

Caz fatal de abces cerebral produs de *Scedosporium apiospermum*

A.G. KRASOUDAKIS^{*1}, A. S. MARAKI², E. PAPADOMANOLAKI¹, A. VAKIS²,
G. ARCHONTAKIS¹, S. KASTANAKIS¹

(1) General Hospital Chania, Crete, Greece

(2) University Hospital of Heraklion, Crete, Greece

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Fatal case of brain abscess due to fungus *Scedosporium apiospermum*

Abstract: *Scedosporium apiospermum* - the asexual form of *Pseudallescheria boydii* are ubiquitous saprophytic fungi that commonly cause cutaneous infections. However in certain circumstances can also cause invasive disease which can involve the central nervous system. We described the case of an 86-year-old previously healthy man that developed acute sinusitis and was treated in ENT department. Cultures of sinus drainage specimens were negative for both fungi and bacteria. Ten days later the patient presented again in the emergency department, lethargic with a right side hemiparesis. Cranial CT and brain MRI with contrast medium revealed a left parietal intracerebral ring-enhanced lesion with surrounding brain edema. After surgical drainage of the abscess a microbiological examination of the purulent material was done and a fungal species (*Scedosporium apiospermum*) was isolated. An antifungal therapy was initiated after these results but despite this the patient's condition worsened more and finally he died due to multiple organ failure 20 days after his first admission.

Keywords: brain abscess, *Scedosporium apiospermum*, voriconazole

Rezumat: *Scedosporium apiospermum* – forma asexuată a speciei *Pseudallescheria boydii*, este un fung saprofit ubicuitar care în mod obișnuit produce infecții cutanate. Totuși, în anumite circumstanțe poate cauza infecții invazive cu interesarea sistemului nervos central. Prezentăm cazul unui bărbat de 86 ani, anterior sănătos, care a dezvoltat o sinuzită acută și a fost tratat în departamentul de O. R. L. Culturile efectuate din drenajul sinusal au fost negative atât pentru bacteria, cât și pentru fungi. După 10 zile, pacientul s-a prezentat la unitatea de urgențe, letargic și cu hemipareză dreaptă. CT-ul cranian și RMN-ul encefalic cu substanță de contrast au relevat o leziune circulară intracerebrală, cu localizare parietală stângă, circumscrisă de o zonă de edem. După drenajul chirurgical al abscesului cerebral s-a procedat la analiza microbiologică a materialului purulent extras izolându-se o tulpină fungică aparținând speciei *Scedosporium apiospermum*. Terapia antifungică a fost imediat inițiată, dar în ciuda acesteia starea pacientului s-a înrăutățit continuu și în final acesta a decedat cu insuficiență organică multiplă, la 20 zile după prima sa internare.

Cuvinte cheie: abces cerebral, *Scedosporium apiospermum*, voriconazol

Introduction

Scedosporium apiospermum and its sexual form - *Pseudallescheria boydii*, are ubiquitous saprophytic fungi that commonly cause cutaneous infections (1). However in certain circumstances can also cause invasive diseases which can involve the central nervous system (CNS) (2). When the CNS becomes involved, treatment is difficult, therapeutic options are limited and the prognosis is poor (3). We report a lethal case of *Scedosporium*

apiospermum brain abscess treated with surgical drainage and systemic voriconazole.

Case Report

An 86-year-old previously healthy man developed acute sinusitis and was admitted to ENT department for more investigations and treatment. Physical examination was notable for fever, headache and left orbit cellulites. CT scan revealed sphenoid sinusitis (figure 1).

