enhanced by reversal of this neutropenia along with inducing remission of the underlying disease. Thus, it is not surprising that to date invasive aspergillosis is not commonly associated with the acquired immunodeficiency syndrome which often affects homosexuals, Haitians, drug addicts, and hemophiles.

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To the Editor:

In presuming to comment on the recent article by K. B. Lake et al (Chest 1983; 83:138-39), I chose to consider the particular circumstances of asthmatic patients stricken with pneumonia and respiratory failure, and the pronounced effects of corticosteroids on T-cell function. Dr. Gilmore and collaborators, and Drs. Peters and Atkinson remind us that there are many other epidemiologic and immunologic aspects of Aspergillus infections, for which I thank them. As to the likelihood of invasive aspergillosis affecting patients with the acquired immunodeficiency syndrome, Dr. Peters may well be right—time will tell.

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Nitroglycerin Therapy of Asthma

To the Editor:

A 12-year-old steroid-dependent asthmatic boy with iatrogenic Cushing's disease, was receiving theophylline sufficient to produce therapeutic blood levels. He was also taking metaproterenol orally, as well as inhaled albuterol, beclomethasone and ipratropium bromide, an investigational bronchodilator. His dose of prednisone ranged between 50 and 100 mg per day. Sodium cromolyn had been ineffective when given prophylactically in a relatively asymptomatic period. Short-term inhaled albuterol did not improve results of pulmonary function tests. It was decided to try the nonspecific smooth muscle dilator, nitroglycerin, continuing all other medications at their previous dosages.

Prior to administration of 0.15 mg of nitroglycerin sublingually, the FEV₁ was 1.54 (54% of predicted) and the patient was in moderate respiratory distress. Five minutes later the FEV₁ was 2.11 (74% of predicted) and the patient was symptomatically improved. He is now using a 10 cm² transdermal patch containing 25 mg of nitroglycerin daily with minimum side effects (very mild intermittent dizziness), and has tapered his steroid dosage to nothing. There has been no orthostatic hypotension. Follow-up has been three months.

It would appear that nitroglycerin dilates bronchial smooth muscle by a mechanism unrelated to that usually affected by current bronchodilating medications. The patient's spirometric results were not altered by inhaled albuterol, indicating maximal adrenergic effect and probable nonresponsiveness to parenteral epinephrine. Although there is little information on its use in pediatric patients, the literature gives conflicting reports about the efficacy of nitroglycerin in acute asthma.1,2 I was unable to discover any reports of long-term therapy. It seems that nitroglycerin may have therapeutic benefit when given on a long-term basis, as well as short-term, although tachyphylaxis to its antiangiinal effects is known to occur in adult patients.

The mode of action of nitroglycerin on bronchial smooth muscle can only be speculated upon. It is known to relax tracheal smooth muscle when given intravenously.3 Nebulized isosorbide dinitrate, a related drug, was found to be effective in seven patients aged 14-49 with extrinsic and reproducible exercise-induced asthma.5 This compound has been found to produce vasodilation in the endothelium of coronary artery smooth muscle by the reproduction of nitric oxide which stimulates guanylate cyclase, producing cyclic GMP.6

Nitroglycerin has also been shown to stimulate production of prostacyclin in human endothelial cells, thereby stimulating adenyl cyclase.1 It has been suggested7 that this enhancement may be caused by inhibition of thromboxane A₂ synthesis, thereby preferentially shunting precursor into the prostacyclin synthetase pathway. Caution should be used when prescribing nitroglycerin for the hypovolemic patient, since it may produce hypotension, an effect which may even occur in the normovolemic patient.

Nitroglycerin treatment of pediatric asthma is worthy of further trials and may be indicated in selected patients.

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Noninvasive Measurement of Mixed Venous Pco₂

To the Editor:

We would like to comment on the report on mixed venous Pco₂ in the article "Non-invasive monitoring of arterial blood gases: a report of the ACCP Section on Respiratory Pathophysiology" (Chest 1983; 83:666-70). We have been using the equilibrium rebreathing technique for measurement of mixed venous Pco₂ (Pvco₂) in patients for many years and have published several articles designed to help the physician understand and use this technique. We feel, however, that Drs. Burki and Albert's description of the two rebreathing techniques for measurement of Pvco₂ may confuse the reader, and also contains some inaccuracies.

Two methods of estimating the Pvco₂ by rebreathing are in common clinical use. The Campbell and Howell technique1 is a two-stage procedure, in which the patient breathes for 15 minutes from a bag containing pure oxygen, breathes air for 2 min, then rebreathes from the bag for 20 sec. The Pvo₂ is the Pco₂ in the bag at the end of the second period of rebreathing. The choice and latitude of these times and volumes are explained in a later paper.2 This two-stage method has the advantage of not requiring a rapidly responding analyzer, but it does require constant practice. We find it quite satisfactory when performed by trained technicians and use it in the general wards and clinic.