Adiaspiromycosis Causing Respiratory Failure and a Review of Human Infections Due to *Emmonsia* and *Chrysosporium* spp.

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We report a case of a 27-year-old male who presented with respiratory distress that required mechanical ventilation. Transbronchial biopsy revealed adiaspores of the fungus *Emmonsia crescens* within granulomata, a condition known as adiaspiromycosis. The patient received amphotericin products and corticosteroids, followed by itraconazole, and made a full recovery. *Emmonsia crescens* is a saprobe with a wide distribution that is primarily a rodent pathogen. The clinical characteristics of the 20 cases of human pulmonary adiaspiromycosis reported since the last comprehensive case review in 1993 are described here, as well as other infections recently reported for the genus *Emmonsia*. Pulmonary adiaspiromycosis has been reported primarily in persons without underlying host factors and has a mild to severe course. It remains uncertain if the optimal management of severe pulmonary adiaspiromycosis is supportive or if should consist of antifungal treatment, corticosteroids, or a combination of the latter two. The classification of fungi currently in the genus *Emmonsia* has undergone considerable revision since their original description, including being grouped with the genus *Chrysosporium* at one time. Molecular genetics has clearly differentiated the genus *Emmonsia* from the *Chrysosporium* species. Nevertheless, there has been a persistent confusion in the literature regarding the clinical presentation of infection with fungi of these two genera; to clarify this matter, the reported cases of invasive *Chrysosporium* infections were reviewed. Invasive *Chrysosporium* infections typically occur in impaired hosts and can have a fatal course. Based on limited *in vitro* susceptibility data for *Chrysosporium zonatum*, amphotericin B is the most active drug, itraconazole susceptibility is strain-dependent, and fluconazole and 5-flucytosine are not active.

Adiaspiromycosis is primarily a pulmonary infection of rodents, fossorial mammals, and their predators and is caused by the soil fungi *Emmonsia crescens* and *Emmonsia parva* (17, 30, 35, 53). It is a rare human infection. In this infection, inhaled *Emmonsia* conidia enlarge to form nonreplicating adiaspores. As in other mammals, the infection in humans usually involves the lungs, with only a few other cases of infection at other sites (17, 30, 35, 53). About 70 cases of human adiaspiromycosis have been described, but much of the literature on this infection has been dispersed in less-accessible, non-English journals. Furthermore, the inconsistent nomenclature and taxonomy of *Emmonsia* species and their confusion with *Chrysosporium* species has resulted in an overall lack of consistent information on adiaspiromycosis and *Chrysosporium* infections. Herein, we report a case of adiaspiromycosis that resulted in respiratory failure. We also review the true cases of adiaspiromycosis that have been reported since the seminal monographs of England and Hochholzer in 1993 (21) and Sigler in 2005 (53) or omitted from those reports. Furthermore, we differentiate the cases of adiaspiromycosis from the true and probable cases of invasive disease due to the genus *Chrysosporium*. In 2011, Pelegrin and coworkers (44) also reviewed cases of adiaspiromycosis, but again, the nomenclature adopted by the authors was inaccurate, and the genera *Emmonsia* and *Chrysosporium* were not appropriately distinguished.

**CASE REPORT**

A 27-year-old Hispanic male presented in July 1998 with a 5-day history of nonproductive cough, dyspnea, pleuritic chest pain, and weight loss. Initial vital signs were temperature of 99.2°F, blood pressure of 112/67, pulse of 104 per minute, and respiration rate 22 breaths per minute. On exam, there were crackles throughout both lung fields. A chest X-ray showed marked bilateral interstitial infiltrates (Fig. 1). The white blood cell count was 15,800/mm³ (85% polymorphonuclear leukocytes, 6% lymphocytes, 4% monocytes, 5% eosinophils). The hemocrit, platelet count, and routine serum chemistry values were within normal limits, except for aspartate and alanine transaminase levels of 45 and 104 U/liter, respectively. An arterial blood gas measurement on room air showed pH 7.49, P CO₂ 31 mm Hg, and P O₂ 50 mm Hg. The impression was miliary tuberculosis or pneumocytosis, and the patient receivedisoniazid, rifampin, pyrazinamide, ethambutol, and trimethoprim-sulfamethoxazole. The patient had emigrated from Mexico 2 years prior to his presentation and had worked at a construction site near San Antonio (TX). He denied recent travel.

Bronchoscopy with transbronchial biopsy was performed on hospital day 3. Acid-fast stain and culture of the biopsy specimen were negative. The Gomori’s methenamine-silver (GMS)-stained and hematoxylin and eosin-stained biopsy specimens showed greater-than-10 thick-walled, capsulated structures (either empty or with a few internal globules) centrally in nonnecrotizing granulomas (Fig. 2). The structures were 35 to 40 μm in diameter. The initial impression was coccidioidomycosis. The patient received one dose of fluconazole and then amphotericin B 40 mg intravenously (i.v.) per day. The antimycobacterial drugs and trimethoprim-sulfamethoxazole were discontinued.

