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Letter to the Editor

Cladophialophora bantiana infection mimicking neuromyelitis optica

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ABSTRACT

Cladophialophora bantiana (*C. bantiana*) is a life-threatening melanized mycelial fungus causing brain abscess. *C. bantiana* is usually observed in tropical countries, including India. We report a Japanese case of *C. bantiana* presenting with myelitis mimicking neuromyelitis optica (NMO) and brain abscess. A 73-year-old man was administered prednisolone (30 mg/day) for antineutrophil cytoplasmic antibody (ANCA)-related vasculitis 100 days before admission. He had right side-dominant paraplegia and sensory loss in the right leg. T2-weighted spinal cord MRI revealed longitudinal high-intensity signals at the T7 to T12 levels. A ring-enhancing lesion at the T10 level was detected on gadolinium (Gd)-enhanced MRI. He was tentatively diagnosed with NMO, and steroid pulse therapy was performed. One month later, an abscess at the right cerebropontine angle was noted on Gd-enhanced brain MRI. Two months later, several subcutaneous intramuscular tumors were detected. Based on the morphological study of the cultured organelle obtained by tumor enucleation and the internal transcribed spacer sequence of ribosomal RNA, the pathogen was identified as *C. bantiana*. Although he received liposomal amphotericin B treatment, the patient died of respiratory insufficiency. *C. bantiana* infection should be considered in patients with myelitis presenting with longitudinal lesions and CNS abscess in an immunocompromised state.

Dear Editor

1. Introduction

Cladophialophora bantiana (*C. bantiana*) is a fungus that is dark in color due to melanin in the cell wall and is predominantly found in soil [1]. *C. bantiana* is known to cause central nervous system (CNS) abscess in humans [2], and has a high mortality rate of up to 70% regardless of combined surgical and antifungal therapy. *C. bantiana* infection is usually observed in subtropical regions with high humidity. Indeed, among the 124 cases of brain abscess by culture-confirmed *C. bantiana* infection between 1952 and 2014, 50% (62 cases) were from India [1]. Due to the increased use of immunosuppressive therapy and organ transplantation, the incidence of this rare fungal CNS infection has increased. Recently, even in the countries outside of India, including the USA, Canada, and European countries, *C. bantiana* infection has been reported [1].

As mentioned above, *C. bantiana* infection frequently causes brain abscess [2], while complication of myelitis with *C.bantiana* infection is rare [3,4]. We report here a Japanese case of *C. bantiana* infection presenting with myelitis mimicking neuromyelitis optica (NMO) and brain abscess.

2. Case report

A 73-year-old Japanese man was admitted to our hospital due to bilateral leg edema and difficulty in moving his right leg. He had a past history of hypertension, chronic kidney disease, benign prostatic hyperplasia, and diabetes mellitus. He had traveled to Guam 8 years ago, and to Europe, including France, Monako, and Italy, 10 years ago. Three months ago, when he developed coughing, a pulmonary lesion was found on lung CT, and his serum was positive for myeloperoxidase-antineutrophil cytoplasmic antibody (MPO-ANCA). He was therefore tentatively diagnosed with antineutrophil cytoplasmic antibody (ANCA)-related vasculitis, and prednisolone (30 mg/day) was administered at that time at the local hospital. On admission, the neurological examination revealed right side -dominant bilateral leg weakness and touch sensation loss in the right leg. T2-weighted spinal cord MRI demonstrated high- intensity signals in the central portion of the spinal cord at the T7 to T12 levels (Fig. 1A). T2 weighted axial imaging also revealed high-intensity signals at the T10 level (Fig. 1B). A ring-enhancing lesion was noted at the T10 level on T1-weighted gadolinium (Gd)-enhanced spinal cord MRI (Fig. 1C). Mild elevation of protein (58 mg/dl) with normal cell counts ($< 5/mm^3$) was found on cerebrospinal fluid (CSF) examination. Methylprednisolone pulse therapy (1000 mg/day) was performed twice to treat transverse myelitis of unknown origin. One month later, diffusion-weighted imaging of brain MRI detected a high-intensity signal at right cerebropontine angle (Fig. 1D). Ring-enhancement of that lesion was noted on Gd-enhanced brain MRI (Fig. 1E). Blood tests, laboratory tests, viral infectious tests, immunological examination, fungal examination, including serum Aspergillus antigen, Cryptococcus antigen, and *Candida albicans* antigen, and CSF examination did not reveal the cause of these manifestations. Anti-aquaporin 4 (AQP4) antibody was confirmed negative in this patient. Two months later, several tumors were detected at the upper back and bilateral thigh, spanning subcutaneous to muscle layers, and tumor enucleation was performed. The microorganism was cultured in Mycosel culture medium at 27 °C or potato dextrose agar (PDA) culture medium at 40 °C. Based on morphology, Genus *Cladophialophora* (*Cladophialophora arxii*, or *C. bantiana*) was suspected (Fig. 1F). The pathogen was finally identified as *C. bantiana* by the internal transcribed spacer sequence of ribosomal RNA [5].

