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Fatal Cerebral Mycoses Caused by the Ascomycete *Chaetomium strumarium*

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Three cases of fatal cerebral mycosis in males with prior histories of intravenous drug use from the United States and Australia are reported. Infection in each case was limited to brain abscess; no other sites of infection were observed. The fungus seen by histopathology and isolated from the brain tissue in each case was identified as *Chaetomium strumarium*. This is the first report of human infection by this species, and *C. strumarium* is the second species of *Chaetomium* known to cause primary brain infection. *Chaetomium strumarium* is unusual among members of the genus *Chaetomium* in forming ascocarps covered with pale, thin-walled, flexuous hairs, a feature leading to its original placement in the genus *Achaetomium*. Presence of pinkish exudate droplets and/or crystals associated with hyphae or ascocarps, sometimes accompanied by a pinkish diffusible pigment; good growth at 42°C; and production of small conidia further distinguish this species. The brain abscess isolates were compared with isolates from prior cases of cerebral infection which had been identified as either *Chaetomium atrobrunneum* or *Chaetomium globosum*. With reidentification of one isolate originally identified as *C. globosum* to *C. atrobrunneum*, only *C. strumarium* and *C. atrobrunneum* have been confirmed to cause infection involving the brain.

The genus *Chaetomium* is a member of the subphylum Ascomycotina (family Chaetomiaceae) in which the ostiolate ascocarps (or perithecia) are covered with thick-walled, pale to dark brown, straight, elaborately branched, or coiled hairs or setae (10, 35). *Chaetomium* species are widespread in soil and plant debris, where they are important agents of cellulose degradation. Species of *Chaetomium* are occasionally encountered as contaminants in clinical specimens; however, they sometimes go unrecognized since they can present as sterile moulds. Cases of confirmed human infection are rare. Systemic mycoses have been reported to occur in three patients with acute leukemia (3, 12, 25). Isolates from the first two cases were not definitely identified, but one was tentatively identified as *Chaetomium cochliodes* (12) since ascospores were lacking. In the most recent case, attributed to *Chaetomium atrobrunneum* (25), infection involved multiple organs, including the brain. Anandi et al. (2) identified *C. globosum* as the cause of primary cerebral infection in a renal transplant recipient. Earlier, Huppert et al. (13) detected fungal hyphae in brain tissue of a patient from whom a *Chaetomium* species had been isolated from a blood clot; however, since the *Chaetomium* sp. had not been isolated from the brain, they were unable to rule out the possibility of contamination. Other infections include peritonitis caused by *Chaetomium globosum* in a patient with renal failure on chronic ambulatory peritoneal dialysis in whom resolution of the infection occurred after removal of the catheter (4), subcutaneous fistulous nodules in the perineum and lower abdomen occurring after superficial injury which were caused by *Chaetomium funicola* (15), and subcutaneous lesions caused by *C. globosum* (8) and an unidentified species (9). Although most cases of onychomycosis have been caused by *C. globosum* (21, 26, 31), one was attributed to *Chaetomium perpulchrum* (8). *Chaetomium* species also have been implicated as human allergens (17), and many species are known to produce mycotoxins (10, 27, 33).

This report describes three cases of fatal primary brain abscess caused by *C. strumarium* (1). The Australian case was reported previously but not described in detail (19). A report on the forensic aspects of the New Mexico case is in preparation (20a). *Chaetomium strumarium* is a rarely encountered but widely distributed species which was originally placed in the genus *Achaetomium* (24). The cases discussed here provided an opportunity to reexamine the taxonomy of *C. strumarium*, to describe the features which distinguish this new pathogen from other human-associated species of *Chaetomium*, and to critically reexamine two available isolates from prior cases of cerebral infection (2, 25).

MATERIALS AND METHODS

Case 1. A 28-year-old Hispanic male was admitted to Medical Center Hospital, San Antonio, Tex., on 21 December 1991 with sudden onset of left hemiplegia. He reported that about a week prior to admission, his left leg had begun feeling heavy, and approximately 4 days prior to admission, he had a seizure and fell from his bed. During the seizure, he felt both lower extremities jerk, and the jerking seemed to ascend up the trunk and to the left upper extremity. Following the seizure episode, the patient developed a progressive left hemiparesis. On admission, he complained of a frontal headache which had begun at the time of the seizure. The patient was confined in a correctional facility because of marijuana possession and had a past history of intravenous drug use and sharing of needles. He denied any homosexual behavior. He had a history of a head injury

