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What is This?

CNS cryptococcoma in an HIV-positive patient

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Abstract

This is the first case of brain cryptococcoma in an AIDS patient reported in Argentina. The patient was a 28-year-old white heterosexual man with AIDS who presented with altered mental status, seizures, visual hallucinations, headache, and fever without significant focal neurological deficit. He had a lumbar puncture, and was treated for cryptococcal meningitis. Subsequent brain CT scanning and MRI disclosed a mass lesion in the occipital lobe. Histopathological examination of biopsy was compatible with cryptococcoma, and tissue culture revealed *Cryptococcus neoformans*. Resolution of the mass and edema resulted after treatment with intravenous amphotericin B for six weeks, which was followed with maintenance oral fluconazole.

Intracranial mass is an uncommon complication in AIDS patients with cryptococcosis, and cryptococcoma should be considered as differential diagnosis of brain mass lesion in these patients. The etiologic diagnosis is necessary because central nervous system (CNS) toxoplasmosis, lymphoma, and tuberculoma can produce similar clinical syndromes and MRI or CT findings to cryptococcoma. Also, these pathologies may coexist with meningeal cryptococcosis.

Key words: cryptococcoma, HIV infection, central nervous system, neurologic complications

Introduction

Cryptococcosis is the most frequent systemic mycosis observed among AIDS patients at the Francisco J Muñiz Hospital in Buenos Aires, Argentina, where approximately 100 new cases are diagnosed annually. Its prevalence is 15 percent of HIV/AIDS cases.¹

Correspondence and request for reprints to: Alcides Troncoso, MD, PhD, Infectious Diseases, Francisco Muñiz Hospital, Uspallata 2272-1282, Buenos Aires, Argentina. E-mail: alcidestr@hotmail.com JIAPAC 2002;1(4):131-133. © 2002 IAPAC. Cryptococcal infection of the CNS may produce symptoms and signs of meningitis, meningoencephalitis, or manifest as single or multiple space-occupying lesions with focal neurologic deficit, which is referred to as cryptococcoma.^{1,2} Three different forms of focal lesions have been described as intracerebral abscesses, gelatinous pseudocysts, and rarely septated lesions within the intraventricular spaces around the choroid plexus.²

Cryptococcosis is present in most AIDS patients at our hospital as meningitis or meningoencephalitis with clear cerebrospinal fluid (CSF), and is only occasionally observed as mass, or space-occupying lesion.³ We report on an HIV-positive patient with cryptococcal meningitis and CNS cryptococcoma, diagnosed by microscopy and cultures of tissue after stereotactic brain biopsy.

Case report

A 28-year-old white heterosexual man with a history of intravenous drug use had been diagnosed with HIV infection eight years earlier. He became ill two weeks prior to his admission with symptoms of fever, severe headache, visual hallucinations, seizures, and altered level of consciousness. At the time, his medications included double-strength trimethoprim-sulfamethoxazole tablets three times weekly. His only previous opportunistic infection had been tuberculosis.

Physical examination showed reduced alertness, hepatoand splenomegaly, pseudomembranous oropharyngeal candidiasis, hairy leukoplakia, tachycardia, and fever. Kernig, Brudzinski, and Romberg signs were negative, and the Babinski reflex and nuchal rigidity were absent. Pupils were equal and reactive. There was no papilledema. Skin sensation, reflexes, muscle tone, and cranial nerves were intact. Deep tendon reflexes were normal without clonus.

Blood chemistry was unremarkable except for a white blood cell count of 2,100/ μ L, and hemoglobin of 10.9 g/dL. CD4 lymphocyte count was 28 cells/ μ L, and HIV-1 plasma viral load greater than 750,000 copies/ μ L. Lumbar puncture was done. The CSF fluid was under

Figure 1. Contrast-enhancing mass lesion, in the left occipital lobe, with significant surrounding edema, associated with mild mass effect

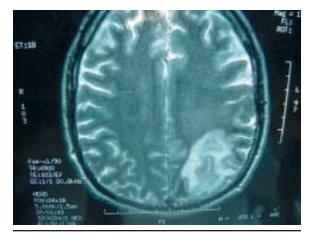


Photo courtesy of Luis Trombetta

increased opening pressure of 300 mm H₂O, and contained 5 cells/ μ L (100 percent lymphocytes). The protein content was 49 mg/ μ L with normal glucose. CSF India ink stain revealed encapsulated budding yeasts cells, and the culture grew *C. neoformans*. The latex agglutination tests for *C. neoformans* capsular polysaccharide antigen were positive in serum, and in CSF at high titer (1:100,000 and 1:10,000, respectively). The patient was treated, but did not improve, with amphotericin B.