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doi:10.1128/JCM.00226-11
Serologic studies for coccidioidomycosis, however, were repeatedly negative. Other negative studies included the following: viral and routine cultures, urine *Histoplasma* and *Legionella* antigens, serum cryptococcal antigen, and serologic tests for human immunodeficiency virus, *Mycoplasma*, *Toxocara*, and *Chlamydia*.

Despite treatment with amphotericin B, the patient’s respiratory status deteriorated. On day 13, methylprednisolone at 100 mg i.v. four times daily was started. Later that day, the patient went into respiratory failure and required mechanical ventilation. On day 16, amphotericin B was changed to amphotericin B lipid complex at 5 mg/kg/day, because the patient developed renal tubular acidosis. An open lung biopsy was performed on day 18, and it showed only scattered fragments of GMS-positive material.

At this point, the histopathology specimen from the original transbronchial biopsy was reviewed again, and a diagnosis of adiaspiromycosis due to *Emmonsia crescens* was made, based on the size of the adiaspores (35 to 40 μm). The patient’s pulmonary status was gradually improving. He was weaned from mechanical ventilation after 6 days. Amphotericin B lipid complex was discontinued on day 25, and itraconazole 200 mg orally each day was started. A computed tomography scan performed on day 26 showed diffuse bilateral interstitial thickening (Fig. 3). Three days before hospital discharge, pulmonary function tests showed a moderate restrictive defect. The patient was discharged on tapering prednisone and itraconazole 200 mg orally daily for 12 days. At follow-up 3 months after discharge, the patient was asymptomatic, and he had returned to his previous weight.

With the diagnosis of this unusual mycosis, the patient was interviewed again about exposures. He reported that 2 weeks prior to the onset of his illness he disposed of a partially decomposed cat carcass at his construction worksite and that some debris showered down upon his face at that time.

**MATERIALS AND METHODS**

To find previously published cases of infection due to the genera *Emmonsia* and *Chrysosporium*, MEDLINE was searched from 1965 to August 2011. Additional cases were found by bibliographic branching. Papers in non-English languages were translated into English by using the program Babel Fish (Yahoo).

**RESULTS AND DISCUSSION**

Review of adiaspiromycosis: history of the description of the organisms and their nomenclature and taxonomy. The nomenclature and taxonomy of the fungi involved in adiaspiromycosis has been a source of ongoing confusion, which has caused many authors to lump infections due to *Chrysosporium* species together with those caused by *E. crescens* and *E. parva*, and so the clinical presentation of disease caused by the two genera has been quite muddled in the literature (40, 41, 44, 63, 68, 69).

The circuitous history of the taxonomy of these organisms has been recounted by Sigler (53). In 1939, Kirschenblatt described cystic structures in the lungs of rodents from the former Soviet Union and proposed that these were due to a fungus, which he named *Rhinosporidium pulmonale* (28). In 1942, Emmons and Ashburn observed spherical nonbudding cells of up to 14 μm in diameter in the lungs of rodents in Arizona; they thought this fungus was a zygomycete, and so they placed it in the genus *Haplosporangium* and used the species epithet *H. parvum* because of the small size of its sporangium (19). In 1947, Dowding observed fungal cells, of up to 300 μm in diameter, in the lungs of rodents...
from Alberta (16). Although this fungus resembled *H. parvum* in its culture characteristics and microscopic appearance, it formed both larger cells in vivo and larger chlamydospores when grown at 37°C. In 1951, it was determined that *H. parvum* was not a zygo-/mycete and was closely allied to the genus *Blastomyces* on the basis of conidial characteristics (7). Ciferri and Montemartini created the new monotypic genus *Emmonis* for *H. parvum* in 1959 (10), and in 1960 Emmons and Jellison (20) added *E. crescens* (the fungus from the Alberta rodents). The two species were differentiated by the size of their adiaspores and maximum growth temperatures (53).

The confusion commenced in 1962 when Carmichael broad-/ened the genus *Chrysosporium* to include all fungi that produce aleuroconidia, solitary single-cell conidia that are released by dis-/integration of the supporting structure (8), which included *Emmonis*. Furthermore, Carmichael treated *E. parvum* and *E. cres-/cens* as varieties of the same species. Thus, *E. parvum* and *E. cres-/cens* were renamed *C. parvum* var. *parvum* and *C. parvum* var. *crescens*, respectively (8). Some mycologists embraced the reclass-/ification (33), but others advocated retaining the genus name *Emmonsia* but also designating the two species as varieties, i.e., *E. parvum* var. *parvum* and *E. parvum* var. *crescens* (66).