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after a fall 14 years previously, but his wife reported no residual sequelae from it and the patient had no history of prior surgery. A computed tomography (CT) scan and magnetic resonance imaging (MRI) showed a right parietal area with white-matter edema. The patient remained hemiplegic on the left but presented no other symptoms until day 3, when he became febrile with a temperature of 38.8°C. He had a questionable systolic murmur at the pulmonic valve area. A workup for the fever, including sputum, urine, and blood cultures and a chest X ray, gave negative results. An angiogram for a possible hemorrhagic event was negative, and culture of fluid taken by lumbar puncture showed no bacteria. However, because of an increased leukocyte count on cerebrospinal fluid analysis he was treated with oxacillin, cefotaxime, and flagyl. The patient's condition began to deteriorate, but the cause of the hemiplegia and progressive lethargy remained unknown despite aggressive workup, including an echocardiogram, repeat MRI and CT scan, and tests for human immunodeficiency virus, tuberculosis, hepatitis, and *Toxoplasma* infection, all of which were negative. On 27 December 1991, he underwent a right frontal brain biopsy which showed diffuse acute cerebritis. Necrotic brain tissue and a syringe of liquefied tomato soup-colored material were sent for virus, bacterial, and fungus culture and pathology. A fungus but no bacteria grew in culture. The patient became progressively lethargic; he required intubation and became unresponsive. The repeat MRI and CT scan showed marked progressive cerebral edema with midline shift and necrotic lesions. The patient was pronounced dead on 31 December 1991. Autopsy showed several large yellow-orange abscesses (3 to 6 by 3 cm) with ragged outlines and semiliquid necrotic centers, all in the cerebrum.

The biopsy specimen consisted of a single piece of very soft tan-white tissue. Sections showed sheets of polymorphonuclear leukocytes among white-matter tracts, producing a variegate pattern of purulent material and intervening brain tissue. Gomori methenamine-silver and periodic acid-Schiff stains showed hyphal elements having periodic bulbous enlargements. Many hyphae occurred around blood vessels. A Masson-Fontana stain was only faintly positive. Acid-fast bacillus and Gram stains were negative.

The fungus isolated from the brain biopsy specimen (F3224) was sent to the University of Texas Health Science Center, San Antonio (UTHSC) (strain UTHSC 92-32), and then referred to the University of Alberta Microfungus Collection and Herbarium, Edmonton, Alberta, Canada (UAMH) (strain UAMH 7135), where it was eventually identified as *C. strumarium*.

Case 2. A 25-year-old male student who lived in Western Australia was admitted to hospital on 23 December 1986 with a 36-h history of confusion, disorientation, drowsiness, a temperature of 39.5°C, and mild neck stiffness. He had been an inmate of prison for 10 days. He was known to be a chronic multiple drug user, and on a previous admission to hospital in September 1986 for a traffic-related injury to the abdomen, he showed stigmata of intravenous drug use. He was on an extended drug withdrawal program and was thought to have ceased drug use in the month prior to his December admission. He reported prior homosexual activity and had spent some time in Malaysia. A CT scan on admission showed localized cerebral edema of the left parietal and occipital regions. An elevated lumbar puncture pressure, cerebrospinal fluid microscopy, and protein glucose suggested either viral or bacterial encephalitis, and treatment with amoxil, chloramphenicol, and acyclovir was begun. However, the fever continued and no bacteria or viruses were isolated. He also showed episodes of severe agitation which required sedation with haloperidol and diazepam and later with morphine. By 29 December 1986, the patient was comatose with irregular respirations, bradycardia, and hypertension and showed no response to painful stimuli on the right side, which was flaccid. He was then transferred to a neurosurgical unit at a different hospital. Differential diagnosis at the time of admission was encephalitis due to herpes simplex virus or *Mycobacterium* infection, and treatment with rifampin, isoniazid, and pyridoxine was added to the earlier regimen.

A brain biopsy was performed on the evening of 29 December 1986, and specimens were sent for bacterial, viral, mycobacterial, and fungal culture and for histopathology. Cultures were negative except for the fungal culture, which yielded a fast-growing fungus within 2 days. Treatment with amphotericin B was commenced, but the patient's condition had deteriorated. He had epileptiform left-side twitching; he developed an acute rise in intracranial pressure; and on 4 January 1987, he died of respiratory arrest. The diagnosis was fungal encephalitis with edema and brain stem compression.

At autopsy, the brain was markedly swollen and dry and showed multiple acute abscesses involving the centrum semioval on the left and right sides and pulvinar of the thalamus on the right. Large, roughly circular areas, in which the brain tissue was partly liquefied and hemorrhagic, were present in the left centrum, the white matter of the parieto-occipital region, and the right cerebral hemisphere. In the lower pons, a small irregular zone of tissue was discolored brown, and a similar area of discoloration was present in the lateral basis pontis on the left side. The only other abnormalities detected were modest pulmonary congestion and edema and slight enlargement of the spleen. Initial brain sections failed to show hyphae of the fungus, but recut sections demonstrated branched, septate hyphae, often with slight swellings (Fig. 1).

The fungus was recognized as an ascomycete and sent to Paul F. Cannon, International Mycological Institute, Egham, United Kingdom (IMI), (IMI 313435), where it was identified as *C. strumarium*. Susceptibility testing showed the isolate to be susceptible to amphotericin B, miconazole, and ketoconazole. A 0.4-ml suspension of ascospores of the fungus was inoculated intercranially into each of eight female ARC(s) weaned mice (random outbred strain). Three died on day 4 and one died on day 5, and *C. strumarium* was grown from brains from all of them. On day 12 two mice were euthanized, one showing spasms and the other with swelling of the brain area; *C. strumarium* was isolated from each brain. The remaining two mice were not affected.