Subsequent MRI of the brain (Figure 1) revealed a 2 cm left occipital mass that was hypointense on T1 weighted images, hyperintense on T2 weighted images, ringenhancing with gadolinium, with substantial surrounding edema, and little displacement or mass effect.

Differential diagnosis included other causes of cerebral mass lesions, principally toxoplasmosis, tuberculosis, and primary CNS lymphoma. A stereotactic brain biopsy was performed. Histopathologic evaluation revealed granulomatous lesions with numerous encapsulated yeast organisms, and the oval and rounded yeasts (4-10 μ in diameter) appeared light pink with hematoxylin and eosin stains. The capsule of C. neoformans stains showed positive with Mayer's mucicarmine stain. Cultures revealed Cryptococcus neoformans. Brain biopsy was uncomplicated, and the patient had been started on high-dose amphotericin B (0.7 mg/kg/day) for *Cryptococcus neoformans* infection. Dexamethasone (28 mg/day) was added. Antifungal treatment was changed after six weeks to oral fluconazole 200 mg/day as maintenance dose.

The patient is currently on oral lifelong fluconazole (200 mg/day) therapy, and a repeat MRI scan at 12

weeks showed reduction in the size of the brain lesion. He was discharged eight weeks after admission following subjective and objective improvement.

Discussion

Brain mass is a common cause of neurologic deficit in HIV-infected patients, who may also characteristically present with headaches, fever, or seizures.² The diagnostic workup for an HIV-positive patient who presents with these symptoms should include a cranial CT or MRI scan. This should be obtained as soon as possible, and preferably before a lumbar puncture.³ Diagnostic imaging may narrow the differential diagnoses, guide empiric therapy, and identify undue risks of lumbar puncture.

It is initially useful to divide potential causes of CNS mass lesions into infectious or non-infectious groups, with attention to CNS lymphoma and to other neoplasms that may metastasize to the brain.⁴

During the early years of the HIV epidemic, toxoplasmosis was the most common infectious cause of cerebral masses, followed by mycotic abscess such as cryptococcoma and tuberculoma.^{5,6} Tuberculosis of the CNS without obvious lesions elsewhere may be the most difficult disease to identify. In such cases the diagnosis is usually not made until after neurosurgical biopsy.⁷

C. neoformans causes CNS infection in patients with AIDS, and is generally associated with basal meningitis. CNS cryptococcosis rarely presents as a single lesion or multiple mass lesions.⁸ Clinical presentation ranges from headache to acute obstructive hydrocephalus.⁹ Cryptococcoma is an uncommon cause of seizures and must be considered in the differential diagnosis.¹⁰ This fungal disease may mimic almost any other condition affecting the central nervous system.¹¹

Treatment of cryptococcoma consists of amphotericin B and adjunctive steroid therapy for management of elevated intracranial pressure. The benefit of steroid therapy is not well established¹² and is controversial as an adjunctive treatment of infection. However, its use is often recommended in circumstances where elevated intracranial pressure may precipitate rapid neurological deterioration.

The clinical manifestations of CNS mass lesions are quite variable with presentation ranging from indolent to a neurologic catastrophe. The classic triad of headache, fever, and focal deficit occur in less than 50 percent of patients with mass lesions. Lumbar puncture is usually nonspecific, and may be contraindicated due to the potential for transtentorial herniation and death.⁶

CT and MRI have revolutionized the diagnosis and management of CNS mass lesions. The radiological evaluation of the lesions included both CT scan and MRI with gadolinium enhancement, that are shown to be more sensitive than a standard MRI in identifying focal brain lesions of specific cause, or in the evaluation of patients with meningeal findings when other studies are inconclusive. Contrast enhancement is also beneficial in differentiating a mass lesion from surrounding edema in preparation for a stereotactic biopsy, and in defining multiple lesions that may not be apparent or that appear as solitary lesions on a CT scan.¹³

Our patient had a subacute presentation of illness. CSF was negative for *Toxoplasma gondii* DNA by polymerase chain reaction (PCR). The lesion did not have a typical appearance of a lymphoma or a metastatic carcinoma, and there was no evidence of a primary tumor outside the CNS. We considered Mycobacterium tuberculosis and non-tuberculous mycobacterial infections in the differential diagnosis, particularly in this setting of HIV and past turberulosis. Mycobacterial abscesses are also frequently multiple and occur in the setting of meningitis or disease outside the central nervous system.^{1,14,15} We performed the stereotaxic procedure to obtain the etiologic diagnosis because of the similarity among the lesions produced by different etiologic agents in the brain, the occasional concomitance of these various lesions, and a lack of initial therapeutic response observed in our patient.

