

- Bertherat E, Talarmin A, Zeller H. République Démocratique du Congo: Entre guerre civile et virus Marburg. *Med Trop (Mars)*. 1999;59:201-4.
- Zeller H. Les leçons de l'épidémie à virus Marburg à Durba, République Démocratique du Congo (1998-2000). *Med Trop (Mars)*. 2000;60(2S):23S-6.
- Bourée P, Bergmann JF. Ebola virus infection in man: a serological and epidemiological survey in the Cameroons. *Am J Trop Med Hyg*. 1983;32:1465-6.
- Johnson ED, Gonzalez JP, Georges A. Filovirus activity among selected ethnic groups inhabiting the tropical forest of equatorial Africa. *Trans R Soc Trop Med Hyg*. 1993;87:536-8.
- Gonzalez JP, Nakoune E, Slenczka W, Vidal P, Morvan JM. Ebola and Marburg virus antibody prevalence in selected populations of the Central African Republic. *Microbes Infect*. 2000;2:39-44.

Address for correspondence: Matthias Borchert, London School of Hygiene and Tropical Medicine, Infectious Diseases Epidemiology Unit, Keppel Street, London WC1E 7HT, United Kingdom; fax: 44-20-7299-4720; email: matthias.borchert@lshtm.ac.uk

Disseminated Coccidioidomycosis

To the Editor: Coccidioidomycosis, an infection caused by the dimorphic fungus *Coccidioides immitis*, is endemic in the southwestern United States, parts of Mexico, and Central and South America (1). Patients with *C. immitis* infection may have chronic pneumonia, fungemia, and extrapulmonary dissemination to skin, bones, meninges, and other body sites. The clinical features of coccidioidomycosis may mimic those of melioidosis, penicilliosis marneffeii, and tuberculosis, which are commonly seen in some southeastern Asian countries, including Taiwan.

A previously healthy, 71-year-old retired gynecologist from Taiwan, visited Los Angeles in August 2003 and

traveled to the San Joaquin Valley in November 2003. He had smoked 1 package of cigarettes daily for 50 years. He noted fever 5 days before returning to Taiwan on December 1, 2003. He came to a local hospital on December 4 with a temperature of 39°C and a history of 1 month of night sweats, productive cough, and weight loss of 10 kg. Chest radiograph showed diffuse nodular lung lesions bilaterally (Figure, panel A). His leukocyte count was $16.65 \times 10^9/L$ (neutrophils 85.6%, lymphocytes 6.2%), and C-reactive protein was 21.5 mg/dL (reference value, <0.8 mg/dL). Empiric antimicrobial drugs (amoxicillin/clavulanic acid and ciprofloxacin) and antituberculosis therapy (isoniazid, rifampin, ethambutol, and pyrazinamide) were administered. Blood and sputum specimens

were negative for bacteria; HIV antibody test results were negative, but the fever persisted. A follow-up chest film showed a left pleural effusion. The pleural effusion aspirate was exudative with $3.6 \times 10^9/L$ leukocytes (73% neutrophils). Computed tomographic scan of the patient's chest showed collapse of the left lower lung with central necrosis, bilateral pleural effusions, and mediastinal lymphadenopathy. Pleural biopsy by video-assisted thoracoscopic surgery showed no evidence of malignancy, but heavy lymphoplasmacytic infiltration and chronic necrotizing granulomatous inflammation were found (Figure, panel C). On December 17, 2003, 30 mg/day prednisolone orally was prescribed for intermittent fever. Biopsy material and cultures of blood samples taken at admission grew an