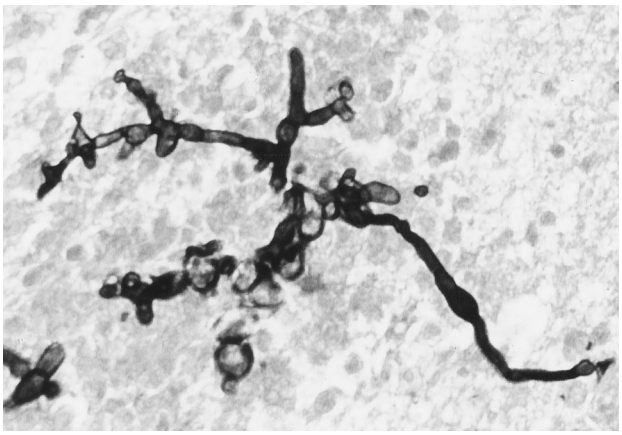

FIG. 1. Section of brain (case 2) stained with Gomori methenamine-silver showing branched septate hyphae of irregular width. Magnification, ×900.

Case 3. A 20-year-old male who had been in prison for 6 days began to have seizures and fell from his bed. The next day he was comatose. On 30 September 1994, he was admitted to Memorial Medical Center, Las Cruces, N.Mex. He had a past history of drug use, including heroin (intravenous), cocaine, and marijuana, and of use of volatiles. He was human immunodeficiency virus negative and reported no homosexual activity. A CT scan was inconclusive. Acute bacterial meningitis or herpesvirus-induced encephalitis was suspected, and the patient was treated empirically with ceftriaxone and penicillin; 4 days later, acyclovir was added to the regimen. He died 6 days after admission.

A complete autopsy was performed. Cause of death was determined as cerebral edema with herniation due to fungal encephalitis. Sections from the right and left cerebral hemispheres and deep white matter showed necrosis and dense acute inflammation and were positive for fungal elements by hematoxylin and eosin, Gomori methenamine-silver, and periodic acid-Schiff stains. Two separate specimens of the occipital cortex were positive by culture for a fast-growing fungus. The two isolates (FG-227 and FG-224) obtained by the State Laboratory, Albuquerque, N.Mex., were forwarded to UTHSC (94-2398 and 94-2399) and subsequently to UAMH (7804 and 7804A), where they were identified as *C. strumarium*.

Mycologic studies. The brain isolates were compared with ex-type cultures of *C. strumarium* (originally described as *Achaetomium strumarium*) and *Achaetomium cristalliferum* and with human-associated and saprobic isolates of *Chaetomium* species (Table 1). All strains are maintained in the UAMH. For all tests, a straight needle was inserted aseptically into a suspension of ascospores prepared for each strain in semisolid detergent agar (23) and then the needle was stab inoculated into the center of 100-mm-diameter petri plates containing various media. Since production of ascocarps (perithecia) is crucial to the identification of *Chaetomium* species, it is important to employ one or more nutritionally deficient media to obtain sporulation. For studying morphology and time to ascosporulation, cultures grown on Takashio agar (TAK) (32) and homemade cornmeal agar (HCMA) (20) were compared with those grown on Sabouraud dextrose agar (SAB; Difco Laboratories, Detroit, Mich.). Plates were examined at 7-day intervals for 4 weeks. Colonial features were recorded, and colors were determined by using the color standards of Kornerup and Wanscher (16). Microscopic preparations for detecting the presence of conidia were obtained from slide cultures grown on Pablum cereal agar without antibiotics (29) for 7 to 35 days. Mounts of whole ascocarps were prepared in polyvinyl alcohol or lactofuchsin mounting medium (29); ascospores were released by gentle pressure upon the coverslip. Ascospore germination was examined on potato dextrose agar (Difco) by the Dalmau technique (20). Growth rates were determined by measuring colony diameters on CMA (Difco) at 25, 35, and 42°C after 5, 7, and 14 days. Tests for salt tolerance at concentrations of 0, 3, 5, and 7%, tolerance of cycloheximide at 400 μg/ml, and tolerance of benomyl at 2 μg/ml were done by the methodology of Sigler et al. (30). Selected specimens were prepared by vapor fixation in 2% osmium tetroxide, dried to the critical point, and examined with a Hitachi S-2500 scanning electron microscope (SEM).

RESULTS

Morphology of *C. strumarium*. Numerous ascocarps developed on HCMA at 30 or 37°C after 14 to 21 days, but ascocarps

