Medical Mycology Case Reports 23 (2019) 43–45

Contents lists available at ScienceDirect

Medical Mycology Case Reports

journal homepage: www.elsevier.com/locate/mmcr

Brain abscess caused by Cladophialophora bantiana: Total remission after full resection and short-course Voriconazole treatment

Li-Anne Schweizer[a,*], Lorenz Bärlocher[a], Anne Graber[b], Katia Boggian[c]

[a] Department of Internal Medicine, Hospital of St.Gallen, Rorschacherstrasse 95, 9007 St.Gallen, Switzerland
[b] Institute of Pathology, Hospital of Baselland, Mühlmattstrasse 11, 4410 Liestal, Switzerland
[c] Division of Infectious Diseases and Hospital Epidemiology, Hospital of St.Gallen, Rorschacherstrasse 95, 9007 St.Gallen, Switzerland

ARTICLE INFO

Keywords:
Cladophialophora bantiana
Brain abscess
Resection
Antifungal
Voriconazole

ABSTRACT

We report on a brain abscess in an immunocompetent man caused by *Cladophialophora bantiana*, a black mold known to prefer the brain for abscess-formations with a mortality rate up to 65%. The published cases so far show different therapeutical approaches and outcomes, whereby a standardized treatment could not yet be established. We report on a case of *Cladophialophora bantiana* brain abscess with total remission of the abscess after full resection and a short antifungal treatment.

1. Introduction

Cladophialophora bantiana belongs to the group of phaeohyphomycoses ("phaeo"= greek for "dark") which are characterized by their highly neurotropic spreading due to melanin production, that allows to bind to receptors of the blood-brain barrier and penetrate into the parenchyma [1]. Fungi containing melanin in their cell walls are also called dematiaceous, phaeoid or darkly pigmented fungi. *Cladophialophora bantiana* is the commonest cause of cerebral phaeohyphomycosis [1]. It is especially known to affect immunocompetent male individuals with no special medical history and the mortality rate is reported as high as 65% [2].

Similar to bacterial brain abscesses, also in cerebral phaeohyphomycoses there is a male predominance of 70% with an average age of 35 years [3]. Half of the cases occur in non-immunosuppressed patients.

Cladophialophora bantiana is an ubiquitous soil fungus with predominance in subtropical areas, but it can also occur in moderate climate zones [2,4]. The entry point of the fungus still remains unknown. Inhalation and haematogenous spread from an unrecognised pulmonary focus has been hypothesised, as well as chronic sinusitis [5].

In literature reviews, early diagnosis and full resection of the lesion has been associated with higher cure rates, but antifungal treatment duration is reported for 6 months or longer. We report on a case of an abscess caused by this pathogen with a favourable outcome after surgical and short antifungal treatment.

2. Case

A 53-year old man was referred to the neurology department of a tertiary care hospital in Switzerland by his ophthalmologist due to bitemporal peripheral visual loss (day 0). The symptoms began with a flickering in the eyes, accompanied by a typical migraine-pain (day -6), which was known to the patient and of which the last occurrence was 15 years ago. Apart from migraine and asthma bronchiale the patient's history was unremarkable and the only medication at that time was inhaled steroids. Travel history was unremarkable.

The peripheral visual loss was the only neurological defect and the patient did not report fever, seizures nor neck rigidity. Laboratory parameters were all normal including C-reactive Protein (CRP).

A CT scan of the brain revealed a demarcated area and therefore an MRI was done, which showed a singular lesion with slight enhancement and edema, so that primarily a tumor was suspected and the patient was referred to the neurosurgery department (day 1).

A navigation- and ultrasound-controlled macroscopically full resection of the lesion was performed with an osteoplastic mini-craniotomy (day 7). After one night in the neurosurgical ICU the patient was transferred to the normal ward. The postoperative MRI showed a full resection of the lesion and the patient was discharged in good condition while awaiting the histological results.

Unexpectedly the histology revealed an acute abscess with fungal elements but without specification. The patient was immediately rehospitalized (day 15), a lumbar punction was performed with culturing the liquor and empirical treatment with liposomal Amphotericin B and

* Corresponding author.
E-mail address: lianne.schweizer@gmail.com (L.-A. Schweizer).

https://doi.org/10.1016/j.mmcr.2018.12.001
Received 5 November 2018; Received in revised form 2 December 2018; Accepted 10 December 2018
Available online 11 December 2018

Voriconazole was started. Galactomannan and Cryptococcus neoformans-antigen in the serum were negative. The liquor culture remained sterile.

A panfungal PCR was done on the paraffin embedded biopsy and the PCR revealed *Cladophialophora bantiana* (day 20).

