Candida tropicalis as an emerging pathogen in *Candida* meningitis: case report and review

ABSTRACT

Candida species are an uncommon cause of meninigitis. Given the rarity of this infection, the epidemiology, prognosis, and optimal therapy for *Candida* meningitis are poorly defined. The authors report on a paraplegic patient due to spinal cord injury who developed *C. tropicalis* meningitis. In addition, we review and discuss other reported cases of *C. tropicalis* meningitis in the medical literature.

Keywords: *Candida*; meningitis.

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INTRODUCTION

Candida species are an uncommon cause of meningitis. Given the rarity of this infection, the epidemiology, prognosis, and optimal therapy of *Candida* meningitis are poorly defined. Risk factors for meningitis are similar to those associated with invasive candidiasis. The risk of developing this complication is unknown. It occurs in immunosupressed patients, in patients treated with broad-spectrum antibiotics and receiving parenteral nutrition or result of disseminated disease.[1-4] In addition, two specific patient groups, premature neonates and neurosurgical patients, are at increased risk.

The case of a paraplegic patient due to a spinal cord injury who developed *C. tropicalis* meningitis is herein reported and the cases reported in the medical literature are reviewed and discussed medical literature.

CASE REPORT

A 26-year-old man was admitted to *Hospital das Clínicas*, Porto Alegre, Brazil, in February 2009 complaining of nausea, vomiting, headache and fever (39°C). Physical exam revealed neck stiffness without any focal neurological signs. Previous medical history included paraplegia due to a spinal injury (2002), decubitus ulcers (2002), pelvic osteomyelitis (2006) and recurrent urinary tract infections. A lumbar puncture yielded cerebrospinal fluid (CSF) with 2,500 leukocytes/mm^3 (100% neutrophils), an elevated protein level of 98 mg/dL, and a reduced glucose level of 34 mg/dL. No fungi and bacteria were seen on Gram stain. CSF cultures were negative for bacteria and fungi. Chest-X ray, head CT scan, and transesophageal echocardiogram results were normal. Blood cultures and HIV serologic test results were negative. Urine cultures grew a mixed flora of Gram-positives and negatives, but urinary Gram-stain revealed innumerous yeasts compatible with *Candida* spp. Despite broad-spectrum 96-hours antibiotic therapy including cefepime, vancomycin, and metronidazole, the patient persisted with fever and headache. Repeated lumbar puncture showed 106 leukocytes/mm^3 (70% neutrophils, 30% lymphocytes), a protein level of 40 mg/dL, and a glucose level of 24 mg/dL. At 24 hours, the primary plates and broth culture grew a budding yeast that was identified with a 99% probability as *C. tropicalis* on API 20C (bioMérieux). The isolates fluconazole MIC was 0.025 µg/mL on disk diffusion susceptibility testing. The patient was treated with amphotericin B deoxycholate (1.0 mg/kg/day) for five days but progressed to respiratory insufficiency, coma and death.

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We declare no conflict of interest.

DISCUSSION

C. albicans accounts for 70%–100% of all fungal meningitis isolates.[3,4] Other reported species include *C. glabrata*, *C. tropicalis*, *C. parapsilopsis*, and *C. lusitaniae*. As shown in Table 1, there have been few cases of *C. tropicalis* meningitis described in the medical literature.[4-17] In contrast to meningitis caused by *C. albicans*, *C. tropicalis* meningitis has been increasingly reported in adults. Most cases of *C. tropicalis* are postoperative complications of head and neck surgery, including

Table 1. Reported cases and series of* C. tropicalis *meningitis

Cases/ Series	Age	Sex	Characteristics	Treatment	Outcome	Reference
1	54	Male	Mastoid exploration; otitis chronic	AmB1	Alive	Chattopadhyay[5]
2	49	Male	Occipital craniotomy; cerebellar hemorrhage	FCZ	Alive	Dawson *et al.*[6]
3	Full-term newborn	Male	Intracranial hemorrhage; respiratory distress; prolonged antibiotic therapy	AmB+5´Flu2	Alive	Ahuja *et al.*[7]
4	54	Male	Mastoid exploration, chronic otitis	AmB+5´Flu	Alive	Chalwick *et al.*[8]
7	43	Male	Hodgkin's lymphoma; chemotherapy	AmB	Death	Hernig *et al.*[9]
8	2	Female	Myelomeningocele correction; ventricular-peritoneal shunt	AmB+FCZ3	Alive	Byers *et al.*[10]
9	66	Female	Corticosteroids	-	Death	Gorell *et al.*[11]
10	63	Male	Syringomyelia	AmB+5´Flu	Alive	Phanthumchinda *et al.*[12]
11	51	Female	Neurinoma, ventriculo-peritoneal shunt, hydrocephalia	AmB+5´Flu	Alive	Miñambres *et al.*[13]
12	-	-	7 children with widespread, leukemia neutropenia, total parental nutrition,costicosteoids, broad sprectrum antibiotics	Yes	Death	Flynn *et al.*[14]
13	-	-	11 children with leukemia, TPN, neutropenia	Yes	Death	McCullers *et al.*[15]
14	Newborn	Male	Sepsis, broad spectrum antibiotics	Yes	Death	Aldress K *et al.*[16]
15	-	-	Ventriculo-peritoneal shunt, bacterial meningitis	Shunt removal	Alive	O´Brien *et al.*[17]
16	68	Female	Cavernous sinus tumor; lumbar drainage, bacterial meningitis, broad spectrum antibiotic therapy	AMB+5FC, shunt removal	Alive	Nguyen *et al.*[4]
17	1	Female	Prematurity, hydrocephalus, peritoneal-ventricular shunt malfunction	AMB+ 5FC, shunt removal	Alive	Chiou *et al.*[18]

AMB, amphotericin B deoxycholate; 5´Flu, 5'Fluorocytosine; FCZ, fluconazole.

mastoid exploration, craniotomy, and ventricular-peritoneal shunt. Additional cases of *C. tropicalis* meningitis in adults have been reported in immunosupressed patients, patients taking prolonged broad-spectrum antibiotic therapy or as a result of disseminated disease, as observed in our case, which developed a possible *Candida* urinary tract infection with later dissemination to the central nervous system.

Symptoms such as those presented by our patient are similar to other *Candida* meningitis and include fever, headache, altered mental status, and meningism. Focal neurologic signs are rare. The diagnosis of meningitis is established by a positive CSF culture. Multiple CSF specimens may be required. CSF parameters are variable, with a mild lymphocytic or polymorphonuclear pleocytosis and an increased protein level. Fungal elements are generally not seen. Thus, CSF abnormalities are indistinguishable from cryptococcal, tuberculous, and some bacterial meningitides. Although fluconazole resistant isolates of *C. tropicalis* have been occasionally reported, the isolate of our case was fluconazole-susceptible.

Despite appropriate therapy with amphotericin B plus 5´fluorocytocine, mortality was seen in 5 of 17 patients (30%) with *C. tropicalis* meningitis. In addition to head and neck postoperative procedures, physicians should have a high index of suspicion for *Candida* meningitis in patients taking broad-spectrum antibiotics who also present an initial source of *Candida* infection. Non-*albicans* species identification and appropriate susceptibility tests should be considered for appropriate management of *Candida* meningitis.

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