TABLE 1. *Chaetomium* species and strains examined

Species and strain	Source[a]	Reference
C. strumarium		
UAMH 5407	Ex-type strain[b] of *A. cristalliferum*; arid, somewhat saline soil; southwest Egypt; L. Faurel; obtained from CBS as 781.84 (=ATCC 58164)	18
UAMH 5523	Ex-type strain of *A. strumarium*; soil; Uttar Pradesh, India; obtained from J. Vederas as ATCC 58165 (=CBS 333.67 = IMI 82624 = NRRL A-10898)	24
UAMH 7135	Case 1: biopsy, fatal brain abscess, 28-yr-old male with history of drug use; Texas; =UTHSC 92-32	
UAMH 7758	Antelope dung; Kenya; J. Krug; obtained from ATCC as 58406	
UAMH 7797	Case 2: biopsy, fatal brain abscess, 25-yr-old male with history of drug use; Western Australia; obtained from IMI as 313435	19
UAMH 7804	Case 3: autopsy, fatal brain abscess, 20-yr-old male with history of drug use; New Mexico; =UTHSC 94-2399 (UTHSC 94-2398)	
C. atrobrunneum		
UAMH 7372	Fatal disseminated infection, 15-yr-old female with acute lymphoblastic leukemia; =UTHSC 90-849	25
UAMH 7760	Received as *C. globosum*; fatal brain abscess in 32-yr-old diabetic male following renal transplant; Vellore, India; T. John; obtained from ATCC as 64497 (also received from CDC as B-4561 = UAMH 7305)	2
UAMH 7761	Ex-type strain of *C. atrobrunneum*; mattress cover; Solomon Islands; G. Martin; obtained from ATCC as 58409	
C. globosum		
UAMH 7142	Indoor air by Reuter centrifugal sampling; Edmonton, Alberta, Canada; L. Sigler	
UAMH 7762	Lesion on forearm; Brazil; C. Lacaz; obtained from ATCC as 66562	8
UAMH 7763	Received as *C. perpulchrum*; fingernail; Brazil; C. Lacaz; obtained from ATCC as 66563	8

[a] Abbreviations for collections: ATCC, American Type Culture Collection, Rockville, Md.; CDC, Centers for Disease Control, Atlanta, Ga.; IMI, International Mycological Institute; NRRL, National Center for Agricultural Utilization Research, U.S. Department of Agriculture, Peoria, Ill.; UAMH, University of Alberta Microfungus Collection and Herbarium; UTHSC, University of Texas Health Science Center.

[b] Culture derived from type specimen.

were rare at 22 or 42°C up to 21 days. Ascocarp production varied among the strains. Ascocarps were sparse on TAK after 21 to 28 days and absent on SAB up to 28 days. The following observations apply to cultures after 7 days at 22°C unless noted. Colonies on HCMA grew to 65 to 70 mm in diameter and were white, with young cultures often developing a strong pink diffusible pigment (10C/D3-5 to 12C/D3-5) which turned to brown (5E/F4-5) within 14 to 28 days. Ascocarps developed in patches, appeared pallid yellowish green (3B4) to yellow (4B7), and were often associated with pink exudate droplets on setae or surrounding hyphae and with dark brown diffusible pigmentation occurring below. Although production of a pink to brown diffusible pigment is a prominent characteristic of this species, production of the pigment was highly variable on different media and at different temperatures among the studied strains. Colonies were similar on TAK but grew slightly more slowly, reaching 40 to 55 mm in diameter, and remained white with the reverse uncolored or with patches of localized brown pigment. On SAB, colonies were 65 to 72 mm in diameter, white to cream, slightly raised in the center, and cottony, with the reverse developing amber, purplish, or reddish brown pigment after 14 days. Ascocarps (perithecia) (Fig. 2 and 3) were 100 to 250 μm in diameter, subglobose, pale brown, and ostiolate with a cell wall consisting of interwoven hyphae (textura intricata [see reference 11]) or irregularly shaped cells (textura epidermoidea). Ascocarps bore many thin-walled, hyphalike appendages (setae) (Fig. 2 and 3) which measured up to 300 μm long and 3 to 4 μm wide. Setae were straight or flexuous (slightly curved), verruculose (finely roughened), septate, pale brown, and slightly thickened at the base but with hyaline tips. Asci (Fig. 4) were hyaline, cylindrical to cylindroclavate, eight spored, and evanescent. Ascospores (Fig. 5 and 6) were initially hyaline, becoming dark brown at maturity, and were smooth, fusoidal, and rarely inequilateral. They had a single apical germ pore (Fig. 6) and contained one or (rarely) several oil droplets (guttules), which were most readily visible in immature spores. Ascospores measured 13 to 17.5 (up to 21) by 8.5 to 11 μm. Crystals of various sizes and shapes were associated with hyphae or ascocarps and were most abundant at 37°C. Conidia (Fig. 7) were visible in all strains, primarily in slide culture preparations held for 14 to 35 days, but production was sparse. Conidia were produced from short, slender phialides (adelophialides, like those of *Lecythophora* species) and were hyaline, smooth, and irregularly ellipsoidal. Conidia measured up to 6 μm long by 3 μm wide.