The panfungal PCR is a single run PCR which amplifies the variable region ITS2 of fungal rRNA gene [6,7]. Two Primers (ITS6 and ITS7) were designed in the Institute of Pathology, Kantonsspital Baselland to obtain shorter products as indicated in the mentioned publications (manuscript in preparation).

The PCR Product of *Cladophialophora bantiana* had a length of 251 bp and was sequenced using both primers. The obtained sequences were aligned and the complete sequence without primer-sequence was blasted at NCBI Nblast suite.

Cladophialophora bantiana with the following sequence IDs: KY312527.1; KY310641.1, KY310640.1, KY310639.1, LN813025.1, KM525668.1, KP131826.1, KP131825.1, KP131824.1, KF800891.1, AF397182.1, AF131079.1 was identified with 207 of 207 homolog base pairs, 100% identity and 100% query coverage.

The entry point of the pathogen still remained unknown. As revealed in MR Images, there was chronic sinusitis as possible entry point but as the brain lesion was situated in the occipital cortex we presume that there was haematogenous spread from an unrecognised pulmonary focus. The patient remained hospitalized for intravenous antifungal treatment.

After 7 days of treatment, liposomal Amphotericin B was stopped due to increase of serum creatinine. Knowing that *Cladophialophora bantiana* in the literature is described as susceptible to Voriconazole, we continued with Voriconazole monotherapy (day 27). Drug monitoring showed good therapeutic levels (between 3.8 mg/l and 5 mg/l).

The patient was always in a good condition, showed no fever, and the visual peripheral loss remained stable. He was followed in an outpatient setting.

After 3 months of peroral Voriconazole treatment a repeat MRI showed a normal postoperative site, without any intraparenchymal lesions or enhancement. At that time, due to an increasing skin rash, which developed under Voriconazole, we stopped the treatment.

In further follow-up MRI's another three months later and one year after stopping treatment, no lesions are seen, and the patient is in good condition without any complaint. (Fig. 1)

3. Discussion

Brain abscesses caused by *Cladophialophora bantiana* remain difficult to treat with a high mortality rate. Screening the published reports, the favourable outcome of our patient remains noteworthy in view of the short duration of antifungal treatment.

Since 1911 there have been 120 cases of culture-proven *Cladophialophora bantiana* CNS-infections reported in medical literature. In the earliest cases, mortality was 100%, as the patients were not treated at all or only by surgery. So far there have been 21 patients described without therapy, and none of them survived [2].

Reduction of mortality is noted in the literature since the seventies, when antifungal therapy was applied, but significantly since 2002 when Voriconazole was firstly available [1,8,10]. Voriconazole is an azole with good penetration in the cerebrospinal fluid and good activity against *Cladophialophora bantiana* [9]. Survival rates for cerebral phaeohyphomycosis treated with Voriconazole have been reported as high as 50% for two years [1].

The role of surgery to achieve complete cure is discussed in literature, especially if the lesion is fully resected [10–13]. In a recent metaanalysis of Kantarcioglu et al., 120 cases of proven cerebral phaeohyphomycoses were reviewed, but as numerous therapeutic approaches have been used, the impact of full resection could not be established. The lowest mortality rate appeared to be in patients treated by both antifungals and surgery [2].

Recommendations for type and length of antifungal therapy are still lacking and so far only one case of favourable outcome with a short duration of drug therapy has been published [14].

Summarizing for our report, the cases described in the past 100 years are too few to draw conclusions about treatment modalities influencing outcomes. Different approaches for achieving a favourable outcome are discussed, such as early diagnosis and full resection combined with antifungal therapy, which have all been applied in our case.

After publication of only one case of a survivor of a *Cladophialophora bantiana* brain abscess after a relatively short antifungal treatment, our case thus confirms that with full resection of the abscess, a duration of antifungal treatment of 3 months can be adequate.

Acknowledgements

The authors of this paper did not have any financial support for reporting on this case.

Conflict of interest

There are none.

