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Case Report

Candida Albicans Dural Granuloma: Case Report

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Candida albicans dissemination to the central nervous system (CNS) may occur in immunocompromised patients even without prior cranial surgery. In such cases, intracerebral lesions are most frequent, meningeal or cerebrospinal fluid involvement being rare. We, here, describe a case of *Candida albicans* granuloma developing exclusively inside the width of the dura mater, successfully treated by surgical excision followed by antimycotic therapy. A 75-year-old man, previously affected by urinary sepsis from *Candida albicans*, was admitted to the emergency department of our hospital because of the acute appearance of sensory obtundation, blurred speech, and right hemiparesis. Emergency computed tomography (CT) scan and magnetic resonance imaging (MRI) with and without contrast enhancement disclosed a huge, left fronto-parietal mass, causing severe brain compression. At surgery, the lesion appeared to develop exclusively inside the dural envelope, and was completely removed. At pathology, a totally intradural *Candida albicans* granuloma was observed and appropriate antimycotic treatment was started. After an uneventful postoperative course the patient was sent to rehabilitation. Five months later he was admitted again because of a bone flap infection, leading to bone removal and further cranioplasty, with full neurological recovery. At 2 years follow-up, no neuroradiological or clinical evidence of residual/relapsing intracranial infection was found. Isolated intradural granuloma from *Candida albicans* has never been described before. Even though surgical excision may lead to complete resolution of mass effect in these patients, prolonged observation should be maintained, to disclose further, potentially lethal, complications.

Keywords: candida, infection, intracranial fungal masses, dura mater, granuloma

Introduction

Mycotic involvement of the central nervous system (CNS) is a rare event even in countries where these infections are largely diffused.[1–3] Different presentation modalities may be observed in affected patients, including development of intracranial granulomas, meningitis, ventriculitis, and anterior cranial base invasion.[4] *Aspergillus fumigatus* and *Cryptococcus neoformans* are the most frequently reported causative organisms of intracranial fungal masses.[5,6] Nonetheless, the raising incidence of diabetes mellitus has resulted in an increased occurrence of intracranial involvement by Candida species.[7,8]

Patients may manifest symptoms only at an advanced stage of the disease, so that lethality is quite high (40–92%). Surgical treatment aimed at mass removal is usually considered only for well circumscribed and superficial lesions and must always be associated with prolonged antimycotic therapy.[9–11]

We report an unusual case of intracranial granuloma from *Candida albicans*, developing exclusively within the dural envelope and causing severe neurological symptoms leading to emergency neurosurgical treatment.

Case Report

On March 2009, a 75-year-old male patient, with previous history of diabetes mellitus and hypertension, was admitted to the Department of Urology of our hospital complaining of left flank pain, dysuria, and high fever. Laboratory values disclosed minimal blood urea nitrogen (BUN) (63 mg/dl) and creatinine increase (1.60 mg/dl). Urine analysis showed glycosuria (100 mg/dl), albuminuria (30 mg/dl), and leukocyturia (1.505 thous/mcl). Urine culture documented an infection from *Candida albicans* (5×10^5 CFU/ml). Antimycotic treament by fluconazole (200 mg twice a day) was started, associated to wide spectrum antibiotic coverage with meropenem (1 g three times a day). Abdominal ultrasound evidenced multiple bilateral kidney stones and a left early hydronephrosis. Because of persistent oliguria, a left pyelostomy was positioned. Three days later he was transferred to the intensive care unit (ICU) because of the development of septic shock. One week later, renal function improved and the patient was readmitted to the urology department, where a double J ureteral stent was placed. Two months later the stent was removed with no further complications and intact renal function, antimycotic treatment was stopped and the patient was discharged home.

On September 2009 he came to our emergency department because of a 3-day history of sensory obtundation, blurred speech, and development of weakness in the right arm and leg. On neurological examination he was stuporous but arousable, with a right hemiparesis (F3, both in the arm and leg) and sensory-motor aphasia. Laboratory examinations revealed only a slight erythrocyte sedimentation rate (ESR) increase (42 mm/hr) and modest monocytosis (12%).

