



Note

Candida parapsilosis meningitis in a patient with AIDS. Report of a case and review of the literature

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ABSTRACT

Background: *Candida parapsilosis* is an important species in the genus *Candida* that plays a significant role in hospitalized patients with nosocomial infections. In patients with HIV infection or AIDS, central nervous system involvement by *Candida* species is exceptional.

Case report: Here we report a case of an acute meningoencephalitis due to *C. parapsilosis* in an adult patient with AIDS. We describe the clinical manifestations, the diagnosis methods, antifungal therapy and outcome.

Conclusions: *C. parapsilosis* is uncommonly reported as a cause of meningitis in AIDS patients. A higher index of suspicion and culture is necessary to confirm the diagnosis of candidal meningoencephalitis.

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Meningitis por *Candida parapsilosis* en un paciente con sida. Informe del caso y revisión de los estudios publicados

RESUMEN

Antecedentes: *Candida parapsilosis* es una importante especie del género *Candida* que tiene un papel fundamental en el desarrollo de infecciones nosocomiales. En pacientes con infección por VIH, el compromiso del sistema nervioso central por hongos del género *Candida* es infrecuente.

Caso clínico: En este artículo se presenta el caso de un paciente adulto con sida que desarrolló una meningoencefalitis por *C. parapsilosis*. Se describen las manifestaciones clínicas, los métodos de diagnóstico, el tratamiento antifúngico y la evolución.

Conclusión: *C. parapsilosis* es un patógeno infrecuente como causa de meningitis en pacientes con sida. Un alto índice de sospecha y la realización de cultivos son necesarios para confirmar el diagnóstico de meningoencefalitis por levaduras del género *Candida*.

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Palabras clave:

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Candida is the fourth most common cause of hospital-related bloodstream infections.² Although *Candida albicans* is the most frequent isolated yeast, other species are also identified with increasing frequency, including *Candida parapsilosis*.¹⁶

C. parapsilosis is an important *Candida* species which compromise hospitalized patients, particularly in critically ill neonates and

surgical intensive care unit patients, in association with parenteral nutrition and central venous lines.^{10,17} These characteristics may be important risk factors for *C. parapsilosis* infections in cancer patients with indwelling access devices.¹²

Here we describe an unusual case of meningitis caused by *C. parapsilosis* in a patient with advanced human immunodeficiency virus (HIV) infection. In addition, a literature review in PubMed, Cochrane, Scielo, Latindex and Science Citation Index was made including the following words: *C. parapsilosis*, central nervous system (CNS), meningoencephalitis, meningitis, AIDS and HIV.

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Case report

A 35-year-old heterosexual man, intravenous drug user (cocaine), with diagnosis of HIV infection since 1993 was admitted in the AIDS division of our hospital with fever, weight loss (approximately 12 kg in the last 2 months) night sweats and malaise. He had been diagnosed of AIDS because he had a history of recurrent bacterial pneumonia in 2007 and cytomegalovirus meningoencephalitis in 2009. He started antiretroviral therapy based on zidovudine plus lamivudine plus efavirenz, with poor adherence.

On admission, physical examination revealed fever, cachectic status and mucocutaneous paleness. Respiratory and cardiovascular systems were normal; abdominal examination revealed hepatosplenomegaly.

Initially, relevant laboratory findings were anemia with hematocrit 23%, hemoglobin 8 g/dL, leukocytes 2400/mm³ (64% polymorphonuclear and 24% lymphocytes), platelet count 175 000/mm³, erythrocyte sedimentation rate 140 mm in the first hour, and glycemia 94 mg/dL. Renal function, coagulation tests and liver enzymes levels were normal. Phosphatase alkaline was elevated (816 U/L). The CD4 T cell count was 104 cell/ μ L (18%). A chest X-ray was normal. Abdominal ultrasonography showed homogeneous hepatosplenomegaly. Computerized tomography brain scan showed no abnormalities.

Since the patient presented prolonged fever without evidence focus, a lumbar puncture was performed. Cerebrospinal fluid (CSF) biochemical examination showed hyperproteinorrhachia 3.4 g/L, glucose concentration 35 mg/dL with less than 5 cells/ μ L. Direct microscopic examination with India ink, Gram and Ziehl–Neelsen stains were negative. Polymerase chain reaction to herpesvirus and JC virus were also negative. CSF culture on Sabouraud dextrose agar at 28 °C and 37 °C showed non capsulated yeast cells and culture consistently grew with a yeast identified as *C. parapsilosis*.

Intravenous fluconazol treatment at doses of 800 mg/day was initiated with a good clinical response. CSF examination after 14 days of treatment was negative for yeasts. It was his own decision not to follow the indicated treatment and to stop the visits to the hospital.

