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Scedosporium apiospermum brain abscesses in a patient after near-drowning – a case report with 10-year follow-up and a review of the literature

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ABSTRACT

Scedosporium apiospermum is known to be a fungal pathogen affecting immunocompromised as well as non-immunodeficient patients. Although this fungus is found rarely, an infection can lead to severe and even fatal disease. Here, we describe the case of a 41-year-old female who developed multiple Scedosporium apiospermum brain abscesses after near-drowning with aspiration of contaminated mud and water. She showed various neurological symptoms. The patient recovered after removal of abscesses in combination with long-term antifungal treatment.

1. Introduction

Scedosporium apiospermum is a saprophytic fungus formerly known as *Monosporium apiospermum* [1]. The genus *Scedosporium* consists of two medically important species: *Scedosporium apiospermum* and its teleomorph or sexual state *Pseudallescheria boydii* and *Scedosporium prolificans* [2]. Both species are found worldwide in sewage, manure, polluted waters, indoor plant pots and greenhouses. Clinical manifestations show a great variety from cutaneous to disseminated diseases [3–5]. In the literature, many cases of *Scedosporium apiospermum* infections in immunocompromised patients [6–8], in transplanted patients [9], children [10] and other manifestations have been described [11–14]. Because of the variety of symptoms, the diagnosis remains to be difficult and early initiation of appropriate medication is critical.

2. Case

A 41-year-old otherwise healthy female experienced a car accident in October 2004, in which she was thrown out of her car and fell into a moat. Her head got underwater and she aspirated water and mud. After six minutes, she was successfully resuscitated by lay passers-by. In the hospital, she had to be treated on Intensive care Unit (ICU) due to severe aspiration pneumonia. The day of accident and hospital admission on ICU are defined as day 0. Within days, she developed additional cognitive impairment leading to cranial MRI examination which showed several brain abscesses on day +5 (Fig. 1a,b). Because of suspicion of cerebral mycosis a therapy with voriconazole 300 mg IV daily and amphotericin B 250 mg IV daily was started immediately on day +5. One big abscess in the left occipital cortex was removed via osteoplastic craniotomy an day +7, but no pathogen could be identified upon histological analysis. Since bacterial infection could not be ruled out at that time, antifungal therapy was temporarily combined with ceftriaxone 2 g IV daily and metronidazole 1 g IV daily since day +7 for two weeks. Amphotericin B therapy was terminated after 8 weeks. Eleven months into voriconazole mono-therapy with 300 mg/day isolated focal epileptic convulsions occurred which could be controlled by gabapentin treatment. On day +331, the patient deteriorated presenting with a series of focal epileptic convulsions, trunk myoclonus and gait disturbances. MRI scans showed no new abscesses but increased perifocal oedema. Dosage of antiepileptic medication was elevated and convulsions suspended. For detection of the pathogen species, another brain biopsy of a superficial cerebral focus was performed. Histological analyses using specific stainings (haematoxylin and eosin stain, Periodic acid–Schiff stain, Grocott-Gomori's methenamine silver stain, Gridley stain) were performed and the histological characteristics and sequencing of the internal transcribed spacer 1 (ITS1) region revealed the diagnosis. Impressively, confirmation of *Scedosporium apiospermum* infection via polymerase-chain reaction and blood culture failed under continued antifungal therapy.

Unfortunately, control MRI scans on day +433 showed at least one new cerebral lesion in the right occipital cortex with a distinct perifocal oedema. Based on the current literature on fungal infections caused by *Scedosporium apiospermum* and also considering the patient's elevated liver enzymes which most likely appeared due to antimycotic