Admission computed tomography (CT) scan disclosed a left parietal epidural mass (A-P diameter: 7 cm) with focal calcifications, compressing the underlying brain and displacing the contralateral horn of the left lateral ventricle

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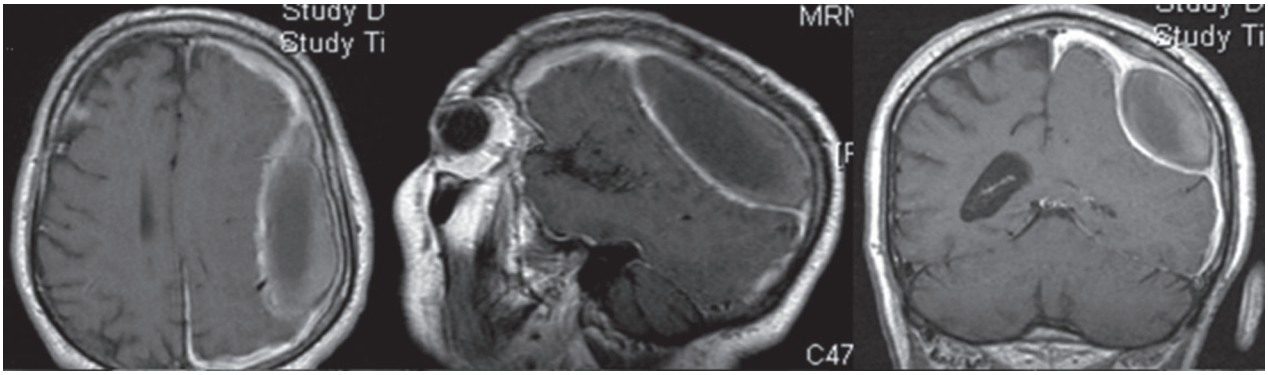

Fig. 1 Axial, sagittal, and coronal preoperative magnetic resonance images with gadolinium, showing a left fronto-parietal lesion apparently located in the epidural space and compressing the underlying brain with left lateral ventricle distortion and severe mass effect on the surrounding brain. Cerebral sulcations are no more visible and leptomeningeal enhancement is observed along the entire left hemisphere.

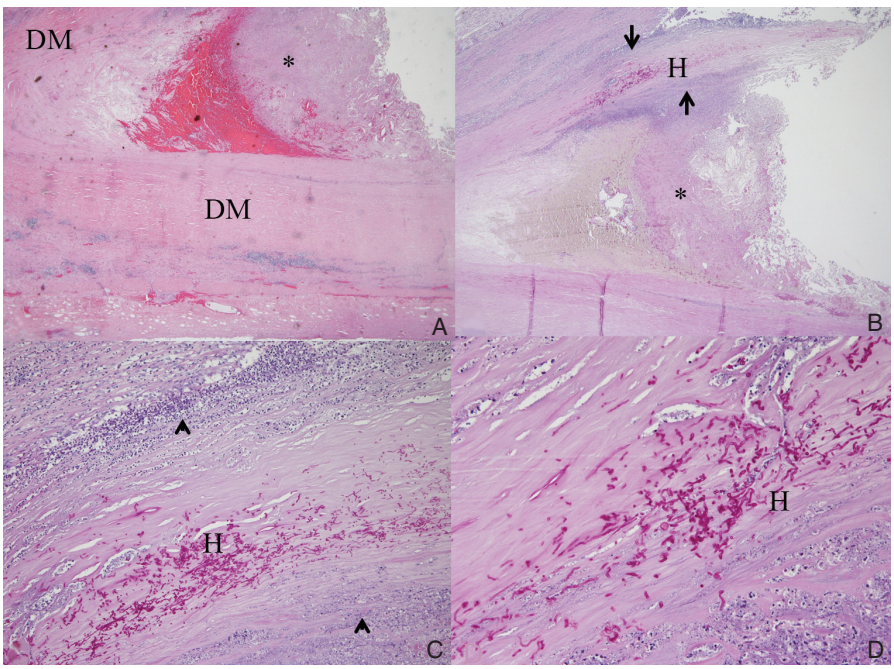

Fig. 2 A, B: Histology—Sagittal sections under periodic acid-Schiff (PAS) stain, magnification ×2.5 (A) and ×4 (B). Dura mater (DM) is split by a central core of necrotic material (black asterisk). Fungal hyphae (H) are clearly visible, surrounded by neutrophils infiltrate (black arrow). C, D: Histology—Under higher magnification, ×10 (C) and ×20 (D) the chronic inflammatory tissue (black arrowhead) encircles the fungal hyphae (H).