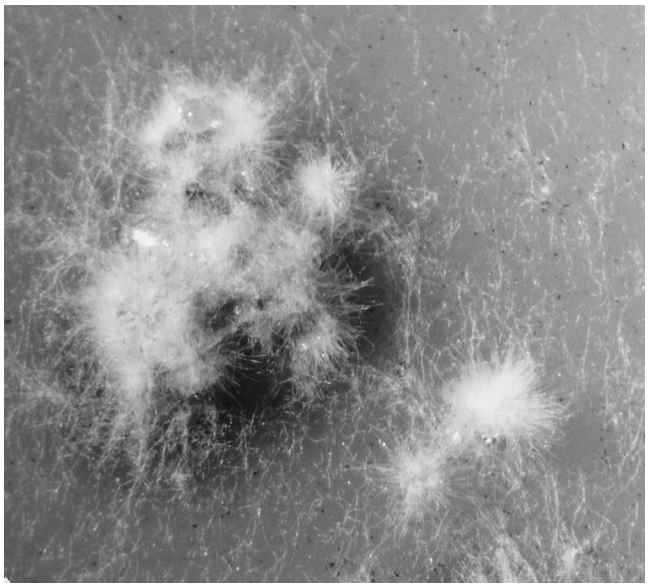

FIG. 2. *C. strumarium* UAMH 7135. Ascocarps covered with thin-walled setae viewed are visible with a dissecting microscope. Magnification, ×16.

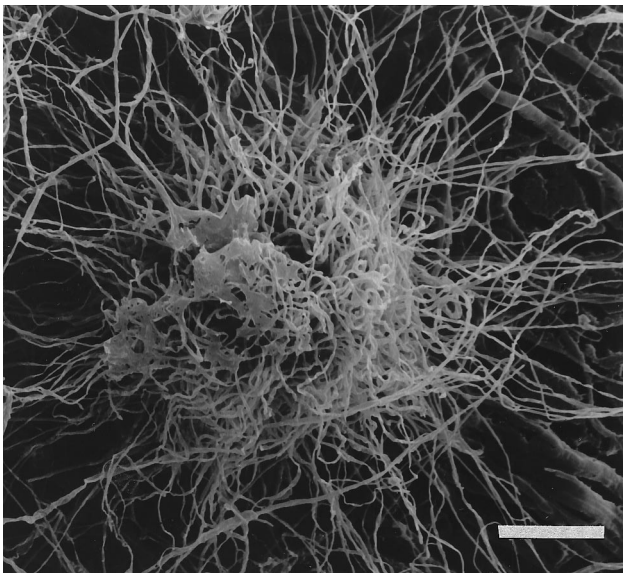

FIG. 3. *C. strumarium* UAMH 7797. SEM showing ascocarp with thin-walled setae. Bar = 50 μm.

Thermotolerance and physiologic features of *Chaetomium* species. *C. strumarium* grew fastest at 35 or 42°C, with colonies reaching the edge of the petri dish by 5 days (Table 2). *C. atrobrunneum* demonstrated a similar thermotolerance but a slower growth rate. One of these isolates (UAMH, Table 1) had been initially identified as *C. globosum* (2). No isolate of *C. globosum* grew at 42°C.

Isolates of *C. strumarium* were weakly salt tolerant (Table 2). Growth of all strains was markedly inhibited at a concentration of 3% NaCl (colony diameter range, 4 to 17 mm after 7 days). *C. atrobrunneum* and *C. globosum* were slightly more salt tolerant, but each showed some variability among strains. One isolate of *C. atrobrunneum* (UAMH 7372) was strongly inhibited at 3%. Two isolates of *C. globosum* demonstrated similar growth rates on media amended with 5 and 7% salt, but growth was markedly reduced compared with that of the control. All isolates were susceptible to cycloheximide (at 400 μg/ml) and benomyl (2 μg/ml).

DISCUSSION

The taxonomy of *C. strumarium* has been the subject of some confusion since its original description as *A. strumarium* (24).

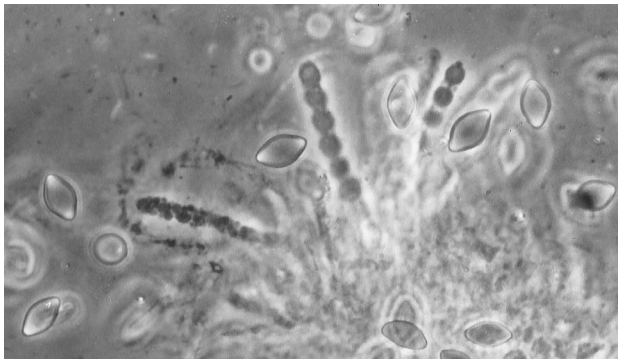

FIG. 4. *C. strumarium* UAMH 5523. Shown are cylindrical asci. Magnification, ×610.

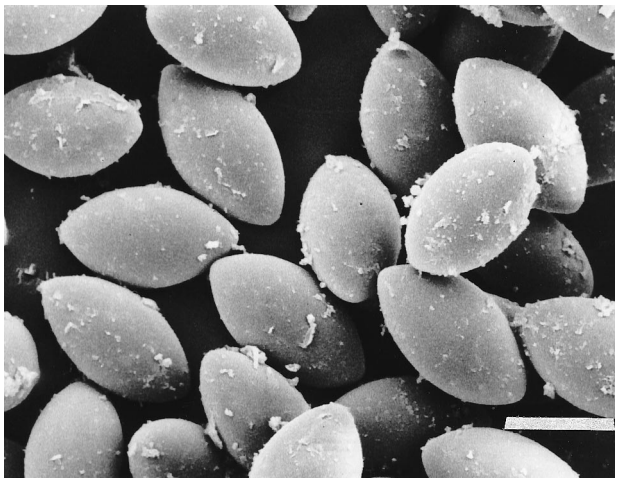

FIG. 5. *C. strumarium* UAMH 7135. SEM showing fusoidal ascospores. Bar = 10 μm.