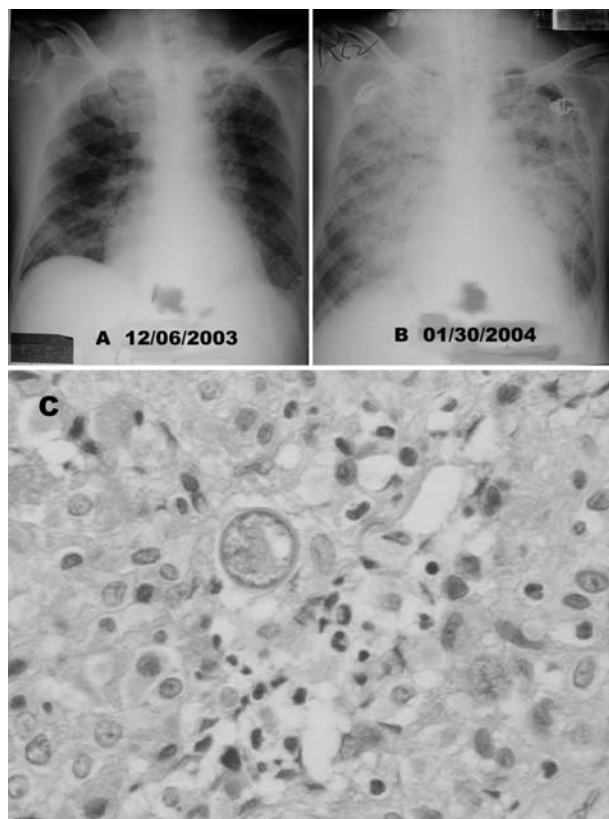


Figure. A) Chest radiograph shows diffuse nodular lesions in both lungs. B) Chest radiographic scan taken 2 months later shows coalescence of nodular shadows and almost complete white-out of bilateral lung fields. C) Hematoxylin and eosin staining of the wound specimen from pleural biopsy site showed spherules of *Coccidioides immitis* and chronic necrotizing granulomatous inflammation (400x).

unidentified mold, which was also isolated from the biopsy wound. The patient was discharged afebrile from the hospital on January 20, 2004. The fever recurred, with a disturbance in consciousness on January 25, 2004. Computed tomographic scan of the brain revealed no obvious organic lesions. He was referred to our hospital on January 26, 2004.

After the patient was admitted, fever persisted and respiratory distress worsened rapidly. He developed severe headache, seizures, and loss of consciousness. He was transferred to the intensive care unit for aggressive management of acute respiratory distress syndrome and deterioration of renal function. Chest radiograph showed coalescence of nodular shadows and almost complete white-out of bilateral lung fields (Figure, panel B). Meropenem, antituberculosis agents, and intravenous voriconazole, 200 mg every 12 hours, were administered.

Both the unidentified mold, which was sent to our hospital for further identification, and a mold cultured from the previous biopsy wound at our hospital were identified as *C. immitis* by their characteristic gross and microscopic morphotypes in standard slide cultures incubated at 28°C for 10 days. Hematoxylin and eosin staining of the biopsied tissue showed many spherules.

Lumbar puncture was performed on January 30, 2004, and showed an elevated opening pressure of 380 cm H₂O and a few destructed large spherules in the cerebrospinal fluid (CSF). However, cultures of CSF were negative for bacteria and fungi. After the diagnosis of disseminated coccidioidomycosis (pneumonia, fungemia, and meningitis), voriconazole was replaced by intravenous fluconazole, 400 mg/day. The patient's intensive care course was complicated by *Pseudomonas* pneumonia and repeated episodes of upper gastrointestinal bleeding. A second lumbar puncture was conducted on February

13, 2004, and also showed an elevated opening pressure (290 cm H₂O). Uncontrolled coccidioidomycosis meningitis was suspected, and intrathecal amphotericin B treatment was planned. Refractory shock with bradycardia developed when an intrathecal catheter was implanted. The patient did not respond to therapy and died on February 16, 2004. The MIC of fluconazole for the *C. immitis* isolate was 48 µg/mL, and the MIC of amphotericin B was found to be 1 µg/mL for by using the Etest (ABiodisk, Solna, Sweden) according to manufacturer's information.