(midline shift: 7 mm). Lesion's walls enhanced after contrast administration. At magnetic resonance imaging (MRI) a diffuse ipsilateral hemispheric leptomeningeal enhancement was observed (Fig. 1). The lesion, appearing as a cyst with necrotic content, seemed confined to the epidural space, so that a diagnosis of epidural abscess was made. Because of rapid clinical worsening (progression of hemiparesis to hemiplegia, followed by coma and left anisocoria) the patient underwent emergency surgery at the left fronto-temporal-parietal craniotomy. After bone removal, a large, discoid mass, involving the dura mater, was observed. Durotomy was started 2 cm beyond lesion's border. The lesion developed exclusively inside the dural envelope with no adhesion to the arachnoidal layer, so that en bloc removal was possible. The removed bone was unaffected. Duroplasty was performed by Tutopatch™ (Tutogen Medical, Inc., Alachua, Florida, USA). We decided not to use any autologous tissue because of defect size and the need of a second surgical incision, which we felt not comfortable with because of poor patient's conditions, potentially predisposing to further infection. Bone was repositioned by titanium miniplates. Postoperative course was uneventful, with CT and MRI scans confirming full lesion removal. After a 5-day ICU staying the patient was re-admitted to our department conscious, still aphasic and with a persistent right hemiparesis, both of which rapidly improved in the following days. At pathology, intraoperative specimens showed the presence of *Candida albicans* hyphae surrounded by neutrophils infiltrate inside the dural lesion (Fig. 2A–D). Antimycotic treatment with amphotericin B (3 mg/kg a day) and meropenem (1 g 3 times a day) was started. Full midline re-alignment and a small subdural hygroma were observed at 2 weeks postoperative CT and MRI. The patient, fully awake, with minimal residual hemiparesis (F4+) and complete language recovery,

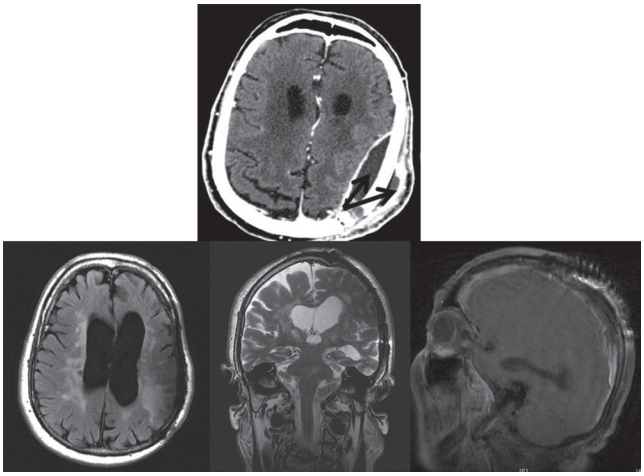

Fig. 3 Contrast enhanced computed tomography at the time of second patient's admission. A collection of purulent material was immediately evident in the subcutaneous and epidural compartments (black arrows). Underlying brain sulci are compressed. Pre-cranioplasty magnetic resonance imaging, showing no further contrast enhancement of the meninges and full brain re-expansion.

was discharged to a rehabilitation facility, where he remained 2 months before going home. Five months later he came back again to our attention because of the sudden appearance of high fever (body temperature 39°C), impaired consciousness, and aphasia. At inspection, a fluctuating subcutaneous collection was observed underneath the previous cranial flap, with overlying skin reddening and tenderness. Enhanced CT scan showed the presence of a subcutaneous and epidural empyema (Fig. 3). During re-surgery, a huge, purulent collection was found overlying the repositioned bone, which appeared eroded, and was removed. Pus was also found overlying the rebuilt dural layer, from which the scar tissue was removed until isolating the rebuilt dural layer. Large spectrum antibiotics were started (ceftriaxone 2 g/2 times a day, teicoplanin 200 mg 2 times a day). No growth of bacteria or fungi was observed from cultures and therapy was interrupted 4 weeks after. Two months post-operative CT scan showed no residual contrast enhancement and the patient was discharged again to a rehabilitation facility. On September 2010, a contrast enhanced MRI was found negative (Fig. 3), so a premodeled titanium cranioplasty was positioned. The patient was discharged home with no residual deficits and no complications at immediately postoperative CT and 6-12-24 months' neuroradiological investigations.

