Case Report

Fungal Granuloma of the Brain in a Case of Chronic Mucocutaneous Candidiasis

Seyed Mojtaba Miri MD[1], Ali Tayebi Meybodi MD•[1], Zohreh Habibi MD[1], Meysam Mohseni, MD[1]

Abstract

Although fungal brain infections are not uncommon, intracranial granulomas due to fungi are rare. Immunodeficiency is considered to be the main predisposing factor. We have presented the case of a 21-year-old lady admitted to the emergency ward with the clinical picture of impending brain herniation. She was a known case of chronic mucocutaneous candidiasis (CMCC) since childhood and had been under oral topical nystatin treatment which she had arbitrarily discontinued for the past ten years. The patient underwent emergent craniotomy and resection of the lesion. Pathologic exam revealed its fungal granulomatous nature. Cultures documented Candida albicans as the offending pathogen. The history of immunodeficiency was a useful clue in this case. To the best of our knowledge, this was the first case of fungal granuloma of the brain in the setting of chronic mucocutaneous candidiasis.

Keywords: Candida albicans, central nervous system, chronic mucocutaneous candidiasis, fungal infections.

Cite this article as: Miri SM, Tayebi Meybodi A, Habibi Z, Mohseni M. Fungal granuloma of the brain in a case of chronic mucocutaneous candidiasis. *Arch Iran Med*. 2012; **15(7):** 452 – 454.

Introduction

Chronic mucocutaneous cadidiasis (CMCC) is a disease characterized by persistent candidal infections of the skin and mucous membranes due to decreased T-cell and altered cytokine response to candidal antigens.[1] This is a case of cerebral granuloma in a 21-year-old woman presenting with the clinical syndrome of impending brain herniation in the setting of CMCC. To the best of our knowledge, this is the first case of its type in the literature.

Case Report

A 21-year-old right-handed female was admitted to the emergency department of our institution because of progressive deterioration of the level of consciousness (LOC) since eight hours previous. On admission she was stuporous (Glasgow Coma Scale [GCS] score: 7/15). Vital signs were within normal limits. Her response to painful stimuli was asymmetric, indicative of left hemiparesis. Pupillary exam showed a dilated right pupil with no response to light; left pupil was mid-sized with a sluggish response to light. Fundoscopic examination revealed bilateral severe papilledema. The neck was supple. Oral thrush and onycolytic lesions were also found on examination. Emergent computed tomography (CT) of the brain revealed a large slightly hyperdense lesion in the right frontal region with marked peri-lesional edema that caused a midline shift.

The patient had been diagnosed as a case of CMCC at four years of age and suffered from persistent oral thrush for which she took oral topical nystatin. She had discontinued the medication at the age of ten years without medical advice. She had no other problems except nail disfiguration along with patchy hyperpigmented lesions of her upper chest and neck (tinea versicolor) for which she did not seek medical attention. For the past two months she had been suffering from new onset persistent headache, more severe in the morning. During the ten days prior to admission, morning vomiting was added to the clinical picture. She was advised to undergo brain imaging by a consultant neurologist. Magnetic resonance imaging (MRI) of the brain revealed a right fronto-parietal mass lesion (Figure 1) with mixed signal intensity and non-homogeneous contrast enhancement. Marked peri-tumoral edema was also evident. The adjacent brain area appeared to be invaded by the lesion. An initial diagnosis of a high-grade glioma had been assumed and she was referred to a neurosurgeon for tumor resection. She was scheduled for elective surgery during the next week; yet, unexpected rapid deterioration resulted in her emergent admission to our institution.

Laboratory examinations were normal except for mild leukocytosis (WBC: 11,800/µl) and elevated erythrocyte sedimentation rate (65 mm/h). Serology test for human immunodeficiency virus was negative.

The patient underwent emergent right fronto-parietal craniotomy for resection of the lesion and decompression. At surgery, the dura appeared tense, with congestion of the cortical veins and severe cerebral edema noted following durotomy. A frontal lobectomy was done; in the sub-cortical white matter there was a firm non-hemorrhagic lobulated yellowish tissue with gritty texture that invaded the adjacent parenchyma, and was barely distinguishable from the normal brain. Piecemeal resection of the lesion was performed and the specimens were sent for pathologic examination, along with bacterial, fungal and acid-fast staining and cultures.