Currently, fungi of the genera *Emmonsia* and *Chrysosporium* are classified in the ascomycete order *Onygenales*, families *Ajello-/mycetaceae* and *Onygenaceae*, respectively. Other members in the *Ajellomyctaceae* of medical significance include the genera *Bla-/stomyces* and *Histoplasma*, and also *Paracoccidioides brasiliensis*, whereas the genus *Coccidioides* has also been placed in the *Ony-/genaceae* (65). (For a comparison of the genus *Emmonsia* with these genera, see Sigler (53).)

In 1996, Sigler described the telemorph (meiotic stage) of *E. cres-/cens*, *Ajellomycetes crescens*, which is the same genus in which the telemorphs of *Blastomyces dermatitidis* and *Histoplasma capsula-/tum* are contained. Genetic sequencing of these fungi confirmed the relatedness of the genus *Emmonsia* to the genus *Blastomyces* (34, 46); in fact, *E. parva* is more closely related to the genus *Bla-/stomyces* than to *E. crescens*. It would be justified, based on genetic analyses, to place the *Emmonsia* species in the same genus as *Bla-/stomyces*. However, because of the chaos that would ensue from a genus-level name change of these medically significant fungi, the genera *Blastomyces* and *Histoplasma* have retained their current names (46, 53). Also, it is appropriate that *E. parva* and *E. crescens* be considered distinct species (46, 53).

In 1998, a cutaneous mycosis was reported in an AIDS patient; histopathologic analysis of the skin revealed small yeast-like bud-/ding cells (2 to 4 μm in diameter), larger thick-walled cells (8 to 10 μm in diameter), and pseudohyphae. In culture, the fungus was morphologically compatible with the genus *Emgonsia* but was genetically distinct from *E. parva* and *E. crescens* and was described as a new species, *E. pasteuriana* (23).

In a case of a pulmonary infection observed in a rheumatoid arthritis patient, fungi were observed within the macrophages ob-/tained from a bronchoalveolar lavage. The fungus was identified as a possible new *Emmonsia* species based on genetic sequencing, but adiaspores were not observed in the biopsy specimen (74).

Recently, Pelegrin and coworkers (44) reported a case described as disseminated adiaspiromycosis in an HIV-infected liver transplant patient who suffered multiple skin lesions. A skin biopsy revealed multiple GMS-staining organisms; however, these clearly were not adiaspores. The investigators were able to culture the fungus, but the isolate could not be identified to the species level because its genetic sequence did not closely agree with those of the reference strains. There was 95% similarity with *E. crescens*, 94% with *E. parva*, and 91% with *E. pasteuriana* (23), so the fungus was placed in the genus *Emmonsia*.

Thus, the term adiaspiromycosis is correctly applied only when *Emmonsia* adiaspores are observed in tissue and should not be used in cases where *Emmonsia* isolates produce yeast-like (23) or hyphal (44) forms in tissue or for infections due to fungi of the genus *Chrysosporium* (as in reference 57).

**Clinical presentation of human *Emmonsia* infection.** The first human case of *Emmonsia* infection, presenting as a solitary pulmonary nodule, was reported in 1964 (14). Disseminated human pulmo-/nary disease was first observed in 1971 (29). Approximately 67 probable cases of human pulmonary adiaspiromycosis due to *E. crescens* have been described in the literature. England and Hoch-/holzer, in their 1993 case series and review (21), identified 46 cases; there have been 20 other cases reported since that time or that were omitted from the England and Hochholzer review (6, 11, 13, 15, 31, 32, 36, 37, 38, 40, 50, 51, 52, 56, 60, 62) (Table 1). Adiaspiromycosis may be discovered incidentally after histo-/pathologic exam of the lung for other conditions. Alternatively, the disease may have an indolent course, with fever, weight loss, fatigue, cough, hemoptysis, and dyspnea. In such cases, the chest radiograph usually shows bilateral reticulonodular infiltrates sug-gestive of miliary tuberculosis. Disseminated pulmonary infection can have a severe or even fatal course (4, 6, 21, 31, 36, 39, 45, 52, 56). The patient reported herein suffered moderate restrictive lung disease after the infection, as observed in two prior cases (cases 13 and 14 from Table 1).

In 4 of the 21 patients with pulmonary adiaspiromycosis due to *E. crescens*, the disease was discovered incidentally during the eval-/uation of other pulmonary conditions (cases 11, 12, 15, and 16 from Table 1). In the 16 other cases in which a clinical course was described, one case was fatal (case 2 from Table 1), and 5 other patients had severe disease (cases 1, 3, 9, 10, and 17 from Table 1), with 2 of these requiring mechanical ventilation (cases 1 and 17 from Table 1). Host factors were not important in the severity of the infection.