Discussion

Invasive fungal diseases (IFD) are increasingly observed among critically ill patients and are associated with a high index of morbidity and mortality. Although a wide variety of pathogens can be associated with IFD, *Candida* species have historically been the most common causative organisms.¹¹

Candida infections of the CNS are uncommon and represent the manifestation of disseminated infection due to *Candida* species. Risk factors to CNS *Candida* infections include immunosuppressed patients (including AIDS), intravenous drug user (as in our patient), prolonged therapy with broad spectrum antibiotics, parenteral nutrition, peritoneal dialysis catheters, prosthetic heart valves, manipulation of a mucosal site colonized with *Candida* species, diabetes and neurosurgical procedures, including ventriculoperitoneal shunts.^{3,4,22}

The adherence capacity of *Candida* and its ability to form biofilms may be important fungal virulence factors to all *Candida* species and especially for *C. parapsilosis*.^{9,21} Biofilm development was recently related as a reason why patients with *C. parapsilosis* infected catheters had the device or catheter removed.¹⁵ In addition, the hands of healthcare workers are an important source for *C. parapsilosis* hospital outbreaks.¹²

Candida meningitis is more common in neonates and children than in adults.³ CNS *Candida* infections in adults can occur as a manifestation of disseminated candidiasis, as a complication of a

neurosurgical procedure (especially CSF shunt placement) or as isolated chronic infection.^{1,18,19} In some patients, CSF shunt remotion and ventriculostomy drainage should be necessary.¹

Meningitis is the most common clinical presentation, as in our patient, but multiple or single brain abscesses and epidural abscess have been reported.¹⁴ *C. albicans* is the most frequent etiological agent with a few reports of other species as *C. parapsilosis* and *Candida glabrata*.¹⁴

Oropharyngeal and esophageal candidiasis are the most common fungal infections in AIDS patients but CNS involvement due to *Candida* species appears to be rare. Levy et al. reported only 5 cases in a series of 366 neurologically symptomatic patients, including 4 brain abscesses and one meningoencephalitis in an AIDS child.¹³

In another series of 14 cases of *Candida* meningitis in HIV seropositive patients, *C. albicans* was identified in 13 cases and *Candida tropicalis* was the etiological agent in the other one.¹⁴

Dorko et al. reported 13 cases of nosocomial meningitis; *C. albicans* was isolated from 54% of the patients, *C. parapsilosis* from 23%, *C. tropicalis* from 15% and *C. krusei* from 8%. The three cases of *C. parapsilosis* were found from two premature children and the other one in a child with epilepsy.⁸ Recently, Dizbay et al. reported 35 episodes of candidemia in non-neutropenic critically ill patients with a high mortality rate. Only 2 species were isolated, *C. parapsilosis* in 77.1% of the patients and *C. albicans* in 22.9%.⁷

In a series reported by Casado et al.,⁴ active intravenous drug use was a predisposing factor for systemic or CNS candidiasis, as in our patient.

The clinical manifestations of *Candida* meningoencephalitis do not differ from those of meningitis caused by other pathogens: fever, headache, neck rigidity and compromise of the mental status are the most common findings. However, in the majority of the published cases, clinical symptoms of presentation had more than one month. For this reason, many authors have proposed the name of chronic *Candida* meningitis.²⁰ In the patient we describe, the prolonged fever without focus was the motive to make a lumbar puncture.

Cerebrospinal fluid examination generally reveal a mild lymphocytic or polymorphonuclear pleocytosis, hyperproteinorrhachia and low glucose levels.⁴ These findings are similar to cryptococcal or *Mycobacterium tuberculosis* meningitis, the two most frequent opportunistic pathogens that cause meningoencephalitis in AIDS patients.^{5,6}

Liposomal amphotericin B, because of its low risk of nephrotoxicity, at a dosage of 3–5 mg/kg daily, with or without flucytosine at a dosage of 25 mg/kg 4 times daily, appears to be the most appropriate treatment for CNS candidiasis in adults.¹⁴ Fluconazole achieves excellent levels in CSF and brain parenchyma and is useful for the treatment of *Candida* CNS infections after liposomal amphotericin B and flucytosine.¹⁴ Although fluconazole has been used as single therapy, as in our patient, the association with flucytosine has been successfully applied in few patients with *Candida* meningitis.

Therapy should be continued until all signs and symptoms, CSF abnormalities and radiological findings have been resolved.¹⁴

In contrast with other immunocompromised subjects, *Candida* CNS infections, including meningoencephalitis and cerebral abscesses, are a rare complication in AIDS patients.^{3,22} Our case demonstrates the importance of a high index of suspicion and the need to culture the CSF samples to prove the diagnosis of *Candida* meningitis in AIDS patients.

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