Post-operative brain CT showed resection of the lesion with

Authors' Affiliations: [1]Department of Neurosurgery, Imam Khomeini Hospital, Tehran University of Medical Sciences,Tehran, Iran.
•Corresponding author and reprints: Ali Tayebi Meybodi MD, Department of Neurosurgery, Imam Khomeini Hospital, Keshavarz Blvd., Tehran 14197, Iran. Tel: +9821-66939330, Fax: +9821-66939330, E-mail: tayebi_a77@yahoo.com.
Accepted for publication: 8 February 2012

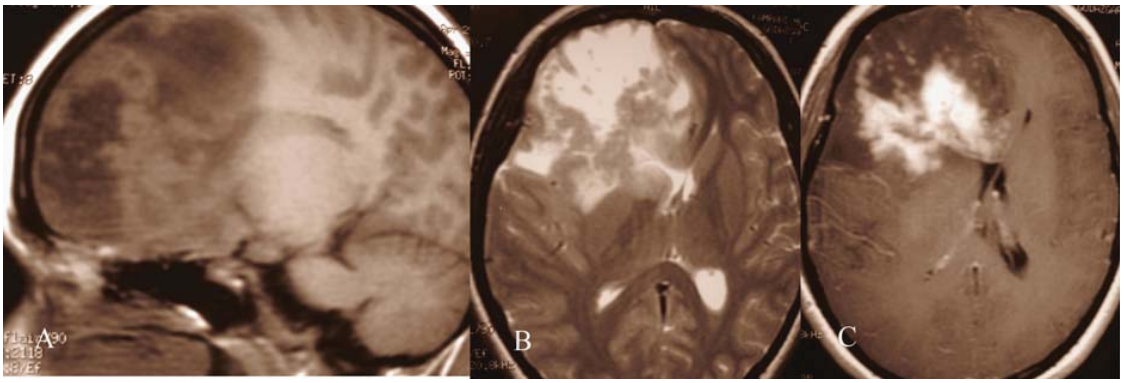

Figure 1. MRI of the brain: (A) T1-weighted, (B) T2-weighted, and (C) Gadolinium-DTPA enhanced showing the enhancing mass lesion.

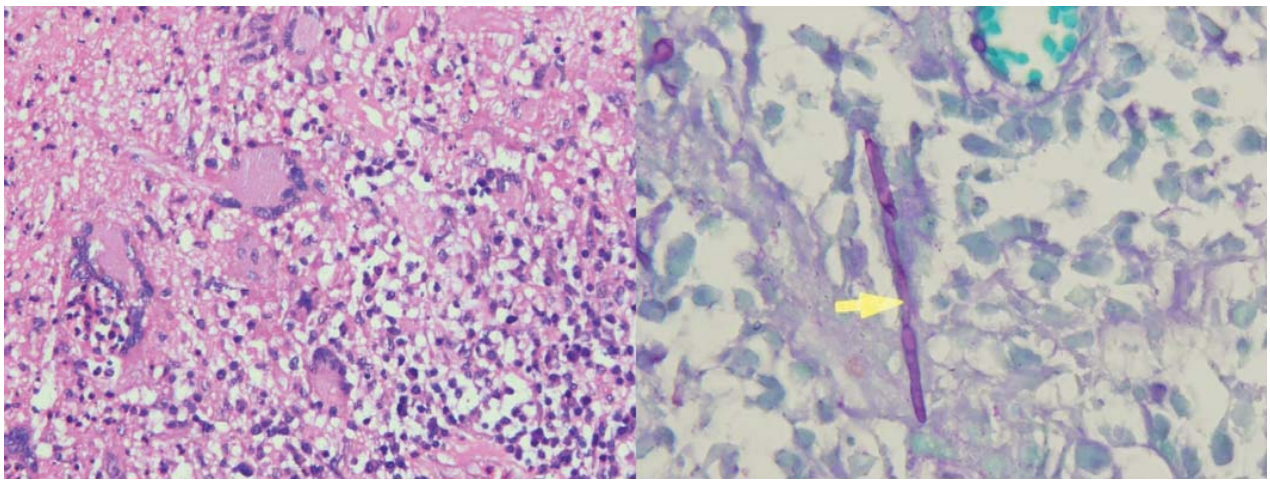

Figure 2. Photomicrograph of the pathologic specimen. Left: Granulomatous reaction. Hematoxylin & Eosin, original magnification 40x. Right: Pseudohyphae of *Candida albicans* (yellow arrow). Periodic acid Schiff staining, original magnification 100x.

marked reduction of the edema and midline shift. A paranasal sinus CT was devoid of any evidence of sinusitis.

Pathologic examination confirmed a fungal granulomatous lesion (Figure 2). Cultures of the specimen further documented *Candida albicans* as the causative agent. Blood, urine, and CSF cultures were negative for bacteria or fungi.

Intravenous amphotericin B was started as was immunotherapy with γ-interferon. On the following days, during which the patient underwent a tracheostomy, she gradually regained consciousness, but developed nosocomial pneumonia. After 40 days of hospitalization she was discharged with oral fluconazole and oral topical nystatin. Six months later, the patient is ambulatory with mild left hemiparesis. She is under periodic imaging surveillance.

