Relapsing aspergillus bronchitis in a double lung transplant patient, ...
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On hospital admission, the temperature was 39.4°C and the pulse rate was 112 beats/min. Findings from physical examination were unremarkable except for mild hepatosplenomegaly. Laboratory tests revealed a serum hemoglobin level of 11.4 g/dl, WBC count of 3.4×10⁹/L, and platelet count of 79×10⁹/L. Results of liver and renal function tests and urinalysis were within normal limits. Findings on chest radiograph were normal.

Thirty-six hours later, the patient had high-grade fever (40.5°C), tachypnea, dyspnea, and acute pain in the anterior chest wall. Blood gas analysis (fraction of inspired oxygen, 0.21) revealed a pH of 7.5, PaO₂ of 64.6 mm Hg, PaCO₂ of 29.1 mm Hg, and HCO₃⁻ of 23.1 mmol/L. The chest radiograph showed bilateral interstitial infiltrates. Two separate peripheral blood smears showed P. citrinum parasitism. No other parasites were observed. Treatment with regular doses of chloroquine (25 mg/kg in 3 days) and oxygen was started. Symptoms quickly improved, and both fever and respiratory symptoms disappeared after 24 h. Values from blood gas analysis normalized and abnormalities on the chest radiograph disappeared.

Pulmonary involvement due to infection by P. falciparum has been widely described and usually presents as lung edema or ARDS. Unlike P. falciparum infection, P. citrinum rarely affects the lung.

After an extensive review of the MEDLINE database (1982 to 1996), only one case of bronchiolitis obliterans organizing pneumonia associated with P. citrinum was found, as was another report of pulmonary uptake of radiocolloid detected by gammagraphy, without evidence of clinical or radiologic disease. This case with gammographic abnormalities might indicate an infection of lesser intensity and, therefore, without evident clinical manifestations. In our patient, the initial symptoms suggested a pulmonary disease, and his clinical condition improved with erythromycin therapy. A possible partial response to this antibiotic may explain the remission of lung symptoms. Cases of in vitro response of P. falciparum with erythromycin and in vivo response of Plasmodium berghei in animals with the same antibiotic effects have been described. The pulmonary interstitial disease evident after the hospital admission was indicative of a lung affection by the parasite, both because it appeared without concomitant respiratory disease and also it cleared promptly with the specific antimalarial therapy. The rapid improvement did not allow us to explore the lung with radiocolloid. However, the apparent radiologic changes with a deep derangement in blood gas analysis are clearly suggestive of pulmonary involvement.

Interstitial pulmonary involvement, although extremely rare, should be considered in patients with P. citrinum malaria and acute respiratory symptoms.

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References

Relapsing Aspergillus Bronchitis in a Double Lung Transplant Patient, Successfully Treated With a New Oral Antimycotic Agent

To the Editor:

Aspergillus infections in transplant patients have been associated with a high mortality rate, quite high in lung transplant recipients. In these latter patients, Aspergillus can lead to the development of an invasive form of ulcerative bronchitis characterized by the presence of membranes associated with hemor- rhagic necrosis. Amphotericin B (AB) is the drug of choice for Aspergillus, but its use is limited by severe side effects and toxicity. Liposomal amphotericin B (LAB) is definitely less nephrotoxic than its conventional form. Its routine administration, however, is limited to the IV route, and it is highly expensive. Ketoconazole and itraconazole are antifungal agents active on Aspergillus, but may be responsible for liver toxicity and interference with cyclosporine A levels.

Terbinafine is a new oral antifungal drug used for the treatment of onychomycosis. This drug, which interferes with the integrity of fungal cell wall membrane, exerts a fungicidal action, inducing an intracellular accumulation of square. Against Aspergillus species, its in vitro action is similar to, or more effective, than those of AB, ketoconazole, or itraconazole.