This case is the first to be reported of disseminated coccidioidomycosis with fulminant pneumonia, fungemia, and meningitis reported from Taiwan (2). Review of the patient's travel history and clinical course indicated that the *C. immitis* was acquired in California and that the initial manifestations had begun before the patient returned to Taiwan. Coccidioidomycosis is commonly diagnosed in disease-endemic areas but frequently overlooked in disease-nonendemic areas because of a low index of suspicion among physicians. The interval from onset of symptoms to disease diagnosis was relatively long (3). Our patient had chills, productive cough, weight loss, and night sweats followed by fever as the initial manifestations of this infection. These symptoms had been most frequently reported in previous coccidioidomycosis cases (4). Radiographic scans of the patient initially showed diffuse reticular lesions, followed by pleural effusion and consolidation. This clinical course was also fully compatible with those of previously reported cases (4). However, the clinical manifestations of chronic pneumonia with pleural effusion, the initial partial response to steroid treatment, and the delay in recognizing the mold contributed to delayed diagnosis of this disease.

The isolate was not susceptible to fluconazole (MIC 48 µg/mL).

Although the National Committee for Clinical Laboratory Standards does not have a standard susceptibility method and MIC breakpoint of fluconazole for defining susceptibility against *C. immitis*. Fluconazole has been recommended as a drug of choice for treating meningeal coccidioidomycosis, particularly in patients with underlying renal disease or with disease-associated renal function deterioration (4,5). Immunocompromise secondary to steroid use, as well as resistance of the isolate to fluconazole, may have contributed to treatment failure in this patient.

With increasing international travel, physicians should consider those diseases that are endemic in regions where their patients have traveled. In addition to tuberculosis, melioidosis, and penicilliosis marneffii, coccidioidomycosis should be included in the differential diagnosis of chronic pneumonia in Taiwan, considering the number of residents who travel. Only then can prompt microbial investigations be conducted to accurately diagnosis and determine the appropriate antifungal treatment.

**Cheng-Yi Wang,* Jih-Shuin Jerng,*
Jen-Chung Ko,† Ming-Feng Lin,†
Cheng-Hsiang Hsiao,* Li-Na Lee,*
Po-Ren Hsueh,*
and Sow-Hsong Kuo***

*National Taiwan University Hospital, Taipei, Taiwan; and †Hsin-Chu General Hospital, Hsinchu, Taiwan

References

1. Kirkland TN, Fierer J. Coccidioidomycosis: a reemerging infectious disease. *Emerg Infect Dis.* 1996;2:192-9.
2. Chen CH, Shih JF, Hsu YT, Perng RP. Disseminated coccidioidomycosis with lung, skin and lymph node involvement: report of a case. *J Formos Med Assoc.* 1991;90:788-92.
3. Desai SA, Minai OA, Gordon SM, Neil BO, Wiedemann HP, Arroliga AC. Coccidioidomycosis in non-endemic areas: a case series. *Respir Med.* 2001;95:305-9.
4. Chiller TM, Galgiani JN, Stevens DA. Coccidioidomycosis. *Infect Dis Clin North Am.* 2003;17:41-57.

5. Galgiani JN, Ampel NM, Catanzaro A, Johnson RH, Stevens DA, Williams PL. Practice guideline for the treatment of coccidioidomycosis. *Clin Infect Dis*. 2000;30:658–61.

Address for correspondence: Po-Ren Hsueh, Departments of Laboratory Medicine and Internal Medicine, National Taiwan University Hospital, National Taiwan University College of Medicine, 7 Chung-Shan South Rd, Taipei, Taiwan; fax: 886-2-23224263; email: hsporen@ha.mc.ntu.edu.tw

Kytococcus schroeteri Endocarditis

To the Editor: Becker et al. recently reported the probable implication of *Kytococcus schroeteri* in a case of acute prosthetic valve endocarditis, on the basis of its recovery from blood cultures drawn at the time of infection (1). *K. schroeteri* was only characterized on that occasion and is a new micrococcal species resistant to penicillins (2). Here, we report the isolation of this organism from prosthetic valve vegetations in a patient who had undergone aortic valve replacement 3 years earlier. The 73-year-old man was admitted with fever (38.8°C) and shortness of breath, which had both increased gradually over the previous 2 months. He had no recent history of intravenous drug administration or catheterization. Laboratory findings showed a leukocyte count of $12 \times 10^9/L$ (90% neutrophils) and a raised C-reactive protein level. Transesophageal echocardiogram revealed several small vegetations on the Carpentier-Edwards aortic bioprosthesis and a voluminous perivalvular abscess. Four sets of blood cultures were drawn before antimicrobial therapy was initiated.

