mykosen | mykosen 27 (11) 535–538
Angenommen/Accepted: 15. Mai 1984

Necrotizing Pulmonary Aspergillosis with Oxalosis

Nekrotisierende pulmonale Aspergillose mit Oxalose

Carol A. Kauffman, K. H. Wilson and D. B. Schwartz

Divisions of Infectious Diseases and Pulmonary Medicine
Department of Internal Medicine Veterans Administration Medical Center and
University of Michigan Medical School Ann Arbor, Michigan

Key words: Aspergillosis - oxalosis - Aspergillus niger
Schlüsselwörter: Aspergillose - Oxalose - Aspergillus niger

Summary: Aspergillus niger has the unique ability to produce oxalic acid. We describe a patient with chronic necrotizing pulmonary aspergillosis due to A. niger who had calcium oxalate crystals demonstrated in sputum, bronchial washings, and lung tissue obtained by transbronchial biopsy. Necrotizing pulmonary infection due to A. niger is uncommon; the presence of calcium oxalate crystals can prove helpful in establishing the diagnosis of serious infection due to A. niger.

Zusammenfassung: Aspergillus niger hat die einzigartige Fähigkeit, Oxalsäure zu produzieren. Wir beschreiben einen Patienten mit einer chronischen nekrotisierenden pulmonalen Aspergillose durch Aspergillus niger. Der Patient hatte Kalziumoxalat-Kristalle im Sputum, in Bronchialabsaugungen und im Lungengewebe, das durch transbronchiale Biopsie gewonnen wurde. Nekrotisierende pulmonale Infektionen durch Aspergillus niger sind selten. Der Nachweis von Kalziumoxalat-Kristallen kann bei der Stellung der Diagnose einer ernsten Infektion durch Aspergillus niger hilfreich sein.

Introduction

Aspergillus niger is common in the environment, but it rarely causes disease in humans (12). When infections occurs, it is usually non-invasive localized growth of fungus, as in external otitis (10) or sinus or pulmonary mycetomas (5, 7). Necrotizing pulmonary infection with cavity formation and pleural involvement is rarely caused by A. niger (11). A niger is unique in its ability to produce oxalic acid when growing in culture in vitro or when causing infection in vivo (3, 7). This capability to produce oxalic acid can provide a valuable clue in the diagnosis of infection due to A. niger.

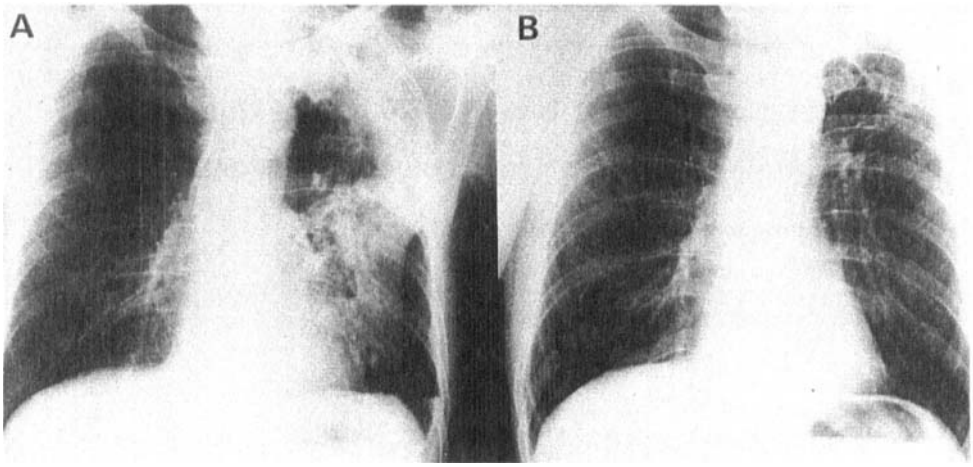

Fig. 1: A. Chest roentgenogram obtained after 14 days of antimicrobial therapy showing left upper lobe cavitary disease, loculated hydropneumothorax, and diffuse infiltrates throughout the left lung. B. Resolution of necrotizing Aspergillus infection after therapy with 2 grams of amphotericin B.

Case Report

A 53 year old man developed fever, night sweats, and cough productive of a cup of rusty sputum daily for 1 month before admission. Several days before admission he had left-sided pleuritic chest pain and hemoptysis. He had a 15 lb weight loss over the preceding 4 months. Approximately 3 to 4 months prior to admission he had helped tear down an old shed. He had a 50 pack year cigarette smoking history and a history of chronic bronchitis, but was otherwise healthy.