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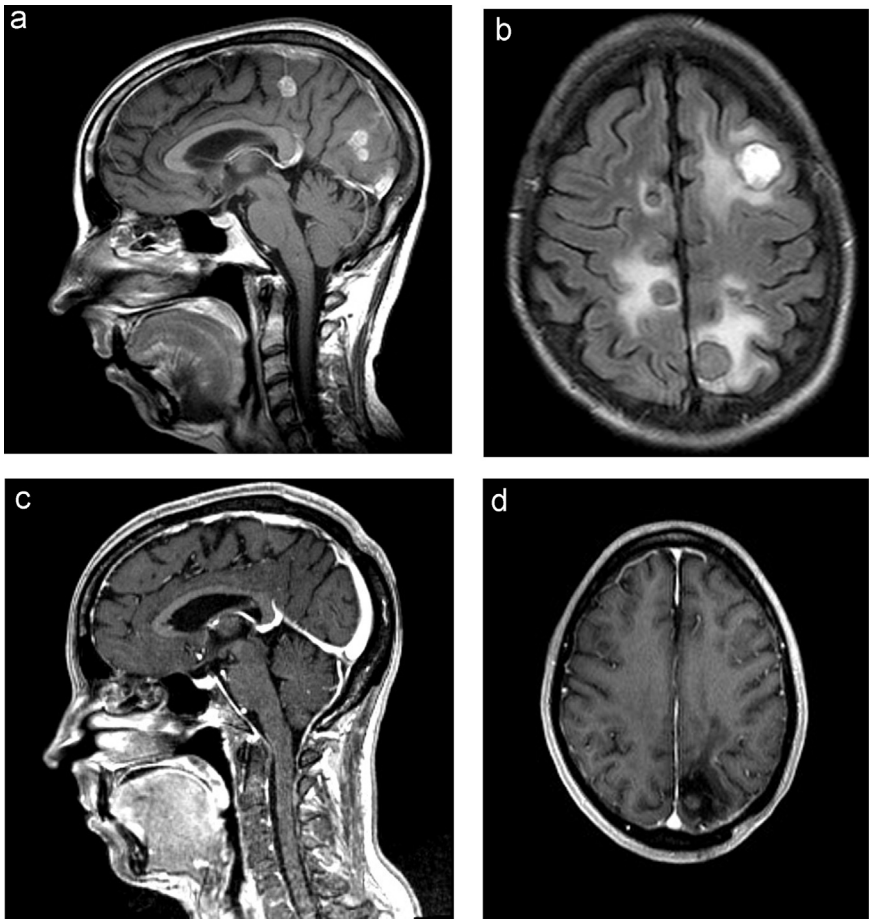

Fig. 1. a, b: MRI in October 2004: The transversal Flair-weighted (a) and sagittal T1-weighted images (b) show multiple *Scedosporium apiospermum* brain abscesses. c, d: MRI in October 2009: The T1-weighted sagittal (c) and transversal (d) images show no brain abscesses but postoperative residual defect areas and gliosis zones can be seen.

treatment, a combined therapy with voriconazole 2 × 300 mg/day and terbinafine 2 × 250 mg/day was applied. At that time, the patient had further deteriorated suffering from spastic left-sided hemiparesis and hemihypesthesia, quadrantanopia and an organic brain syndrome. Development of a manifest depression since day +486 with stable MRI findings showing abscesses detectable in the right temporal, right parietal/parasagittal and left parietooccipital cortex, resulted in termination of terbinafine therapy and initiation of escitalopram (10 mg/day) treatment which resulted in substantial amelioration of depressive symptoms. On day +740, antifungal treatment had to be terminated due to marked phototoxic effects caused by voriconazole leading to a relapse with a new abscess lesion in the right precentral region documented by MRI on day +1161. Control chest X-ray showed densities in the left lung most likely of post-inflammatory origin. At that time, there neither was evidence for acute pulmonal fungal infection nor did the patient show inflammatory blood reaction or positive PCR-analysis for *Scedosporium apiospermum* DNA. Oral voriconazole treatment with 2 × 300 mg/day was resumed accepting the consequence of phototoxic reactions. Within the last two years anticonvulsive and antidepressive treatment had to be changed or adjusted repeatedly but voriconazole treatment could be decreased to a dosage of 100 mg/day given stable findings in MRI scans (Fig. 1c,d), normal CSF results and lack of epileptic activity in EEG. Currently, the patient is in stable neurological condition and the long-term medication with voriconazole could be discontinued on day +3867, i.e. two years ago.