Intravenous vancomycin (2 g twice a day) and gentamicin (240 mg/d) were started empirically. The prosthetic material was replaced promptly and the abscess was debrided extensively. Vegetations from the resected material showed numerous polymorphonuclear neutrophils and gram-positive cocci on microscopic examination. Oral rifampicin (600 mg twice a day) was added to the initial regimen.

The postoperative course was uneventful except for cutaneous intolerance to vancomycin, which was replaced with teicoplanin. The physical condition of the patient improved steadily. Gentamicin and rifampicin were discontinued after 3 weeks. Eight months after completion of the 6-week treatment, the patient had no clinical or biologic evidence of infection, although moderate aortic incompetence persisted.

All blood cultures drawn on admission grew gram-positive cocci

after 72 hours and subcultures on Trypticase soy agar yielded convex, muddy-yellow colonies of heterogeneous sizes. The vegetations, pus samples of the abscess, and prosthetic valve cultures grew the same type of colonies. All isolates displayed identical biotype and antimicrobial susceptibility and were considered as a single strain. The causative organism (designated ROG140) was initially identified as *Micrococcus* sp. based on the morphologic features, resistance to nitrofurantoin, and inability to grow anaerobically. Assignment to the genus *Kytococcus* was suggested by the arginine dihydrolase activity and resistance to oxacillin, 2 characteristics that are not shared by other micrococci (3).

The definitive *K. schroeteri* identification was provided by analysis of the fatty acid content, which was similar to that of the type strain (2), and sequencing of the 16S rRNA genes.

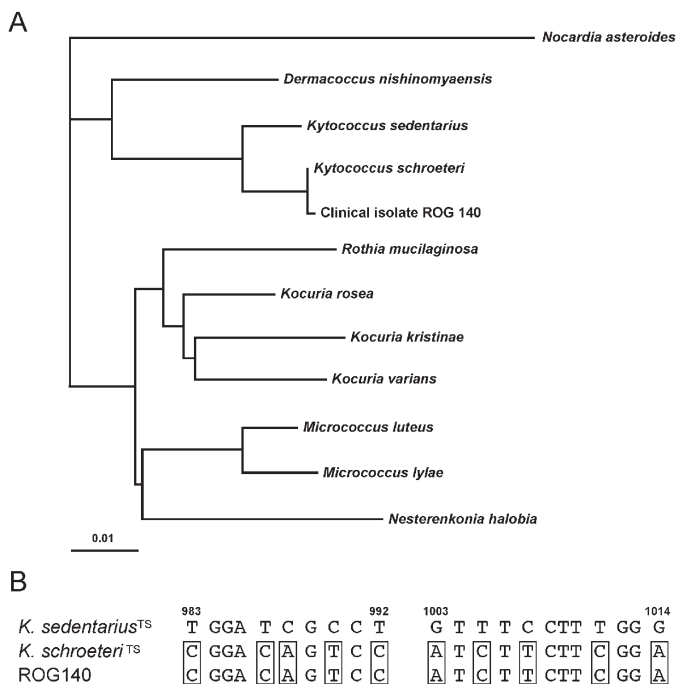


Figure. (A) Phylogenetic tree showing relationships among 16S rDNA sequences of clinical isolate ROG140 and type strains of members of the former *Micrococcus* genus. *Nocardia asteroides* was included as an out-group organism. The scale bar represents 1% differences in nucleotide sequences. (B) Sequence alignment of 16S rDNA nucleotides 983–992 and 1003–1014 of *Kytococcus* sp. type strains (TS) and clinical isolate ROG140. *K. schroeteri* molecular signatures are boxed. Nucleotide numbering refers to the sequence of the 16S rDNA of *E. coli*.