On admission he appeared chronically ill, had mild respiratory distress, and a temperature of 102.4°F (39.1°C). Dullness and rales were noted in the left upper lung field. There was no clubbing or cyanosis. Chest roentgenogram showed the presence of a new left upper lobe infiltrate with a cavity and a pleural-based density in the left mid-lung field. The white blood cell count was 20,300/mm^3 with 81% segmented neutrophils and 11% band forms; hematocrit was 36.6%; albumin was 2.9 g/dl; and arterial blood gases revealed PO_2 68 mm Hg, PCO_2 32 mm Hg, pH 7.51. PPD skin test was non-reactive; Candida skin test was positive. Thoracentesis revealed serosanguinous fluid with a protein of 2.3 g/dl, glucose of 132 mg/dl, 4000 white blood cells, 47% neutrophils and 53% mononuclear cells, and no organisms on Gram's stain. Sputum revealed many neutrophils and mixed gram-positive and gram-negative organisms. Pleural fluid and blood cultures grew no organisms, and sputum yielded normal oropharyngeal flora. He was treated with penicillin and tobramycin for presumed aspiration pneumonia but had no response.

On the 7th hospital day, flexible fiberoptic bronchoscopy revealed purulent exudate in the left upper lobe bronchus. Transbronchial biopsies yielded necrotic tissue with crystals that were seen also in the bronchial washings and transbronchoscopic brushings. The crystals were not further identified at this time. No fungal elements were seen in the biopsy specimens. The biopsy and washings grew A. niger but no bacteria. Sputum cultures yielded Haemophilus parainfluenzae, Candida albicans, and A. niger. In spite of isolation from several sources, the Aspergillus isolate was considered a saprophyte.

He remained febrile to 102°F (38.9°C), produced copious sputum, and continued to lose weight despite a change in antimicrobial therapy to clindamycin and later cefoxitin. His chest

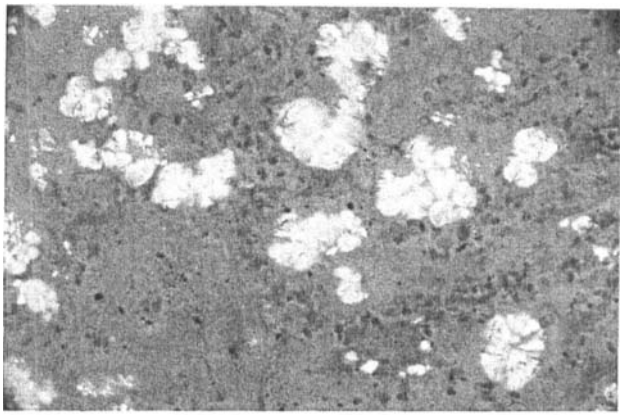

Fig. 2: Lung tissue obtained by transbronchoscopic biopsy showing clumps of birefringent crystals of calcium oxalate. Hematoxylin and eosin stain viewed with polarized light and magnified 25 x.

roentgenogram showed worsening of the left upper lobe cavitary lesions with multiple air-fluid levels, loculated hydropneumothorax, and spread of the disease to the lingula and left lower lobe (Figure 1).

On the 42nd hospital day, repeat bronchoscopy revealed copious purulent secretions from the left upper lobe bronchus, and fluoroscopy demonstrated a cavity, which contained a free-floating mass. Bronchial washings and transbronchoscopic brushings revealed crystals, identical to those seen earlier and identified by appearance and polarity as calcium oxalate crystals. Transbronchial biopsy specimens obtained from lung tissue adjacent to the cavity showed extensive necrosis and fungi with septate hyphae, yeast forms, and bundles of birefringent crystals (Figure 2). Cultures of the bronchial washings grew A. niger and C. albicans and no bacteria.

Serum precipitins to A. niger and other Aspergillus species were negative on 2 occasions. Review of sputum cytologies from the first week of hospitalization revealed the presence of calcium oxalate crystals. Urinary oxalate excretion was 108 mg/24 hr (normal 0–40 mg/24 hr). No oxalate crystals were noted by urinalysis, and renal function was normal.

Amphotericin B was initiated for pulmonary aspergillosis. The patient improved, becoming afebrile and gaining weight after 14 days of therapy. His chest roentgenogram showed steady resolution of the pneumonic process (Figure 1). A total of 2 gm of amphotericin B was given, and the patient has remained well for a year.

Discussion

Chronic necrotizing pulmonary aspergillosis in the non-immunosuppressed host is a discrete clinical entity that has been reported sporadically for decades and has recently been reviewed comprehensively by Binder et al. (2). We think that our patient had this form of aspergillosis since he had biopsy and culture-proved tissue invasion by A. niger and progressive pulmonary infection over a period of at least two months with formation of cavities and mycetomas in addition to widespread infiltrates. After failure of several antimicrobial regimens, his symptoms and roentgenographic changes resolved when he received amphotericin B.