Discussion

Fungi are low virulence organisms, commonly affecting immunocompromised patients. The spreading of mycotic infections to the intracranial compartment is relatively a rare event and rarer is the need of neurosurgical procedures for the removal of fungal masses, either developing inside the brain as abscesses or in the epidural space as granulomas.[1,9–11] The more frequently involved species affecting human brain include *Cryptococcus neoformans*, *Aspergillus flavus*, *Aspergillus fumigatus*, *Actinomyces israeli*, *Nocardia asteroides*, and *Candida albicans*.[1,6] Clinical syndromes with which fungal infections may affect the CNS are protean, occurring alone or in combination, sometimes being specific for peculiar organisms (as for the rhinocerebral form of zygomycosis) and typically present as meningitis, intracranial mass lesions, and anterior skull base granulomas.[2,4,5] Even larger case series include a limited number of patients recruited in a long time interval.[5,11]

Diabetes is one of the most frequent predisposing causes for disseminated fungal infections, which are also frequently associated with immunocompromised status.[8,9] The rising incidence of diabetes, especially in underdeveloped countries, has led to an increase of intracranial fungal masses, intracerebral abscesses, and granulomas due to Candida species. Actually, *Candida albicans* is the fourth more common cause of bloodstream infection, and epidemiological data indicate that at least 72% of all nosocomial fungal infections and 8% to 15% of all nosocomial bloodstream infections are caused by Candida species.[7] Additionally, the 1–6% of patients dying for systemic candidiasis hosts CNS lesions of varying nature, so that it may be postulated that neurocandidosis is more frequent than expected.[3]

Our patient had a previous history of diabetes. The following development of acute renal failure presumably created a predisposing condition to septic dissemination of *Candida albicans*. Nonetheless, the long time elapsed (7 months, from March to September) between full patient's recovery from first hospital admission and the development of neurological symptoms was peculiar and unexpected, especially when considering that antimycotic therapy was protracted for 2 months after his first hospital discharge. It may be supposed that intracerebral colonization from Candida took place during the acute phase of sepsis and that the interruption of antimycotic therapy allowed unhindered fungal growth until the development of mass effect. Such consideration and the above reported incidence of autoptic CNS involvement in disseminated candidosis might raise the question if patients affected by such a condition should routinely undergo neuroradiological examinations to disclose silent CNS fungal colonization.

The development of fungal colonies exclusively inside the width of the dura mater, with no involvement of the epidural and subarachnoidal compartment neither the surrounding skull is the second peculiarity of this case. After an accurate review of the literature, we were not able to find any similar report. The occurrence of a totally intradural granuloma might be explained by fungal meningitis, which is the second most frequent presentation of a fungal infection of the CNS. However, in our patient's clinical history no signs of meningeal involvement were recorded either before or during ICU admission. Unfortunately it is impossible to state if during ICU staying meningitis had developed, because no cerebrospinal fluid cultures or a contrast-enhanced head CT scan were never performed at that time.

A final consideration should be made about the decision of leaving the bone in site at the moment of first surgery.

It might be easily stated that even though the infectious nature of the lesion could be only suspected at that moment, the direct contact between the mass and the overlying bone was a high risk condition. Nonetheless, we felt that the advanced age of the patient, the apparent absence of brain involvement, the integrity of the inner aspect of the bone, and the full brain relaxation observed after lesion removal were all factors suggesting bone repositioning as the best and safer option. We believe that surgical site infection was a complication related to the condition of immunosuppression of the patient, especially when considering the absence of isolation of any microorganism at the time of bone removal.

Conflicts of Interest Disclosure

None of the authors have any financial or personal relationship with people or organizations that could inappropriately influence their work. No actual or potential conflict of interest exists with regard to the above submitted manuscript on behalf of any of the authors. All authors who are member of The Japan Neurosurgical Society (JNS) have registered online Self-reported COI Disclosure Statement Forms through the website for JNS members.

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