There have been two reports of adiaspiromycosis of the appen-/dix that developed after oral ingestion of the fungus (17, 30); in one of these cases, peritonitis was observed after appendiceal rupture (17). However, the reported cases of cutaneous adiaspiromy-/cosis (26, 57) and adiaspiromycosis of the cornea (68) are due to other fungi (53).

An outbreak of ocular adiaspiromycosis was reported from Brazil in 2006. Local ophthalmologists reported 18 children with conjunctival nodules to health authorities. Subsequently, 5,084 children were screened for ocular and visual changes. Active ocular disease was diagnosed in 64 children; 104 had ocular sequelae. Seventeen of the ocular nodules were biopsied; in two specimens, subconjunctival inflammation and adiaspores of *E. crescens* were observed. The investigators hypothesized that exposure to freshwater sponge spicules caused conjunctival irritation; subsequent exposure to airborne conidia of *Emmonsia* caused ocular adiaspiromycosis (35). This is a novel presentation of adiaspiromycosis and may require additional investigation to confirm the identity of the fungus that was involved in these cases.

Two cases of adiaspiromycosis reportedly due to *E. parva* have been described in AIDS patients (cases 1 and 3 in Table 2). In case
<table>
<thead>
<tr>
<th>Case no.</th>
<th>Pub yr (reference)</th>
<th>Patient age(yrs), sex</th>
<th>Location</th>
<th>Host factor</th>
<th>Species (author/nomenclature)</th>
<th>Presentation</th>
<th>Severity</th>
<th>Treatment</th>
<th>Outcome</th>
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<tbody>
<tr>
<td>1</td>
<td>This study</td>
<td>27, M</td>
<td>USA (TX)</td>
<td>None</td>
<td>Emmonsia crescens</td>
<td>Cough, dyspnea, wt loss</td>
<td>Respiratory failure</td>
<td>Ampho, Itra, Methylpred</td>
<td>Recovered</td>
</tr>
<tr>
<td>2</td>
<td>1989 (36)</td>
<td>31, M</td>
<td>Brazil</td>
<td>None</td>
<td>Emmonsia parvum var. crescens</td>
<td>Fever, cough, myalgias, dyspnea</td>
<td>Diffuse pulmonary/severe</td>
<td>Died</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>1989 (36)</td>
<td>37, M</td>
<td>Brazil</td>
<td>None</td>
<td>Chrysosporium parvum var. crescens</td>
<td>Fever, cough, dyspnea, anorexia, wt loss</td>
<td>Diffuse pulmonary/severe</td>
<td>Keto Recovered</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>1997 (11)</td>
<td>43, M</td>
<td>Brazil</td>
<td>None</td>
<td>Emmonsia parvum var. crescens</td>
<td>Fever, cough, wt loss, dyspnea, thorax pain</td>
<td>Diffuse pulmonary</td>
<td>Itra, then Pred</td>
<td>Recovered</td>
</tr>
<tr>
<td>5</td>
<td>1997 (11)</td>
<td>47, M</td>
<td>Brazil</td>
<td>None</td>
<td>Emmonsia parvum var. crescens</td>
<td>Fever, nonproductive cough</td>
<td>Diffuse pulmonary</td>
<td>None</td>
<td>Recovered</td>
</tr>
<tr>
<td>6</td>
<td>1997 (11)</td>
<td>52, M</td>
<td>Brazil</td>
<td>Prior pulmonary histoplasmosis</td>
<td>Emmonsia parvum var. crescens</td>
<td>Fever, productive cough</td>
<td>Diffuse pulmonary</td>
<td>None</td>
<td>Recovered</td>
</tr>
<tr>
<td>7</td>
<td>1997 (32)</td>
<td>35, M</td>
<td>Brazil</td>
<td>None</td>
<td>Emmonsia parvum var. crescens</td>
<td>Fever, cough, wt loss over 2 mos</td>
<td>Diffuse pulmonary</td>
<td>Keto</td>
<td>Recovered</td>
</tr>
<tr>
<td>8</td>
<td>1997 (40)</td>
<td>2, F</td>
<td>Finland</td>
<td>Asthma</td>
<td>Emmonsia parvum var. crescens</td>
<td>Fever, dry cough</td>
<td>Mild</td>
<td>Ampho</td>
<td>Recovered</td>
</tr>
<tr>
<td>9</td>
<td>1997 (51)</td>
<td>26, M</td>
<td>Brazil</td>
<td>None</td>
<td>Emmonsia parvum var. crescens</td>
<td>Fever, night sweats, cough, thorax pain</td>
<td>Diffuse pulmonary</td>
<td>Keto</td>
<td>Recovered</td>
</tr>
<tr>
<td>10</td>
<td>1998 (31)</td>
<td>18, M</td>
<td>Brazil</td>
<td>None</td>
<td>Emmonsia crescens</td>
<td>Thoracic pain, cough</td>
<td>Severe</td>
<td>Keto</td>
<td>Recovered</td>
</tr>
<tr>
<td>11</td>
<td>1999 (62)</td>
<td>51, M</td>
<td>France</td>
<td>Mesothelioma</td>
<td>Chrysosporium parvum var. crescens</td>
<td>Incidental</td>
<td>NA</td>
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<td>NA</td>
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<td>12</td>
<td>1999 (62)</td>
<td>57, M</td>
<td>France</td>
<td>Lung cancer</td>
<td>Chrysosporium parvum var. crescens</td>
<td>Incidental</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
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<tr>
<td>13</td>
<td>2000 (50)</td>
<td>29, M</td>
<td>Brazil</td>
<td>Smoker</td>
<td>Emmonsia parvum var. crescens</td>
<td>Fever, cough, pain, dyspnea, wt loss</td>
<td>Diffuse pulmonary</td>
<td>None</td>
<td>Recovered</td>
</tr>
<tr>
<td>14</td>
<td>2000 (50)</td>
<td>54, M</td>
<td>Brazil</td>
<td>Not specified</td>
<td>Emmonsia parvum var. crescens</td>
<td>Fever, headache, myalgia, nausea, wt loss</td>
<td>Diffuse pulmonary</td>
<td>Keto</td>
<td>Recovered</td>
</tr>
<tr>
<td>15</td>
<td>2001 (38)</td>
<td>45, M</td>
<td>Brazil</td>
<td>None</td>
<td>Emmonsia parvum var. crescens</td>
<td>Incidental</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>16</td>
<td>2004 (37)</td>
<td>60, M</td>
<td>Brazil</td>
<td>Lung cancer</td>
<td>Emmonsia parvum var. crescens</td>
<td>Fever, cough, dyspnea</td>
<td>Mild</td>
<td>Not reported</td>
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<tr>
<td>17</td>
<td>2006 (6)</td>
<td>25, M</td>
<td>Argentina</td>
<td>None</td>
<td>Emmonsia parvum var. crescens</td>
<td>Cough, dyspnea</td>
<td>Respiratory failure</td>
<td>Ampho, Itra</td>
<td>Recovered</td>
</tr>
<tr>
<td>18</td>
<td>2007 (60)</td>
<td>74, F</td>
<td>USA (NY)</td>
<td>Cancer, pulmonary radiation</td>
<td>Emmonsia crescens</td>
<td>Nonproductive cough</td>
<td>Mild</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
<tr>
<td>19</td>
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<td>United Kingdom</td>
<td>Lung cancer</td>
<td>Emmonsia parvum var. crescens</td>
<td>Incidental</td>
<td>NA</td>
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</tr>
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</table>