Delay in specifically diagnosing a treatable spaceoccupying lesion can lead to increased mortality. When assessing these patients, it is important to remember that HIV patients may have concomitant conditions with a variety of noninfectious and infectious diseases that mimic cryptococcoma (eg, toxoplasmosis, lymphoma, tuberculosis). Parasitic causes such as Chagas' disease (*Trypanosoma cruzi*) deserve inclusion, despite being an unlikely pathogen, because they can occur in South America.¹⁶ Biopsy may be helpful in certain contexts, such as lack of a specific diagnosis, or likelihood of identification of a specifically treatable second condition. This case illustrates the presentation, diagnosis, and course of treatment of cyrptococcal meningitis with cryptococcoma in AIDS. ■

References

- Bava AJ, Negroni R, Arechavala A, Robles AM, Bianchi M. Cryptococcosis associated with AIDS in the Muniz Hospital of Buenos Aires. *Mycopathologia* 1997; 140(1):13-7.
- Andreula CF, Burdi N, Carella A. CNS cryptococcosis in AIDS: spectrum of MR findings. J Comput Assist Tomogr 1993; 17(3):438-41.
- Negroni, R, Arechavala A, Robles AM, Bianchi M, Bava AJ. Revisión clínica y evolución terapéutica de pacientes con criptococcosis asociada al SIDA. *Revista Iberoamericana de Micología* 1995; 12:12-5.

- Tirelli U, Spina M, Gaidano G, et al. Epidemiological, biological, and clinical features of HIV-related lymphomas in the era of highly active antiretroviral therapy. *AIDS* 2000; 14(12):1675-88.
- Ammassari A, Murri R, Cingolani A, et al. AIDS-associated cerebral toxoplasmosis: an update on diagnosis and treatment. *Curr Top Microbiol Immunol* 1996; 219:209-22.
- Evaluation and management of intracranial mass lesions in AIDS. Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology* 1998; 50(1):21-6.
- Iacoangeli M, Roselli R, Antinori A, et al. Experience with brain biopsy in acquired immune deficiency syndrome-related focal lesions of the central nervous system. *Br J Surg* 1994; 81(10):1508-11.
- Mitchell TG, Perfect JR. Cryptococcosis in the era of AIDS—100 years after the discovery of *Cryptococcus neoformans*. *Clin Microbiol Rev* 1995; 8(4):515-48.
- Mulanovich VE, Saag MS. Cryptococcal meningitis. In: Berger JR, Levy RM, eds. *AIDS and the Nervous System*. Lippincott-Raven Publishers, Philadelphia, 1997. Pp 661-75.
- Khanna N, Chandramuki A, Desai A, et al. Cryptococcal infections of the central nervous system: An analysis of predisposing factors, laboratory findings and outcome in patients from South India with special reference to HIV infection. *J Med Microbiol* 1996; 45(5):376-9.
- Wispelwey B, Dacey RG, and Scheld WM. Brain Abscess. In: Scheld WM, Whitley RJ, and Durack DT, eds. *Infections of the Central Nervous System*, 2nd ed. Lippincott-Raven Publishers, Philadelphia, 1997. Pp. 463-92.
- 12. van der Horst CM, Saag MS, Cloud GA, et al. Treatment of cryptococcal meningitis associated with the acquired immunodeficiency syndrome. National Institute of Allergy and Infectious Diseases Mycoses Study Group and AIDS Clinical Trials Group. *N Engl J Med* 1997; 337(1):15-21.
- Ammassari A, Scoppettuolo G, Murri R, et al. Changing disease patterns in focal brain lesion-causing disorders in AIDS. J Acquir Immune Defic Syndr Hum Retrovirol 1998; 18(4):365-71.
- Bava AJ, Negroni R. The epidemiological characteristics of 105 cases of cryptococcosis diagnosed in the Republic of Argentina between 1981-1990. *Rev Inst Med Trop Sao Paulo* 1992; 34(4): 335-40.
- Gildenberg PL, Gathe JC Jr, Kim JH. Stereotactic biopsy of cerebral lesions in AIDS. *Clin Infect Dis* 2000; 30(3): 491-9.
- 16. Corti M. AIDS and Chagas' Disease. *AIDS Patient Care and STDs* 2000; 14(11): 581-8.