JOURNAL OF CLINICAL MICROBIOLOGY, Dec. 1997, p. 3335–3337 Vol. 35, No. 12
0095-1137/97/$04.00+0

Necrotizing Pneumonia Caused by *Penicillium chrysogenum*

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Received 12 May 1997/Returned for modification 3 July 1997/Accepted 9 September 1997

We report a case of necrotizing pneumonia due to *Penicillium chrysogenum* in a 57-year-old woman operated on for lung cancer. The residual right lower pulmonary lobe was infiltrated by *Penicillium chrysogenum*. The patient underwent a second pulmonary right lobectomy and was successfully treated with oral itraconazole. To our knowledge, this is the first case of pneumonia due to *P. chrysogenum*.

Fungal infections are an increasing problem in immunocompromised patients (8). The organisms most often responsible for invasive fungal infection are *Candida* and *Aspergillus* species (11). Members of the genus *Penicillium* rarely cause infections and are primarily limited to strains of the species *Penicillium marnaffei* (2, 6, 9, 12, 13). In the past, *Penicillium chrysogenum* has been recognized as an invasive fungus in only two cases of human disease (3, 7). We report here the first known case of necrotizing pneumonia caused by *P. chrysogenum* in a patient with cancer.

Case report. In December 1995, a 57-year-old female with a pulmonary squamous carcinoma was admitted to the Department of Surgery of the University Hospital of Chieti and underwent a right middle-upper bilobectomy. The staging of the cancer, coded as T2N0M0, was more than 3 cm in the greatest dimension, with no regional lymph node metastasis and no distant metastasis. Postoperative recovery was successful, and the patient was discharged on the 12th day of hospitalization. Twenty-five days later, she was readmitted for elevated fever and hemoptysis. Admission laboratory values included a leukocyte count of 18,000/mm^3, with 87% polymorphonuclear elements; serum chemistries and liver enzymes were unremarkable. The erythrocyte sedimentation rate was 54 mm/h, and urinanalysis was normal. Blood cultures did not grow any organism. Hemoptysis culture yielded a pure and heavy growth of *Penicillium*, subsequently identified as *P. chrysogenum* (Fig. 1). The computerized tomography scan showed a necrotizing lesion within an air-filled cavity in the lower right lobe (Fig. 2). The patient underwent a right lower lobectomy. Microscopic examination of a portion of the lung biopsy demonstrated numerous septate hyphae. Cultural examination of necrotic tissue revealed the presence of *P. chrysogenum*. The patient was successfully given oral itraconazole at a dose of 200 mg/day twice a day to maintain serum drug levels at approximately 800 ng/ml. The patient was discharged on the 15th day of hospitalization, and she was still alive 15 months after this episode.

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Laboratory studies. A small sample of the dissected lobe was aseptically collected for histologic and microbiologic studies. Part of this sample was used to prepare tissue sections, stained with hematoxylin and eosin and periodic acid and Schiff's reagent (Fig. 3). The remaining portion of the specimen was partly stored in liquid nitrogen, partly minced with sterile scissors, and homogenized in sterile saline in a biological safety cabinet. Portions of the tissue homogenate were used for microscopic examination. Other portions of the tissue homogenate were cultured for mycobacteria and aerobic and anaerobic bacteria by conventional methods (5). Moreover, aliquots of the specimens described above were directly plated onto Sabouraud glucose agar (SGA) (Difco Laboratories, Detroit, Mich.) and incubated at both 25 and 37°C.

Microscopic studies. Histologic examination of the pulmonary tissue showed a fibronecrotic area with numerous fungal elements, uniformly cylindrical with septate hyphae branching at an angle of 25 to 45°. A few hyphal elements were also observed in stained preparations of the tissue homogenates and were similar to those in the tissue sections.

Mycology studies. Cultures of lung tissue homogenates on Trypticase soy agar (Difco) yielded no bacteria, but mold grew onto the agar plates incubated in an aerobic atmosphere. Direct cultures of biopsy samples on SGA showed a pure growth of multiple colonies. Fungal growth on SGA appeared velvety and was pale greenish-blue, becoming darker with age. A subculture was performed on Czapek Dox agar (Unipath S.p.A., Garbagnate Milanese, Milan, Italy) and incubated at 25°C. Colonies were velvety, grew rapidly (30 to 35 mm in diameter in 7 days), and were pale greenish-blue, becoming darker and somewhat floccose with age. Sporulation was heavy. Yellow drops were produced as exudate. The reverse side was uncolored. Slides were prepared from cultures yielded on Czapek Dox agar (Unipath), stained with lactophenol blue, and examined with an optical microscope. Conidial heads were mononematous and ter- to quareverticillate. In particular, conidiophore structures had the following characteristics. Smooth-walled stripes were 250 to 500 μm high and 2.5 to 3.5 μm wide. Branches were divergent. Metulae were somewhat cylindrical and smooth