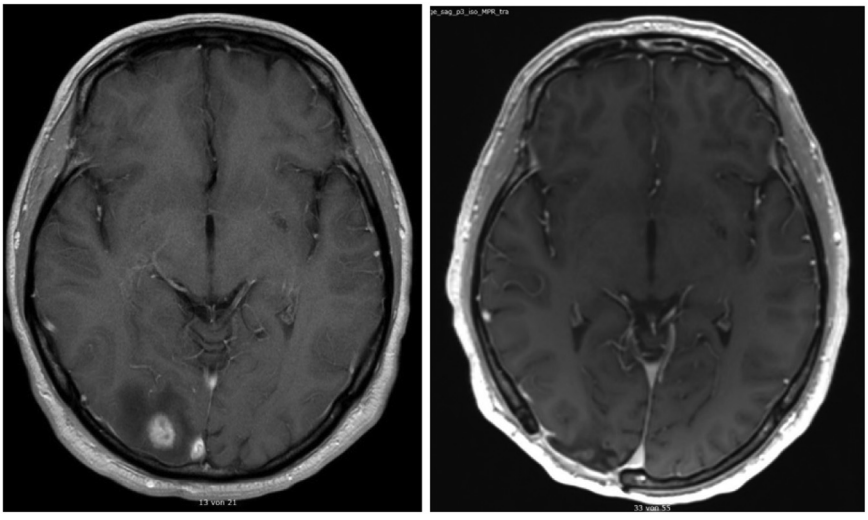

Fig. 1. Imaging of lesion at time of first symptoms (left) and final follow-up MRI (right).

References

[1] S.G. Revankar, D.A. Sutton, M.G. Rinaldi, Primary central nervous system phaeohyphomycosis: a review of 101 cases, Clin. Inf. Dis. 38 (2004) 206–216.

[2] A.S. Serda Kantarcioglu, J. Guarro, S. De Hoog, H. Apaydin, N. Kiraz, An updated comprehensive systematic review of cladophialophora bantiana and analysis of epidemiology, clinical characteristics and outcome of cerebral cases, Med. Mycol. 55 (2017) 579–604.

[3] M.C. Brouwer, J.M. Coutinho, D. van de Beek, Clinical characteristics and outcome of brain abscess Systematic review and meta-analysis, Neurology 82 (2014) 806–813.

[4] C. Garzoni, L. Markham, P. Bijlenga, J. Garbino, Cladophialophora bantiana: a rare cause of fungal brain abscess, Clin. Asp. New Ther. Options, Med. Mycol. 46 (2008) 481–486.

[5] J.W. Brown III, J. Nadell, C.V. Sanders, L. Sardegna, Brain abscess caused by Cladosporium trichoides (bantianum): a case with paranasal sinus involvement, South Med. J. 69 (1976) 1519–1521.

[6] T.J. White, T. Bruns, S. Lee, J. Taylor, Amplification and direct sequencing of fungal ribosomal RNA genes for phylogenetics, in: M. Innis, D. Gelfand, J. Sninsky, T. White (Eds.), PCR Protocols: A Guide to Methods and Applications, Academic Press, San Diego, 1990, pp. 315–322.

[7] C. Muñoz-Cadavid, S. Rudd, S.R. Zaki, M. Patel, S.A. Moser, M.E. Brandt, B.L. Gómez, Improving molecular detection of fungal DNA in formalin-fixed paraffin-embedded tissues: comparison of five tissue DNA extraction methods using panfungal PCR, J. Clin. Microbiol. 48 (6) (2010) 2147–2153.

[8] M. Ahmad, D. Jacobs, H.H. Wu, D.M. Wolk, S.A.J. Kazmi, C. Jaramillo, Cladophialophora bantiana: a rare intracerebral fungal abscess – case series and review of literature, Surg. J. (N. Y) 3 (2017) e62–e68.

[9] M.K. Lyons, J.E. Blair, K.O. Leslie, Successful treatment with voriconazole of fungal cerebral abscess due to Cladophialophora bantiana, Clin. Neurol. Neurosurg. 107 (2005) 532–534.

[10] A. Chakrabarti, H. Kaur, S.M. Rudramurthy, S.B. Appannanavar, A. Patel, K.K. Mukherjee, et al., Brain abscess due to Cladophialophora bantiana: a review of 124 cases, Med. Mycol. 54 (2016) 111–119.

[11] D. Delfino, S. De Hoog, L. Polonelli, M. Benecchi, F. Fanti, S. Galatioto, et al., Survival of a neglected case of brain abscess caused by Cladophialophora bantiana, Med. Mycol. 44 (2006) 651–654.

[12] C. Dash, A. Kumar, R.S. Doddamani, Is complete excision the key to cure for Cladophialophora bantiana brain abscess? A review of literature, Neurol. India 64 (2016) 1062–1064.

[13] M. Roche, R.M. Redmond, S. O'Neill, E. Smyth, A case of multiple cerebral abscesses due to infection with Cladophialophora bantiana, J. Infect. 51 (2005) 285–288.

[14] P. Sood, V. Dogra, A. Thakur, B. Mishra, A. Mandal, S. Sinha, Brain abscess due to Xylohypha bantiana, Scand. J. Infect. Dis. 32 (2000) 708–709.