Rai et al. (24) proposed the genus *Achaetomium* for *Chaetomium*-like fungi having ostiolate ascocarps but lacking ascomatal setae and a dark membranous ascocarp wall. Recognizing that *Achaetomium* species formed hyphalike thin-walled setae and had other characteristics compatible with *Chaetomium* species, Carter (7) accommodated them in a separate subgenus. Cannon (6) transferred *A. strumarium* and *Achaetomium luteum* to the genus *Chaetomium* but retained the genus *Achaetomium* for the type species, *A. globosum*. We agree with Cannon and Carter that *A. strumarium* is appropriately placed in the genus *Chaetomium* on the basis of similarities of asci and ascospores. Although the thin-walled setae are less conspicuous than are those of most other species of *Chaetomium* when viewed by light microscopy, they are abundant and readily visible with a dissecting microscope (Fig. 2) or by SEM (Fig. 3) and thus provide a further feature unifying *C. strumarium* with other members of the genus.

Species delimitation has also been problematic. The omission of *Achaetomium* species from modern monographic treatments of the genus *Chaetomium* (1a, 28, 35) has led to the redescription of *C. strumarium* under other names. Cannon (6) listed *A. cristalliferum* (18) and *Chaetomium spinulosum* (28) as

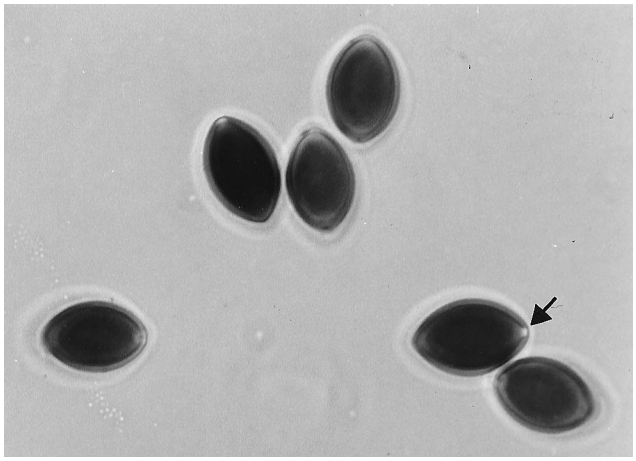

FIG. 6. *C. strumarium* UAMH 7135. Shown are mature ascospores with a single germ pore (arrow). Magnification, ×1,015.

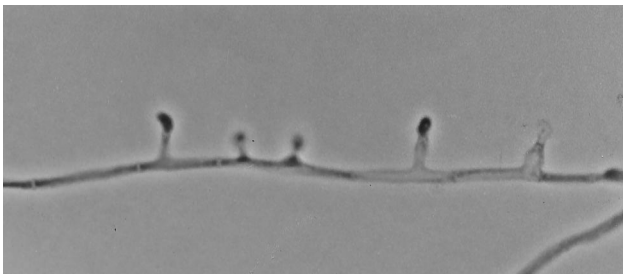

FIG. 7. *C. strumarium* UAMH 7135. Small conidia are formed on short, solitary phialides. Magnification, ×1,015.

synonyms of *C. strumarium*; *Achaetomium brevisemum* was considered a probable synonym. *Chaetomium sulphureum* (28) and *Achaetomium macrocarpum* are other possible synonyms (34).

Initial examination of the isolate from case 1 revealed many crystals in association with the hyphae and ascocarps, leading us to a preliminary identification of the organism as *A. cristalliferum*, originally described as having "crystalliferous setae" (18). However, Cannon (6) found crystal production to be variable in the ex-type culture of *A. cristalliferum* and concluded that no other features warranted specific distinction from *C. strumarium*. Although production of crystals was not reported for *C. strumarium* (6, 7, 24), our studies have shown that all isolates produce them. Their presence varies with age of cultures, temperature of incubation, and type of medium used. Other unifying features include thermotolerance, production of a pinkish exudate, presence of conidia, and a single apical germ pore on ascospores. Pigment production varied at different temperatures on different media but was most common on CMA at 25 or 37°C. Often the pigmentation was visible only as pinkish exudate droplets on the yellowish ascomatal setae. Production of the pigment was apparent also at autopsy in case 1, in which the abscesses were described as yellow-orange and the liquefied material was described as tomato soup colored. Ascospore size varied over a considerable range, even within a single strain. In the isolate from case 1, occasional macrospores, which were irregular in shape and distinctly larger than typical spores in the same mount, were observed. Such variation has been observed previously (6). Although we found variation among strains, we concluded that the brain isolates could not be distinguished from the ex-type cultures of *A. cristalliferum* and *A. strumarium*. Thus, we concur with Cannon's (6) treatment of *A. cristalliferum* as a synonym of *C. strumarium*.