*a* Year of publication and reference number.

*b* Ampho, amphotericin B; Itra, itraconazole; Keto, ketoconazole; Vori, voriconazole; Methylpred, methylprednisolone; Pred, prednisone.

*c* Misidentified; should be E. crescens.

*d* NA, not applicable.

*e* Not specified, but appears to be E. crescens.
<table>
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<th>Case no.</th>
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<th>Patient age (yrs), sex</th>
<th>Location</th>
<th>Host factor</th>
<th>Species (author nomenclature)</th>
<th>Presentation</th>
<th>Organ(s) affected/severity</th>
<th>Treatment</th>
<th>Outcome</th>
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<td>1</td>
<td>1993 (18)</td>
<td>32, M Colombia</td>
<td>HIV infection</td>
<td>C. parvum var. parvum</td>
<td>Wrist pain, swelling</td>
<td>Extensive skin ulcers</td>
<td>Lungs, bones/widespread</td>
<td>Amphotericin B</td>
<td>Recovered</td>
</tr>
<tr>
<td>2</td>
<td>1998 (23)</td>
<td>40, F France</td>
<td>AIDS</td>
<td>E. pasteuriana</td>
<td>Cough, dyspnea, fever, fatigue</td>
<td>Diffuse pulmonary/severe</td>
<td>Skin/widespread</td>
<td>Amphotericin B</td>
<td>Died, unrelated cause</td>
</tr>
<tr>
<td>3</td>
<td>1999 (64)</td>
<td>40, M Israel</td>
<td>AIDS, smoker</td>
<td>E. parva var. parvum</td>
<td>Dyspnea, fever, fatigue</td>
<td>Diffuse pulmonary/moderate</td>
<td>Skin/widespread</td>
<td>Fluconazole, Itraconazole</td>
<td>Recovered</td>
</tr>
<tr>
<td>4</td>
<td>2003 (74)</td>
<td>64, M Germany</td>
<td>RA</td>
<td>E. sp.</td>
<td>Multiple skin nodules, asthenia, anorexia</td>
<td>Chronic, relapsing</td>
<td>L-AB</td>
<td>Amphotericin B</td>
<td>Died</td>
</tr>
<tr>
<td>5</td>
<td>2011 (44)</td>
<td>46, M Spain</td>
<td>HIV, liver transplant</td>
<td>E. sp.</td>
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</table>

*Year of publication and reference number.