Discussion

Fungal infections of the central nervous system may represent numerous illnesses such as meningitis, meningoencephalitis, vasculitis, abscess formation, granuloma formation, arachnoiditis, myelitis, and stroke-like syndromes.[2–4] Fungal infections of the central nervous system are not uncommon. Their incidence is increasing in the current era, mostly due to the increased population of immunocompromised hosts (namely acquired immunodeficiency syndrome [AIDS], transplant patients, malignancies, etc.). Yet, their presentation as intracranial fungal granulomas is a rare occurrence. In general, *Cryptococcus*, *Aspergillus*, and *Candida* are identified as the most common organisms, however in cerebral fungal granulomas *Aspergillus* is reported most frequently.[2] A wide spectrum of neurological findings and presentation syndromes have been previously described.[2,5,6]

Radiological evaluation of brain granulomas is appreciated in two ways: first, the characteristics of the brain lesion in itself, and second the associated extra-cranial findings such as paranasal sinusitis and bony destruction of the medial orbital wall. The MRI features of the cerebral granuloma can take a wide gamut of characteristics.[7,8]

The origin of infection is also variable and can be the result of hematogenous dissemination from a distant focus or contiguous spread (e.g., from a paranasal sinus infection or mastoiditis).[2] The main predisposing factor in fungal infections is reported to be compromised host defense, which could be due to steroid use, prolonged antibiotic therapy, acquired immunodeficiency states (e.g., AIDS, organ transplantation, and advanced age), and diabetes, among others.

CMCC is very rarely reported to be associated with deep infections.[9–11] Our review of the literature did not disclose any patient that has been reported to have intracranial fungal granuloma in the setting of CMCC. It could be hypothesized that, in the shadow of chronic inherent deficient T-cell response in CMCC, hematogenous spread of the fungi to the brain (from the source of persistent oral mucosal lesions) might be the most likely mechanism of development of the brain lesion in our patient. This contradicts

classic characteristics of CMCC in which deep infections are not included in the common scenario of the disease. Yet, the chronicity of the mycotic oral mucosal lesions along with the fact that the patient had failed to comply with anti-fungal therapy may be a basis for possible hematogenous spread of the infectious agent to the brain. Considering the intact bony architecture of the skull base in our patient, contiguous spread of the infection is less likely.

To the best of our knowledge this is the first reported case of intracranial fungal granuloma in the setting of CMCC, which has probably developed in the setting of chronic oral mucosal *Candida* infection that disseminated via a hematogenous route to the brain.

Timely diagnosis of the infectious nature of this malady requires a high degree of suspicion which is brought about by obtaining a thorough clinical history, bringing awareness to a chronic state of immunodeficiency in the relevant clinical picture.

References

1. Lilic D, Gravenor I. Immunology of chronic mucocutaneous candidiasis. *J Clin Pathol*. 2001; **54:** 81 – 83.
2. Dubey A, Patwardhan RV, Sampth S, Santosh V, Kolluri S, Nanda A. Intracranial fungal granuloma: analysis of 40 patients and review of the literature. *Surg Neurol*. 2005; **63:** 254 – 260.
3. Sánchez-Portocarrero J, Pérez-Cecilia E, Corral O, Romero-Vivas J, Picazo JJ. The central nervous system and infection by Candida species. *Diagn Microbiol Infect Dis*. 2000; **37:** 169 – 179.
4. Scully EP, Baden LR, Katz JT. Fungal brain infections. *Curr Opin Neurol.* 2008; **21:** 347 – 352.
5. Murthy JM, Sundaram C, Prasad VS, Purohit AK, Rammurti S, Laxmi V. Aspergillosis of central nervous system: a study of 21 patients seen in a university hospital in south India. *J Assoc Physicians India*. 2000; **48:** 677 – 681.
6. Panda NK, Sharma SC, Chakrabarti A, Mann SB. Paranasal sinus mycoses in north India. *Mycoses*. 1998; **41:** 281 – 286.
7. Akyüz M, Karpuzoğlu G, Açikbaş C, Tuncer R. Candida albicans granuloma imitate clivus chordoma. *Acta Neurochir (Wien)*. 2002; **144:** 505 – 506.
8. Mikhael MA, Rushovich AM, Ciric I. Magnetic resonance imaging of cerebral aspergillosis. *Comput Radiol*. 1985; **9:** 85 – 89.
9. Germain M, Gourdeau M, Hérbert J: Case Report. Familial Chronic Mucocutaneous Candidiasis Complicated by Deep Candida Infection. *Am J Med Sci*. 1994; **307:** 282 – 283.
10. Kauffman CA, Shea MJ, Frame PT. Invasive fungal infections in patients with chronic mucocutaneous candidiasis. *Arch Intern Med*. 1981; **141:** 1076 – 1079.
11. Marazzi MG, Bondi E, Giannattasio A, Strozzi M, Savioli C. Intracranial aneurysm associated with chronic mucocutaneous candidiasis. *Eur J Pediatr*. 2008; **167:** 461 – 463.