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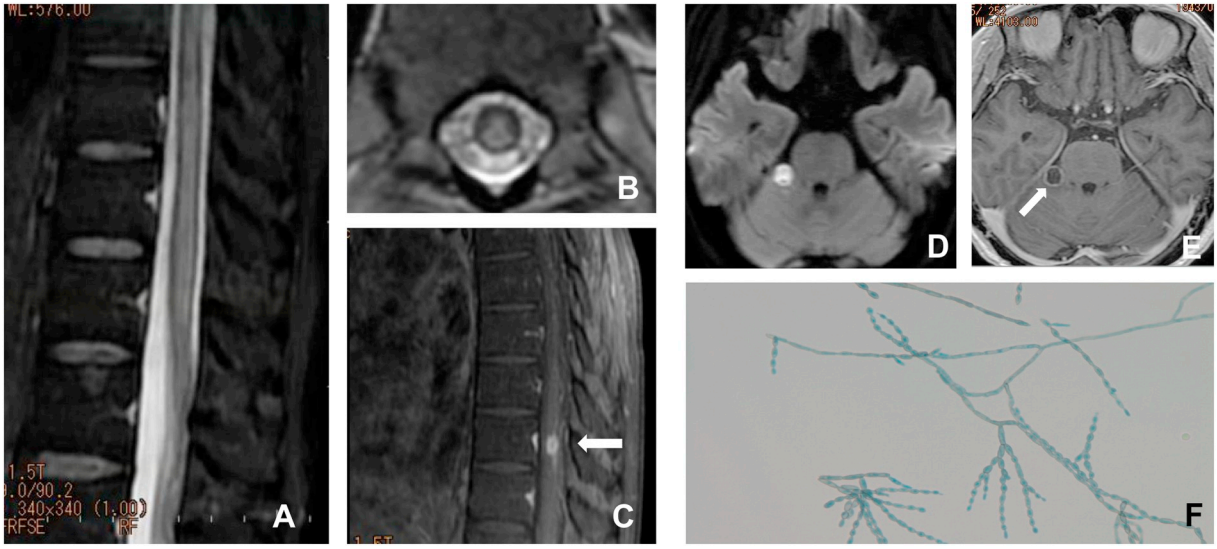

Fig. 1. (A) Spinal cord MRI. Sagittal T2-weitghted imaging (TR/TE: 4199.0/90.2) detected a longitudinal lesion at the T7 to T12 levels (A). Axial T2-weighted imaging detected a central lesion at the T10 level (B). At the T10 level, a ring-enhancing lesion (arrow) was noted by gadolinium (Gd)-enhanced T1-weighted imaging (TR/TE: 7.2/2.2) (C). Brain diffusion-weighted MRI. Diffusion-weighted imaging (TR/TE: 3000.0/63.0) demonstrated high-intensity signal at the cerebellopontine angle (D). Ring-enhancement of that lesion was noted on Gd-enhanced brain MRI (arrow) (TR/TE: 7.2/2.2) (E). Light micrograph showing smooth walled, pale olivaceous, ellipsoidal- to spindle-shaped conidia arranged in long chains (400 × magnification) (F).

Although liposomal amphotericin B (L-AmB) therapy was started, he developed bacteremia, pulmonary edema, hypokalemia, and hemorrhagic rectal ulcer, and his general status remained unstable. Three months later, his respiratory condition deteriorated and he passed away.