Ampho, amphotericin B; Flu, fluconazole; Itra, itraconazole; L-AB, liposomal amphotericin B.

Emmonsia parva, based on nomenclature system used in our study.

RA, rheumatoid arthritis, on corticosteroids.

Based on genetic analysis, this isolate was placed in the genus Emmonsia, but it is not E. crescens or E. parva.
after necrosis, pulmonary nodules due to fungi of the genus Coccioidiodes may contain empty spherules (43). Nevertheless, these are usually smaller than the adiaspores of Emmonsia crescens, with thinner walls. One of the tissue forms of R. seeberi, the sporangium, typically measures 100 to 200 μm but has thinner walls than E. crescens and distinct endosporulation (73). The other tissue form of R. seeberi is the trophocyte, which is 10 to 100 μm in diameter and has a flocculent cytoplasm and a single nucleus. Thus, these tissue forms of R. seeberi have an internal structure much different from the adiaspores of the Emmonsia species (73).

The diagnosis of adiaspiromycosis due to E. crescens for the patient described in this case report is based on the size of the adiaspores (35 to 40 μm) and the absence of endosporulation. Although the adiaspores were smaller than the average size for E. crescens reported by England and Hochholzer (21), the patient was ill for a very short period of time (5 days) before seeking medical attention. The adiaspore size observed in the patient in this case is within the reported size range of 25 to 400 μm for E. crescens adiaspores and larger than those of E. parva (53).

Epidemiology of human adiaspiromycosis. As summarized in Table 1, the average age of the patients was 40 years, with a range of 2 to 74 years; 90% were male, probably because of greater occupational exposures to dusts. Previous cases of adiaspiromycosis have been reported from North America (Guatemala, Honduras, and the United States [Arizona, Georgia, North Carolina, New York, and Oklahoma]), South America (Argentina, Brazil, and Venezuela), and Europe (the former Czechoslovakia, France, Germany, and the former Soviet Union, Spain) (21, 53). New countries from which the disease has been reported are Finland and the United Kingdom (13, 40); however, 62% of the 21 new cases from Table 1 were reported from Brazil (11, 31, 36, 37, 38, 50, 51, 56). It is unclear if E. crescens is more common in Brazil or if this is simply reporting bias. However, because E. crescens has been observed in more than 100 species of mammals on all continents except Africa and Australia (53), it is expected that human cases would be observed in many different locales.

The patient described in this case report probably encountered the organism in his occupation as a carpenter at a construction site. In most previous cases of adiaspiromycosis, the persons had had occupations with soil or dust exposure (21). The patient described here specifically remembered inhalation of soil at his work site 2 weeks prior to the onset of symptoms. A time frame of several weeks is typical for the granulomatous reaction to occur in the lungs in response to the presence of the fungus or for adiaspiromycosis to develop in experimentally induced disease (2, 53).

Treatment of adiaspiromycosis. The most appropriate treatment for adiaspiromycosis is unknown (71). Many human cases are self-limited or asymptomatic, but several cases that have resulted in respiratory failure (including death) have been reported (4, 6, 21, 31, 36, 45, 52, 56). In the cases of adiaspiromycosis reported in Table 1, 57% of the patients were treated with an antifungal agent.

Recently, the susceptibility of an isolate of E. crescens to various antifungal agents was determined (5). The MICs (in μg/ml) of amphotericin B, itraconazole, voriconazole, caspofungin, fluconazole, and 5-fluorocytosine were 0.06, 0.12 to 0.25, 0.06, 0.5, 64, and 8, respectively, with no significant differences in susceptibilities between the aleuroconidia and adiaspores. Only amphotericin B was fungicidal (5). The susceptibility to azoles was similar to that of Histoplasma and Blastomyces (42).

Anecdotally, clinical improvement in patients with adiaspiromycosis has been reported using a number of drugs, including ketoconazole (cases 3, 7, 9, 10, and 14 from Table 1), pimafucin (4, 29), levamisole (4), thiabendazole (4), 5-fluorocytosine (47), itraconazole (cases 1, 4, and 20 from Table 1), voriconazole (case 19 from Table 1), and amphotericin B (cases 1, 2, 8, and 17 from Table 1). However, it is uncertain if antifungal treatment accelerated recovery or if this was merely the natural history of the infection. Patients appeared to benefit from corticosteroids in three previous cases (cases 4 and 21 from Table 1 and a case described in reference 29), and in the case described herein as well; this intervention seems reasonable in the immunocompetent patient because the major pathogenic effect of the fungus is due to the host granulomatous response. In severe pulmonary adiaspiromycosis in the immunocompetent host, it is reasonable to give both antifungal treatment to destroy the organism that provokes the inflammation and corticosteroid treatment to modulate that response. The disease is so rare that controlled clinical trial data will never be available; however, an animal model may be able to suggest if antifungal treatment, corticosteroids, both, or neither may be beneficial.