* A. G. Krasoudakis

15 K.Voulgaridi Street, Chania 73100 Greece, Email: akr@otenet.gr

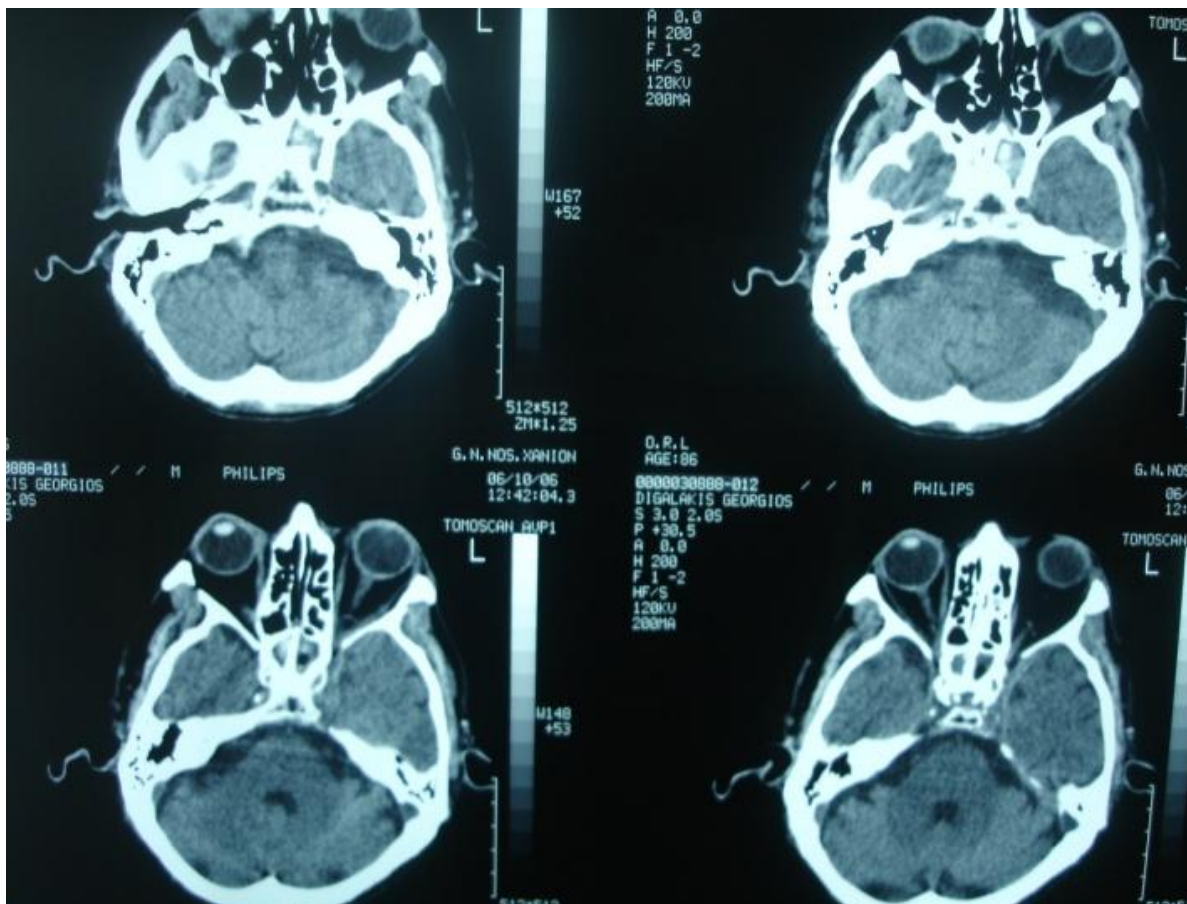


Figure 1. CT image - sphenoidal sinusitis

Blood examination showed marked white cell elevation ($14.87 \times 10^3/\mu\text{L}$), CRPLX elevation (23.0 mg/dL), and the patient was treated with intravenous administration of broad spectrum antibiotics (Ticarcillin and Clavulanic Acid, Amikacin and Metronidazole). Cultures of sinus drainage specimens were negative for both fungi and bacteria.

After 8 days of treatment, the patient improved clinically, and blood tests revealed normalization of white blood cells and CRPLX, and he was discharged. Ten days later the patient was presented again in the emergency department, lethargic with a right side hemiparesis. Cranial CT and brain MRI revealed a left parietal contrast -ring enhancing lesion with surrounding brain edema (figure 2). The patient was admitted in Neurosurgery clinic. Broad spectrum antimicrobial therapy was initiated (Imipenem and vancomycin) and also treatment with amphotericin B was started. Surgical drainage of the abscess was performed via burr hole, and purulent material was sent to laboratory for culture and cytological examination.