3. Discussion

In this patient, CNS abscess and skin lesion were caused by *C. bantiana* infection in an immunocompromised state. *C. bantiana* is a highly neurotropic fungus, and the presence of melanin in its cell wall may function in its localization to the CNS [2].

In general, amphotericin B and L-AmB are most commonly (62.83%) prescribed for the treatment of C. bantiana. However, the survival rate was not improved [1]. Relatively new-generation triazole antifungal compounds, voriconazole or posaconazole, have been reported to improve the survival rates of patients with *C. bantiana infection* [6]. In particular, posaconazole may be a new therapeutic option given its higher tolerance, lower toxicity, and fewer drug-drug interactions. Ta et al. reported the successful treatment of CNS blastomycosis with amphotericin B followed by voriconazole [6].

In this patient, a longitudinal spinal cord lesion was detected on T2-weighted spinal cord MRI. At the T10 level, a ring-enhancing lesion was found by Gd-enhanced imaging. Based on its morphology on MRI, this lesion was similar to NMO [7] or neurosarcoidosis. While in this patient, AQP4 antibody was negative [7]. Similar spinal cord MRI findings by *C. bantiana* infection have been previously reported [3,4], but spinal cord lesions are extremely rare in *C. bantiana* infection.

In this patient, it took 52 days for the clinical diagnosis of *C. bantiana*. NMO was first excluded, as described above. The mean duration for the clinical diagnosis of *C. bantiana* was reported to be 115 days after symptoms developed [1]. It was reported that one-third of phaeohyphomycosis due to *C. bantiana* does not present skin lesions. Thus, if ring-enhancing lesions, which imply CNS infection or brain tumor, are observed, the possibility of *C. bantiana* infection is always considered and empirical therapy is performed in India [1]. *C. bantiana* infection should be considered in patients in an immune-compromised state with possible CNS infection and ring-enhancing lesions in the brain regardless of cutaneous lesions, even in the countries outside of India, including Japan.

Hironaga reported the first case of brain abscess due to *C. bantiana* in Japan in 1980 [8]. To our knowledge, this is the second case of *C. bantiana* with a cutaneous lesion and CNS abscess in Japan. The possibility of *C. bantiana* should be considered in patients exhibiting myelitis similar to NMO and brain abscess, especially in an immune-compromised state.

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Soichi Enomoto[a,f], Hiroko Shigemi[b], Yuki Kitazaki[a], Masamichi Ikawa[a], Osamu Yamamura[a], Tadanori Hamano[a,f,*], Katsunori Tai[c], Hiromichi Iwasaki[c], Haruka Koizumi[d], Minoru Hasegawa[d], Kiminobu Takeda[e], Yasunari Nakamoto[a]

[a] *Second Department of Internal Medicine, University of Fukui, 23-3 Matsuokashimoaizuki, Eiheiji-cho, Yoshida-gun, Fukui 910-1193, Japan*

[b] *Department of Respiratory Medicine, University of Fukui, 23-3 Matsuokashimoaizuki, Eiheiji-cho, Yoshida-gun, Fukui 910-1193, Japan*

[c] *Department of Control & Prevention of Infectious Diseases, University of Fukui, 23-3 Matsuokashimoaizuki, Eiheiji-cho, Yoshida-gun, Fukui 910-1193, Japan*

[d] *Department of Dermatology, University of Fukui, 23-3 Matsuokashimoaizuki, Eiheiji-cho, Yoshida-gun, Fukui 910-1193, Japan*

[e] *Department of Dermatology, Kanazawa Medical University, Uchinada, Ishikawa 920-0293, Japan*

[f] *Department of Aging and Dementia (DAD), Faculty of Medical Sciences, University of Fukui, 23-3 Matsuokashimoaizuki, Eiheiji-cho, Yoshida-gun, Fukui, Japan*

E-mail address: hamano@u-fukui.ac.jp (T. Hamano).

[*] Corresponding author at: Second Department of Internal Medicine, University of Fukui, 23-3 Matsuokashimoaizuki, Eiheiji-cho, Yoshida-gun, Fukui 910-1193, Japan; Department of Aging and Dementia (DAD), Faculty of Medical Sciences, University of Fukui, 23-3 Matsuokashimoaizuki, Eiheiji-cho, Yoshida-gun, Fukui, Japan.