3. Discussion

The pathogen fungus *Scedosporium apiospermum* is found worldwide and known to be able to cause infections in immunocompetent as well as immunodeficient patients [3,6–15]. The infections range from isolated cutaneous infections, osteomyelitis, infections in transplant recipients, leukaemia, sclerokeratitis, endophtalmitis to sepsis [3,6–15]. Unfortunately, the infection itself often remains undetected and early initiation of an appropriate therapy is critical.

This case impressively illustrates the severity and variability of symptoms as well as the therapeutic difficulties in a patient suffering from infection with *Scedosporium apiospermum* which manifested by multiple fungal brain abscesses after near-drowning.

In line with the comparable cases described in the literature, diagnosis can be very difficult and – as in our case – requires interdisciplinary work-up including repeated histological evaluation and sequencing, especially when *Scedosporium apiospermum* escapes detection by PCR. Still, early antifungal therapy should be initiated in suspect of fungal infection after near-drowning to avoid fatality.

As our case indicates, new cerebral abscesses can occur even under sufficient antifungal treatment. Hence, as was reported in a similar case, permanent medication with voriconazole might be necessary and it appears mandatory that early therapy discontinuation has to be avoided [18]. Regarding the literature, surgical debridement combined with voriconazole has shown good results in manifestations in respiratory system, central nervous system, bone marrow and other tissues [14,17,18,20]. In all cases, infections with *Scedosporium apiospermum* showed a high associated mortality and patients required long term voriconazole treatment.

Voriconazole monotherapy also has been successfully used in several cases with infection with *Scedosporium apiospermum* [15,18,20], even in pediatric patients [15,20]. Voriconazole dosage in these studies differed upon the patient's comorbidities, condition and route of administration.

In some reported cases, a combination of voriconazole and terbinafine demonstrated good results, especially when an aggressive

surgical debridement was required and long term antifungal therapy was necessary [16,18,19]. In these case reports, an initial therapy of both agents combined with subsequent long term voriconazole treatment showed good results [16,18,19]. Like in case reports describing voriconazole monotherapy from the beginning, an antifungal combination therapy with both agents differed in dosage due to the same causes described above. Nevertheless, mortality in the described case reports was high and many patients died due to the infection.

Exact duration, dosage and efficacy of antimycotic therapies are not generally known by reason of lack of large studies. As with every antifungal treatment, especially when given as long-term treatment, side effects are to be controlled and regularly follow-up examinations are necessary. In this case, the patient suffered from phototoxic effects due to the therapy with voriconazole under a dosage of 2 × 300 mg/day. Having carefully weighed the advantages and disadvantages of the antimycotic therapy, she handled the side effects by avoiding harsh sun light. Under the final dosage of 1 × 100 mg/day, no phototoxic reactions were reported and lab examinations were all within normal limits. Over the time, our patient took voriconazole in different dosages, with and without combination with antifungal or antibiotic drugs and with different routes of administration for approximately 10 years. Because of recurrent multiple brain abscesses and resulting surgical debridement, she initially got voriconazole and terbinafine. To our knowledge, there is no comparable case of a long term treatment with voriconazole and a long-term survival after *Scedosporium apiospermum* infection in a patient with multiple cerebral abscesses regarding the literature.

In the largest study so far, in which 107 cases of *Scedosporium apiospermum* infections were reported, a median surivival time of 133 days was described. In our case report we describe a patient's 10-year follow-up who is cured under recurrent surgical debridement of brain abscesses and long term voriconalzole therapy. This case impressingly shows that infections with *Scedosporium apiospermum* may consider higher dosages or longer courses as typical for management of cerebral abscesses and invasive fungal disease.

Conflict of interest

There are none.

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