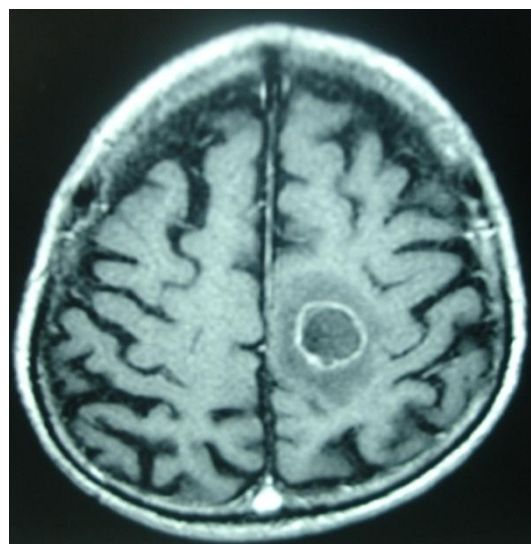


Figure 2. CT image – cerebral abscess surrounded by brain edema

Despite continuation of amphotericin B therapy for the next 4 days (total dose 2.5 grams) the patient's condition worsened. A CT scan of the brain revealed a new developed cerebral abscess caudally to the old one and a second surgical drainage was performed (figure 3).

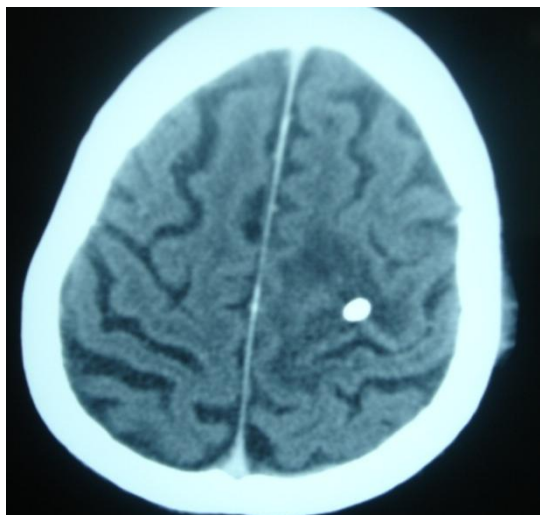


Figure 3. CT image – postoperative secondary brain abscess

Purulent material from the abscess was cultured onto routine bacteriologic media according to usual protocols. After 3 days of incubation cultures on Sabouraud's dextrose agar plates with chloramphenicol grew white cottony colonies, which later turned grey (figure 4). Microscopic examination showed the presence of septate hyaline hyphae and single-celled oval conidia with typical truncated bases. These conidia were formed singly or in small groups on annellidic conidiophores. Based on macroscopic and microscopic characters, the fungus was identified as *Scedosporium apiospermum*.



Figure 4. Culture of *S. apiospermum* – 8 days on SDA

In vitro susceptibility testing revealed resistance against amphotericin B (MIC>32µg/mL), 5-flucytosine (MIC>32µg/mL), itraconazole (MIC>32µg/mL), fluconazole (MIC>256µg/mL),

and caspofungin (MIC>32µg/mL); only voriconazole (MIC 0.19µg/mL) demonstrated excellent *in vitro* activity against the isolate. Voriconazole 400 mg/day every 12 h for 2 doses was initiated after these results but despite this the patient's condition worsened more and finally he died due to multiple organ failure 20 days after his first admission.

Discussion

S. apiospermum is the asexual form of *Pseudallescheria boydii*, a saprophytic fungus frequently isolated from soil manure, decaying vegetation and polluted water. (2, 3, 6). True human infection by *S. apiospermum* in developed countries is uncommon although case reports in recent years emphasize the pathogenic potential of this fungus. They preferably affect immunosuppressed patients either with pathological host defense alterations or associated severe drug induced immunosuppression (1, 4).

The clinical spectrum of *S. apiospermum* infection is variable. Soft tissue infection is mostly the result of inoculation of the mould from the soil. Inoculation can lead to a mycetoma, or more frequently arthritis, osteomyelitis and soft tissue infections of the feet and legs. Moreover, sinusitis and ophthalmic infections (*i. e.* keratitis) have been reported. The ports of entry for the fungus are microlesions or puncture wounds (mainly from thorns) of the skin of the hands, legs, feet or arms. If inhaled, the fungus can also cause infections of the respiratory tract.

Patients with infections other than mycetoma normally are immunosuppressed, or are suffering from malignant lesions or other underlying diseases like cystic fibrosis or tuberculosis. On the other hand, healthy patients can develop an infection by inhalation of large numbers of spores or aspiration of polluted water as in near-drowning incidents (2, 5, 6, 7). According to the literature, infections of the brain due to *S. apiospermum* occur only after aspiration of rather heavily polluted fresh water. The clinical manifestations include predominantly brain abscesses, but also spinal pachymeningitis, chronic meningitis, acute meningitis and epidural abscess. (2, 6, 7).