C. strumarium is the second species of *Chaetomium* known to cause primary fatal brain infection. *C. atrobrunneum* caused a systemic infection which disseminated to the brain (25). We believe that *C. atrobrunneum* was also the cause of a primary fatal brain abscess originally attributed to *C. globosum* (2).

TABLE 2. Growth rates and salt tolerance of *Chaetomium* species

Species (no. of strains tested)	Colony diam (range [mm]) after 5 days on CMA at:			Salt tolerance (%)[a]
	25°C	35°C	42°C	
C. strumarium (6)	45–53	>90	>90	3
C. atrobrunneum (3)	16–21	31–36	41–44	3–5
C. globosum (3)	38–49	30–57	0	5

[a] Salt tolerance was measured as the NaCl concentration causing >50% growth inhibition at 25°C in 5 days.

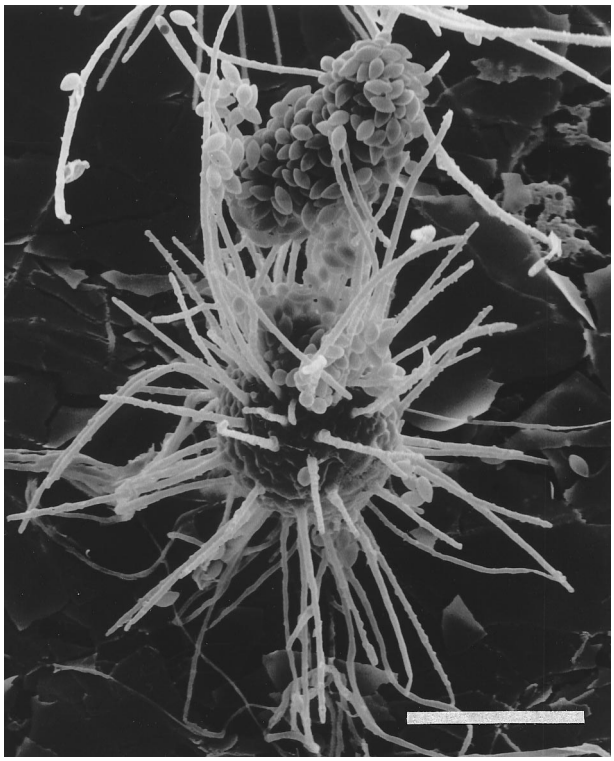

FIG. 8. *C. atrobrunneum* UAMH 7760. Shown is SEM of ascocarps with sparse, short, thick-walled setae. Bar = 50 μm.

After review of the published illustrations and examination of the strain obtained from two sources (ATCC 64497 = UAMH 7760; CDC B-4561 = UAMH 7305), we conclude that the following characteristics place the isolate from that case in the species *C. atrobrunneum*: (i) its thermotolerance; (ii) colonies which were dark grey to black rather than yellowish or greyish green; (iii) the smaller size of the ascocarps (70 to 150 μm in diameter compared with 175 to 280 μm in diameter for *C. globosum*) (Fig. 8 and 9); (iv) fewer setae, which are dark brown rather than olivaceous green, straight rather than undulate, and occasionally branched in age (Fig. 8 and 9); and (v) ascospores which are narrowly fusoidal and measure 9.3 to 10.8 μm long by 4.9 to 6.2 μm wide (Fig. 10 and 11). Our measurements disagree with those previously reported (9 to 12 by 6 to 9 μm) (2), but they agree with the range reported in the literature for *C. atrobrunneum* (9 to 11 μm long by 4.5 to 6 μm wide) (35) and our own observations on the ex-type strain.

Both *C. atrobrunneum* and *C. strumarium* showed a higher optimum temperature for growth than did *C. globosum* (Table 2). *C. globosum* (Fig. 9 and 11), the most common and widely distributed species of the genus, is validly known as a rare agent of onychomycosis (14, 21, 26, 31). Examination of *C. perpulchrum* from a fingernail (8) suggests that this isolate (UAMH 7763, Table 1) should be reidentified as *C. globosum*. Although the potential for opportunistic infection by *C. globosum* appears quite high given the ubiquitous occurrence of this species, its restricted growth at 37°C (optimum, 30°C) (data not shown) suggests that infections may be mainly confined to cooler areas of the body. Other *Chaetomium* species, including *C. funicolum* (subcutaneous) (15) and *C. cochliodes* (systemic) (12), have been reported from single cases of infection. Although we have not studied the isolate from the latter case, *C.*