On the basis of a previous encouraging experience in the treatment of nonimmunocompromised hosts with Aspergillus bronchopulmonary infections, and despite previous treatments with AB and LAB and an itraconazole-intolerance, we treated a double lung transplant patient with relapsing Aspergillus bronchitis with terbinafine. Immunosuppressive regimen included rat antithymocyte globulin for the first 5 postoperative days. cyclosporine A, azathioprine, and steroids. The clinical course was characterized by frequent episodes of acute allograft rejection (AAR) and frequent cytomegalovirus infections inducing onset of pneumonia. The appearance of a bilateral bronchial stenosis was treated by positioning two Gianturo stents in the main and intermedius right bronchus, and one in the main left bronchus. Sixteen months after transplantation, in a condition of increased immunosuppression for a third AAR episode, the patient was hospitalized because of a varicella-zoster virus skin infection, cytomegalovirus pneumonia, and Aspergillus fumigatus bronchitis. Aspergillus fumigatus was obtained from bronchoscopy (bronchial aspirate and BAL) and sputum. BAL was negative for the presence of other opportunistic agents. At bronchoscopy gray-white membranes, spreading on the overall bronchial mucosa, associated with the visible hemorrhagic necrosis, were evident after both anastomoses. Amphotericin B and acyclovir for the varicella infection were started, but a relevant and rapidly evolving nephrotoxicity led to replacement of amphotericin B with its
liposomal form. The patient was treated with LAB (100 mg/d) for 10 days, reaching a cumulative dose of 1,050 mg. Repeated bronchoscopy proved negative for Aspergillus, and LAB treatment was consequently discontinued. Three weeks later, a few Aspergillus fumigatus were isolated again on bronchial aspirate. Itraconazole was started at a dosage rate of 5 mg/kg bid and the cyclosporine A doses decreased by 50%, but the patient presented with an intolerance to these agents with a consequent onset of vertigo, tremors, nausea, and vomiting. A LAB treatment was newly started with a total 2-g dosage and a complete Aspergillus subsidence was observed at repeated bronchoscopic examinations with evidence of normal bronchial mucosa. Two months later, after augmented immunosuppression for two more episodes of AAR, Aspergillus fumigatus reappeared in sputum cultures. Clinical bronchoscopic features were consistent with a diagnosis of Aspergillus invasive bronchitis.

After two relapses following a LAB treatment and episodes of itraconazole intolerance, we decided to start a treatment with terbinafine at the oral dose of 250 mg bid. The treatment was continued for 3 months.

Cyclosporine A levels were monitored, and remained stable; no liver, renal, or other organ toxicity was evidenced, and no untoward side effects were observed. Sputum and bronchial aspirate cultures became negative 9 days after starting the treatment, kept being negative during treatment, and were still negative 14 months after treatment discontinuation. The subsequent clinical course was uneventful.

On the basis of the present case report as well as of our previous experience in nonimmunocompromised hosts, we would suggest the conduction of large trials in order to evaluate the usefulness of this oral antifungal agent in the prevention and in the treatment of Aspergillus infection in immunocompromised and nonimmunocompromised hosts.

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REFERENCES


Errata

In the July 1996 issue (CHEST 1996; 110:180-184), the paper “Intrinsic Positive End-Expiratory Pressure During One-Lung Ventilation for Thoracic Surgery: The Influence of Preoperative Pulmonary Function” by Bardoczky et al contained an error in the Results section. The sentence “There was a significant difference in the incidence of PEEP between the two groups of patients both in the supine (p=0.008) and in the lateral (p=0.001, Mann-Whitney U test) position.” was incorrect. The correct statistical test used was the Fisher’s Exact Test.

In the article “Predicting Eventual Success or Failure to Wean in Patients Receiving Long-term Mechanical Ventilation,” by Eric Gluck, MD, FCCP, and Linda Curgian, RN, PhD (CHEST 1996;110:1018-24), Dr. Curgian’s name is misspelled in the byline. Dr. Gluck was the sole author of the article.