Infection of the brain is usually caused by a vascular spread of the fungal disease from a primary focus (*i.e.* pulmonary) of fungal emboli. In our case the way of life of our aged patient (86-year-old shepherd living next to a lake) was probably a

predisposing factor for the infection as we do not have other information concerning the possible route of infection.

Outcomes associated with disseminated infection with *S. apiospermum* are poor. Mortality rates of approximately 75% have been noted in patients who have hematological malignancies and who developed disseminated infection and in patients with central nervous system involvement (8, 11).

S. apiospermum grows easily and quickly in ordinary media for bacteria and fungi containing cycloheximide. The optimum temperature is 27°C but it can be cultured at room temperature and also at 37°C. It develops quickly as a white cottony mycelium that latter becomes characteristically grey with a reverse between brown and black. At microscopy, the hyphae are septate and branched. The conidia are large, with a pear shape, and they develop individually or in small groups from long anellides, directly from the hyphae or from the ends of simple conidiophores (9, 10).

The correct microbiological diagnosis is essential to the treatment of infections due to *S. apiospermum*. Mimicking the clinical and histological features of invasive aspergillosis, infections due to this pathogen are resistant to conventional amphotericin B. Antifungal triazoles appear to have more intrinsic *in vitro* activity against a wider range of individual isolates (11). Nevertheless, current medical therapeutic strategies for *S. apiospermum* and *Pseudallescheria boydii* are limited. Voriconazole has both oral and intravenous formulations, is widely distributed into body tissues including brain and cerebrospinal fluid, is 60% protein bound and has a low incidence of adverse effects (2, 3, 7, 11). In recent reports voriconazole resulted in improvement of a patient with brain abscess (with surgical drainage), and another case with *S. apiospermum* disseminated infection was successfully treated with voriconazole (12, 13). We believe that voriconazole despite of our patient's outcome is the treatment of choice for *S. apiospermum* infections.

We suggest an early high dose voriconazole treatment of patients at risk (such as immunosuppressed patients, near-drowning victims) together with mycological monitoring to reduce high mortality score of over 75%.

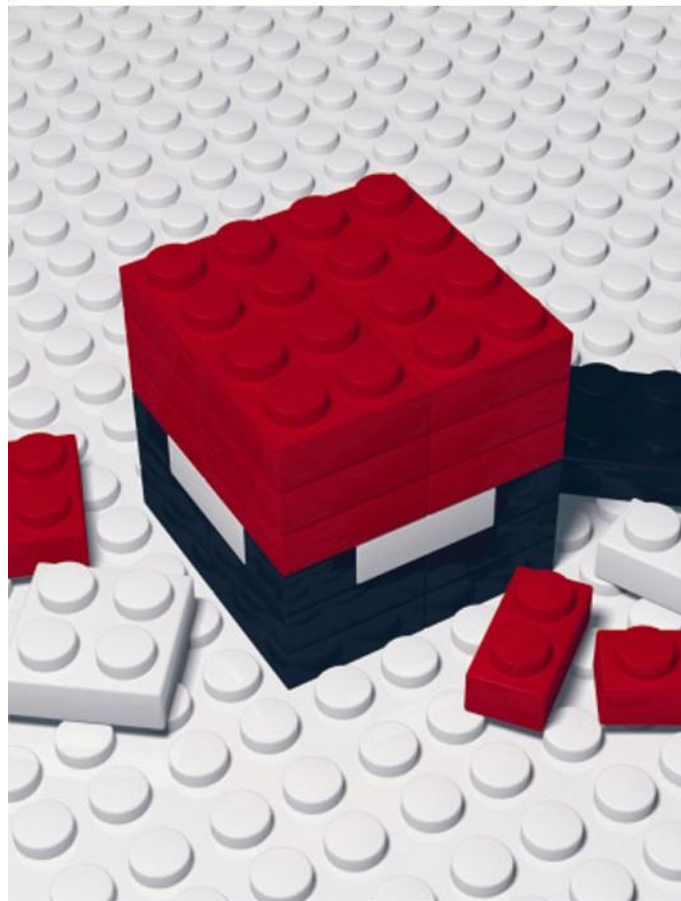
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