Review of Chrysosporium infection. Chrysosporium is a large genus of saprobic soil fungi that includes over 60 species (67). Many of the species are keratinolytic, breaking down shed keratinized residues, such as hair and feathers (1). Chrysosporium species may be encountered in the laboratory as contaminants of cutaneous and respiratory samples but are occasionally isolated as possible agents of human dermatomycoses (12). The most common Chrysosporium species encountered as contaminants or likely to be confused with known pathogens include Chrysosporium anamorph of Arthroderma curreyi, Chrysosporium anamorph of Arthroderma cuniculi, C. georgi, C. lobatum, C. earmichaeli, C. evolceanui, C. keratinophilum, Chrysosporium anamorph of Aphanosus fusivcens, C. articulatum, and C. tropicum (27). The Chrysosporium species that have been isolated from human nail and superficial skin infections include C. keratinophilum, C. tropicum, and C. queenslandicum (12). The Chrysosporium species have rarely been associated with invasive disease, but in immunocompromised patients a few of the species have been shown to be aggressive opportunistic pathogens.

Some of the Chrysosporium species share the teleomorph genus Arthroderma with species of dermatophytes (27, 61). They can be recovered on selective media used for dermatophytes (61) and on potato dextrose agar (1). The common species of Chrysosporium can usually be differentiated by the morphology, location, and size of the conidia (3, 27); however, many species share similar features, and definitive identification may require genetic sequencing (67). The mycology atlases of de Hoog and coauthors (12) and of Kane and coauthors (27) have excellent diagrams to differentiate common species of Chrysosporium from those of Emmonsia. Unlike E. crescens and E. parva, specimens from Chrysosporium infections reveal hyphae within the tissue (49, 59, 69). Unfortunately, in several of the cases of reported Chrysosporium infection, the fungus was not identified to the species level and the specimen was not banked to allow a definitive identification (48).

Table 3 shows the 11 reported cases of invasive or localized Chrysosporium infection. Species reported include C. zonatum (49, 54), C. tropicum (24), the Chrysosporium anamorph of Nannizziopsis vriesii (58), and several unidentified or unclassified spe-

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<table>
<thead>
<tr>
<th>Case no.</th>
<th>Pub yr (reference)a</th>
<th>Patient age (yrs), sex</th>
<th>Place</th>
<th>Host factor</th>
<th>Species</th>
<th>Organ(s) affected</th>
<th>Disease severity</th>
<th>Treatmentb</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1984 (59)</td>
<td>24, M USA (NY)</td>
<td>None</td>
<td>Chrysosporium sp.</td>
<td>Bone</td>
<td>Localized osteomyelitis</td>
<td>Ampho</td>
<td>Recovered</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1986 (63)</td>
<td>61, M USA (IL)</td>
<td>Prosthetic aortic valve</td>
<td>Chrysosporium sp.</td>
<td>Heart valve</td>
<td>Endocarditis</td>
<td>None</td>
<td>Died</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>1991 (69)</td>
<td>18, F USA (MN)</td>
<td>Bone marrow transplant</td>
<td>Chrysosporium sp.</td>
<td>Sinuses, brain, lungs</td>
<td>Disseminated</td>
<td>Ampho, 5FC</td>
<td>Died</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>1998 (54)</td>
<td>NA' Japan</td>
<td>Prior tuberculosis</td>
<td>Chrysosporium zonatum</td>
<td>Allergic pneumonitis/fungal ball</td>
<td>Colonization</td>
<td>Itra, then Ampho</td>
<td>Died</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>1999 (49)</td>
<td>15, M Greece</td>
<td>Chronic granulomatous disease</td>
<td>Chrysosporium zonatum</td>
<td>Lungs, pericardium, bones</td>
<td>Disseminated</td>
<td>Ampho, then Itra, then L-AB</td>
<td>Relapsed, recovered</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>1999 (68)</td>
<td>43, M Saudi Anbia</td>
<td>None</td>
<td>Chrysosporium parva</td>
<td>Cornea</td>
<td>Localized</td>
<td>Surgery, topical Mico, topical Ampho, oral Flu</td>
<td>Relapsing, recovered</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>2002 (22)</td>
<td>50, F Malaysia</td>
<td>Neutropenia</td>
<td>Chrysosporium sp.</td>
<td>Lungs, skin, brain, sinus, blood</td>
<td>Disseminated</td>
<td>Ampho, Itra</td>
<td>Recovered</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>2002 (25)</td>
<td>NA Japan</td>
<td>Prior tuberculosis</td>
<td>Chrysosporium zonatum</td>
<td>Allergic pneumonitis/fungal ball</td>
<td>Colonization</td>
<td>Pred, Itra; intracav. Ampho</td>
<td>Recovered</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>2004 (57)</td>
<td>35, M USA (NY)</td>
<td>Heart transplant</td>
<td>Chrysosporium sp.</td>
<td>Skin</td>
<td>Localized</td>
<td>Topical Ciclopirox, oral Flu</td>
<td>Recovered</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>2005 (58)</td>
<td>38, M Nigeria</td>
<td>AIDS</td>
<td>CANVc</td>
<td>Brain, sinus, lungs</td>
<td>Disseminated</td>
<td>Vori, ARV</td>
<td>Recovered</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>2007 (24)</td>
<td>74, M Spain</td>
<td>Diabetes</td>
<td>Chrysosporium tropicum</td>
<td>Sinus, brain</td>
<td>Severe</td>
<td>Surgery, L-AB, Flu</td>
<td>Recovered</td>
<td></td>
</tr>
</tbody>
</table>