A. niger is rarely a pathogen in humans and has been described as causing chronic necrotizing pulmonary aspergillosis only once before (11). A. fumigatus has a much greater potential to cause disease, and in fact, is responsible for most cases of disseminated infection (12), mycetomas (4), and chronic necrotizing pulmonary aspergillosis (2). A flavus has been

shown to have a propensity to cause upper respiratory tract invasion (12), and has been responsible for invasive pulmonary aspergillosis in patients with leukemia (1).

Although rare, A. niger infection remains noteworthy because this organism has the unique ability to produce oxalic acid (3). When this occurs in tissues, calcium oxalate crystals are formed and can be identified by polarizing microscopy and special histochemical techniques (6). Local deposition of calcium oxalate has been particularly well described with aspergillomas (6, 7, 9). Except for one presumed A. fumigatus infection, with a small amount of calcium oxalate in the surrounding tissues (7), all of these aspergillomas have been caused by A. niger. In one patient with A.niger infection, calcium oxalate crystals were identified in sputum, bronchial washings and pleural fluid (8). In several cases, formation of oxalic acid by the fungus led to deposition of oxalate crystals in the kidney and possible renal insufficiency (7, 9). Our patient had increased excretion of oxalate in the urine, but did not have renal insufficiency.

As exemplified by our patient, and as noted previously, it is difficult to diagnose chronic necrotizing pulmonary aspergillosis. In part this is because Aspergillus is not usually thought of as a pathogen in the non-immunosuppressed host. However, failure to diagnose this infection can result in inappropriate antimicrobial therapy, destruction of lung tissue, and even death. Recognition of the association between A. niger infection and oxalate crystals may be important for two reasons. The presence of oxalate crystals in sputum, pleural fluid, or biopsy specimens should lead one to suspect a serious pulmonary infection with A. niger, allowing earlier institution of proper therapy. In addition, identification of oxalate crystals should alert the physician to the possibility of systemic oxalosis with associated renal damage.

References

1. Aisner, J., J. Murillo, S. C. Schimpff & A. C. Steere (1979): Invasive aspergillosis in acute leukemia: Correlation with nose cultures and antibiotic use. Ann. Intern. Med. 90, 4-9.
2. Binder, R. E., L. J. Faling, R. D. Pugatch, C. Mahasaen & G. L. Snider (1982): Chronic necrotizing pulmonary aspergillosis: A discrete clinical entity. Medicine 61, 109-124.
3. Cleland, W. W. & M. J. Johnson (1956): Studies on the formation of oxalic acid by Aspergillus niger. J. Biol. Chem. 220, 595-606.
4. Glimp, R. A. & A. S. Bayer (1983): Pulmonary aspergilloma. Diagnostic and therapeutic considerations. Arch. Intern. Med. 143, 303-308.
5. Grigoriu, D., J. Bambule & J. Delacretaz (1979): Aspergillus sinusitis. Postgrad. Med. J. 55, 38-40.
6. Kurrein, F., G. H. Green & S. L. Rowles (1975): Localized deposition of calcium oxalate around a pulmonary Aspergillus niger fungus ball. Am. J. Clin. Pathol. 64, 556-563.
7. Nime, F. A. & G. M. Hutchins (1973): Oxalosis caused by Aspergillus infection. Johns Hopkins Med. J. 133, 183-194.
8. Reyes, C. V., S. Kathuria & A. MacGlashan (1979): Diagnostic value of calcium oxalate crystals in respiratory and pleural fluid cytology. Acta Cytologica. 23, 65-68.
9. Severo, L. C., A. T. Londero, G. R. Geyer & P. D. Picon (1981): Oxalosis associated with an Aspergillus niger fungus ball. Report of a case. Mycopathologia. 73, 29-31.
10. Stuart, E. A. & F. Blank (1955): Aspergillosis of the ear: A report of twenty-nine cases. Canad. Med. Ass. J. 72, 334-337.
11. Utz, J. P., J. L. German, D. B. Louria, C. W. Emmons & F. C. Bartter (1959): Pulmonary aspergillosis with cavitation. N. Engl. J. Med. 260, 264-268.
12. Young, R. C., A. Jennings & J. E. Bennett (1972): Species identification of invasive aspergillosis in man. Am. J. Clin. Pathol. 58, 554-557.

Address: Dr. Carol A. Kauffman, Medical Service, Veterans Administration Medical Center, Ann. Arbor, MI 48105.