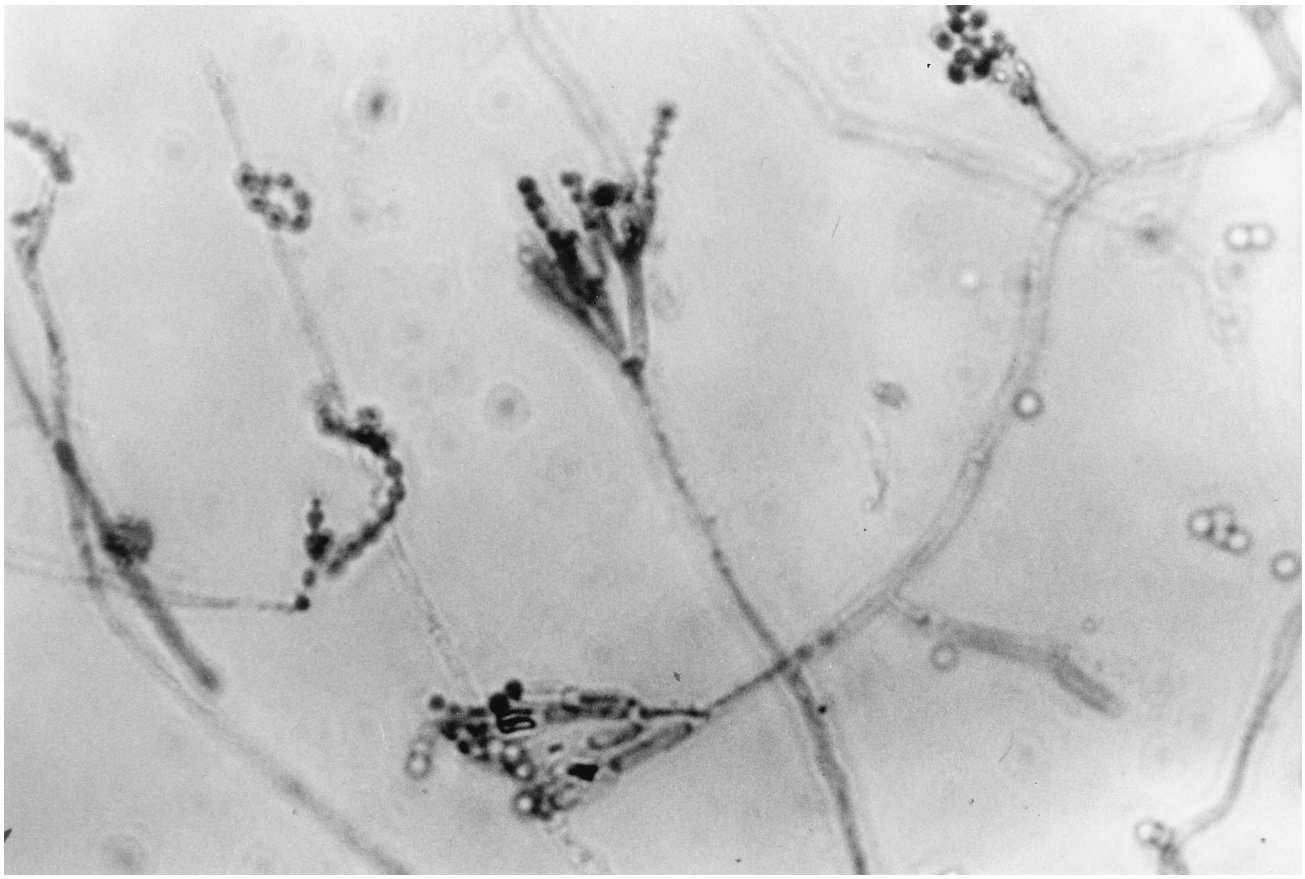

FIG. 1. Slide culture of *P. chrysogenum*. Stain, phenol cotton blue. Magnification, ×200.

walled, measuring 8 to 15 by 2 μm. Bore phialides were three to six per metula, flask shaped, and measured 7 to 10 by 2.0 to 2.5 μm. Conidia were subglobose to globose, smooth walled, slightly greenish, and produced in loose columns. The fungal growth was observed at 25 and 37°C but not at 42°C after a 2-week incubation. The isolate matched with a *P. chrysogenum* Thom strain in all essential characteristics (10).

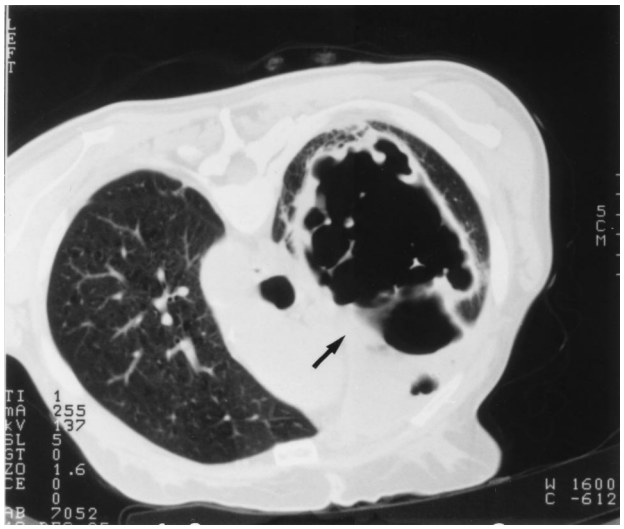

FIG. 2. Computerized tomography scan of the patient showing a necrotizing lesion within an air-filled cavity in the lower right lobe.