a Year of publication and reference number.

b 5FC, 5-fluorocytosine; Ampho, amphotericin B; ARV, antiretroviral therapy; Flu, fluconazole; Intracav, intracavitary; Itra, itraconazole; Mico, miconazole; Keto, ketoconazole; L-AB, liposomal amphotericin B; Pred, prednisolone; Top, topical.

c NA, not available.

d Based on the discussion in the text, this is a misidentification.

e CANV, Chrysosporium anamorph of Nannizziopsis vriesii.
cies. Thermotolerance may be an important determinant of pathogenicity in the *Chrysosporium* species (1). Unlike adiaspiromycosis, invasive *Chrysosporium* infection occurs in the immunocompromised host and is usually disseminated at the time of diagnosis.

Eleven cases of invasive or localized *Chrysosporium* infection have been described in the medical literature (22, 24, 25, 49, 54, 57, 58, 63, 68, 69) (Table 3). Two of these cases were patients with pulmonary fungal balls (cases 4 and 8 from Table 3), and two had localized disease (cases 6 and 9 from Table 3), leaving seven cases of invasive disease (22, 24, 49, 59, 63, 69). In six of the invasive cases, there was a specific host factor that promoted the mycosis; five patients were immunosuppressed (cases 3, 5, 7, 10, and 11 from Table 3), and the other had a prosthetic heart valve (case 2 from Table 3). Five of the seven patients (71%) with invasive disease survived, including three of four patients who were highly immunocompromised (22, 49, 58). *In vitro* susceptibilities for *Chrysosporium* species are limited, and MIC data are available for four strains of *C. zonatum*: amphotericin B (≤0.06 to 0.25 μg/ml); itraconazole (0.25 to 2 μg/ml); 5-flucytosine (>128 μg/ml); fluconazole (32 to 128 μg/ml) (49). Thus, for *C. zonatum*, amphotericin B is the most active drug, with itraconazole susceptibility being strain dependent; fluconazole and 5-flucytosine are not active.

**Conclusions.** Since the seminal review of England and Hochholzer in 1993 (21), 21 cases of human pulmonary adiaspiromycosis have been reported (including the present one). Brazil has emerged as the country with the most reported cases. The new manifestation of disease of ocular adiaspiromycosis has been described but requires additional investigation to confirm the identity of the fungus that was involved in these cases. Additional pathogenic species of *Emmonsia* have been described; these do not cause adiaspiromycosis but have been reported to cause cutaneous and respiratory infections in immunocompromised patients. Molecular genetics has delineated the relationship of the *Emmonsia* species to each other and to the genera *Blastoscyropsis*, *Histoplasma*, and *Paracoccidioides*. The same techniques have also allowed differentiation of *Emmonsia* and *Chrysosporium*, but confusion regarding the two genera persists in the literature. Herein, we have endeavored to clarify the morphological and clinical characteristics of these two genera. Pulmonary adiaspiromycosis has been reported primarily in persons without underlying host factors, and it has a mild to severe course. It remains uncertain if the optimal management of patients with severe pulmonary adiaspiromycosis is supportive care, antifungal treatment, corticosteroids, or a combination of the latter two modalities. Invasive *Chrysosporium* infection typically occurs in impaired hosts and can have a severe or fatal course. Based on limited *in vitro* susceptibility data for *C. zonatum*, amphotericin B is the most active drug, itraconazole susceptibility is strain dependent, and fluconazole and 5-flucytosine are not active.

**REFERENCES**

3. Reference deleted.