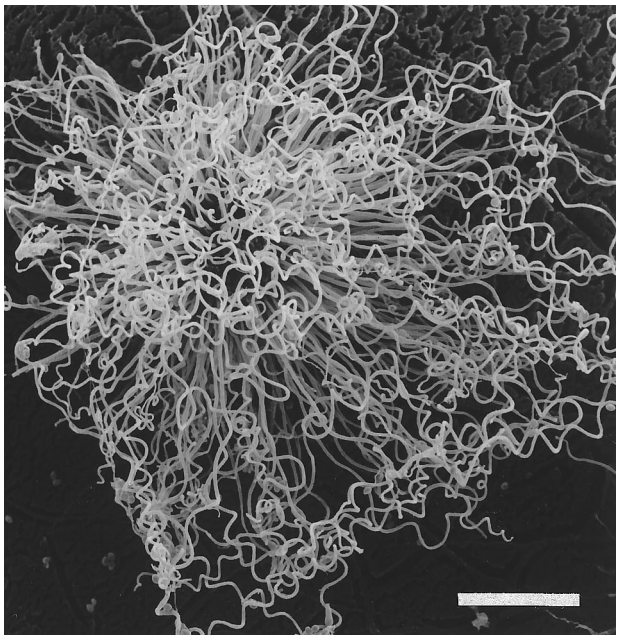

FIG. 9. *C. globosum* UAMH 7762. SEM showing ascocarp with numerous undulate or wavy, thick-walled setae. Note that ascocarps are larger than those of *C. atrobrunneum* and *C. strumarium*. Bar = 100 μm.

cochliodes has been listed as a synonym of *C. globosum* by some authors (35).

C. strumarium has a wide geographic distribution, being found in Asia, northern and southern Africa, the Canary Islands, and parts of Europe, including the United Kingdom and France, and occurs on a wide range of substrates, including soil, plant litter, dung of herbivores (zebras, camels, and gazelles), and cigarettes (6). The infections of men from the southern United States (New Mexico and Texas) and Western Australia described here extend the known distribution of the species. Although the isolation of *C. strumarium* in nature from saline soil and mangrove swamps (6, 18) suggested salt tolerance, *C. strumarium* was found to be weakly salt tolerant. Udagawa et al. (33) showed that *C. strumarium* (as *A. strumarium*) produced cytotoxic metabolites, but the single isolate examined did not produce the most potent mycotoxins chaetoglobosins and chaetomin reported for *C. globosum* (10). Bodo et al. (5) reported a new lactone, achaetolide, of polyketide origin from the ex-type strains of *A. cristalliferum* and *A. strumarium*.

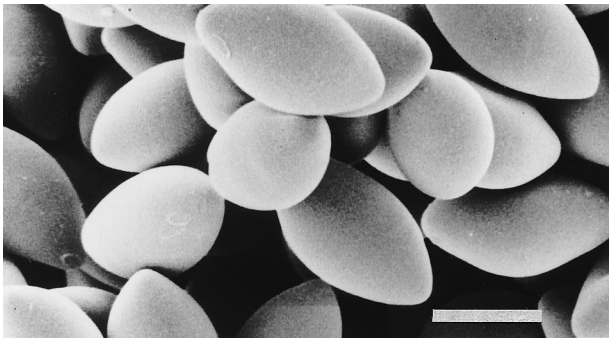

FIG. 10. *C. atrobrunneum* UAMH 7760. Shown is SEM of fusoidal ascospores. Bar = 5 μm.

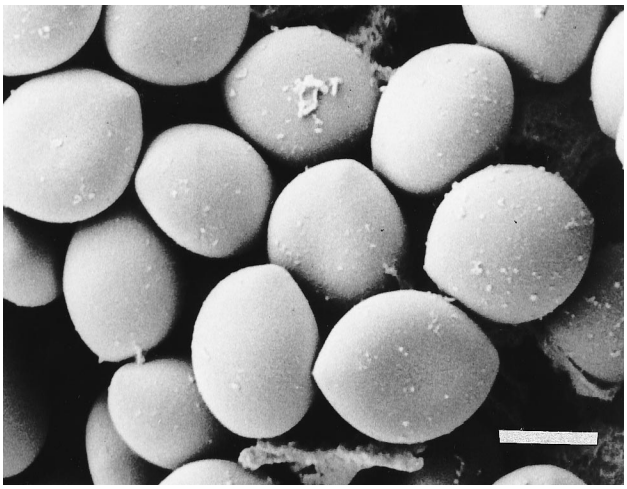

FIG. 11. *C. globosum* UAMH 7762. Shown is SEM of lemon-shaped ascospores. Bar = 5 μm.

Our cases of *C. strumarium* brain infection are remarkable for their similarity in patient history and progression of infection. Each occurred in a young adult male with a history of intravenous drug use who was in prison at the time of presentation. Pierce et al. (22) speculated that cerebral zygomycosis in intravenous drug users was most likely acquired by direct intravenous injection and subsequent hematogenous spread. As in the cases reported here, the mycoses were restricted to the brain and there was no evidence of infection at any other site. Those authors suggested that brain tissue provides an environment for rapid growth and proliferation for these fungi.

Although *C. strumarium* could be isolated without difficulty, etiology of bacterial or viral origin was initially suspected. The rapidity of progression of the infection to morbidity suggests that fungal etiology should be strongly considered in cases of brain abscess when the patient has a history of intravenous drug use. *C. strumarium* infection should be part of the differential diagnostic if the isolated fungus grows rapidly at 37 and 42°C, is white to yellowish-white, and is initially sterile. Such isolates could be confused with sterile *Aspergillus fumigatus* isolates, but transfer to a nutritionally deficient medium such as CMA should promote development of ascocarps.

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