For both strains isolated from hemoptysis and lung biopsy, antifungal susceptibility testing (4) showed the following MICs: amphotericin B, of 0.5 μg/ml; 5-fluorocytosine, 1 μg/ml; itraconazole, 4 μg/ml; and fluconazole, >256 μg/ml.

Discussion. Rarely has a *Penicillium* species been etiologically linked to documented invasive infections, although it is being increasingly recognized as a potential pathogen in immunocompromised hosts. The genus *Penicillium* is ubiquitous, generally saprophytic, and distributed worldwide. It is frequently an airborne contaminant of sterile solutions and culture samples. An etiological diagnosis can be performed only when the laboratory finding is supported by a clear fungal infiltration of the tissue that has been histologically confirmed. In our case, the histological finding was strongly indicative of a fungal infection of the right lower lobe, and the laboratory results showed the exclusive presence of *P. chrysogenum* at the level of the pulmonary lesion. To our knowledge, only two cases of natural human infection with *P. chrysogenum* have been reported. The first isolate of *P. chrysogenum* was recovered in 1973 from the aortic valve prosthesis in a 31-year-old white woman with an endocarditis. The second case was a necrotizing esophagitis unresponsive to oral ketoconazole in a 30-year-old human immunodeficiency virus-infected patient. Our case is the first report of a necrotizing pneumonia caused by *P. chryso-*

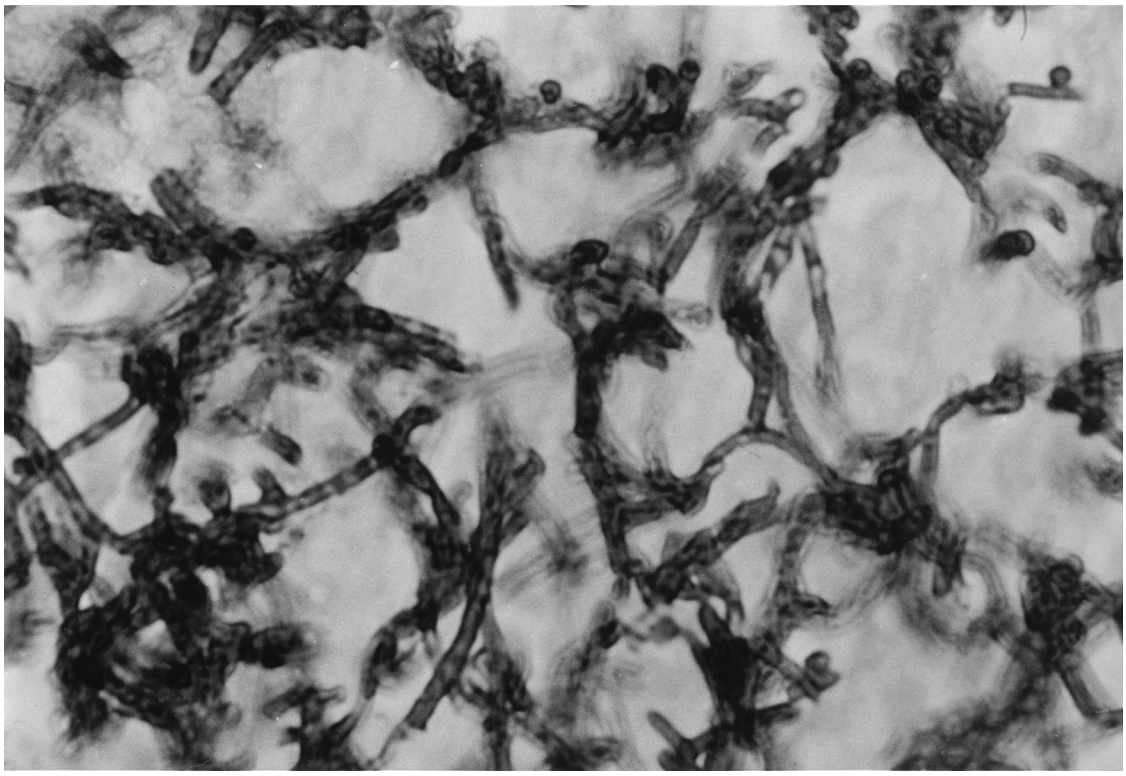

FIG. 3. Hyphae in lung tissue stained with periodic acid and Schiff's reagent. Magnification, ×1,000.

genum, presumably developed at the time of the first pulmonary surgery.

We thank V. Beltrami, Director of the surgery staff of the "Istituto di Clinica Chirurgica," Università "G. D'Annunzio," Chieti, Italy. We are very grateful to R. A. Samson (Centraalbureau voor Schimmelcultures, Baarn, The Netherlands) for confirming the identity of *Penicillium chrysogenum*.

This work was supported in part by the Associazione Donatori Sangue, Pescara, Italy.

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