CASE REPORT

Appearance of CNS histoplasmosis on $^{18}$F-FDG PET/CT with MRI correlation

WILLIAM MAKIS, MD, RAJAN RAKHEJA, MD and STEPHAN PROBST, MD

Department of Diagnostic Imaging, Cross Cancer Institute, Edmonton, AB, Canada
Department of Nuclear Medicine, Jewish General Hospital, Montreal, QC, Canada

Address correspondence to: Dr William Makis
E-mail: makisw79@yahoo.com

ABSTRACT

Disseminated histoplasmosis is an opportunistic infection encountered in immunocompromised patients such as those with human immunodeficiency virus infection/acquired immune deficiency syndrome. Involvement of the central nervous system (CNS) can occur in 5–20% of cases of disseminated histoplasmosis, and CNS histoplasmosis can be very difficult to diagnose via conventional imaging modalities such as CT or MRI. The role of $^{18}$F-fluorodeoxyglucose positron emission tomography/CT scan in the diagnosis of CNS histoplasmosis has not been established. A 66-year-old female presented with dizziness and unsteady gait and was diagnosed with human immunodeficiency virus infection and CNS histoplasmosis. In this report, we present the MRI and $^{18}$F-fluorodeoxyglucose positron emission tomography/CT image findings.

DISCUSSION

H. capsulatum is a thermally dimorphic fungus and infects humans when it is inhaled into the lungs where it germinates into yeast. Disseminated histoplasmosis is an opportunistic infection encountered in immunocompromised patients, such as those with HIV/acquired immune deficiency syndrome (AIDS). While patients with chronic infection often present with pancytopenia and hepatosplenomegaly, patients with AIDS may present with much more serious signs and symptoms, including respiratory distress, shock and hepatic or renal failure.

The CNS is involved in up to 20% of cases of disseminated histoplasmosis and can present as meningitis, multiple focal brain lesions or encephalitis. CNS histoplasmosis is very difficult to diagnose via conventional diagnostic imaging modalities such as CT and MRI, as the presenting brain lesion is often interpreted as a brain tumour or a focus of toxoplasmosis, as was the case with our patient. Diagnosis is usually confirmed by cerebrospinal fluid culture or biopsy, although these tests suffer from low sensitivities (as low as 20% for cerebrospinal fluid culture and 50% for biopsy). Treatment guidelines now recommend induction therapy...
with amphotericin B followed by itraconazole for life in patients with HIV/AIDS.

Azizirad et al reported the only other known case of pathologically proven CNS histoplasmosis imaged with an ¹⁸F-FDG PET/CT scan, where they ascribed the increased glucose metabolism to the patient’s histoplasma lesion; however, careful review of the images showed only minimally increased uptake in the enhancing portion of the lesion when compared with the immediate soft tissue surroundings, and the average uptake of the entire lesion was well below the uptake in the normal grey matter, findings that are very similar to those in our case. Symptomatic CNS histoplasmosis is exceedingly rare and only a few cases have been reported in the imaging literature.

Several studies have shown ¹⁸F-FDG PET/CT scans to be particularly useful in differentiating infections such as toxoplasmosis from malignant lesions such as lymphoma or metastases in HIV-positive patients. In a study of 25 patients by Lewitschnig et al, 10 of 11 patients with a diagnosis of toxoplasmosis were correctly diagnosed by PET/CT scan showing ¹⁸F-FDG uptake by the lesion to be less than that of normal brain cortex with a mean SUVₘₐₓ of 3.5 (range 1.9–5.8), while malignant lesions such as CNS lymphoma showed ¹⁸F-FDG uptake greater than normal brain cortex with mean SUVₘₐₓ of 18.8 (range 12.4–29.9). Interestingly, two patients with tuberculosis also showed low ¹⁸F-FDG uptake. Westwood et al showed that an ¹⁸F-FDG PET/CT scan was able to correctly identify lymphoma and hypometabolic toxoplasmosis in all of their 10 HIV-positive patients.

Our case showed that CNS histoplasma lesions were hypometabolic compared with normal grey matter, similar to ¹⁸F-FDG PET/CT results that have been seen with other CNS infections in HIV-positive patients such as toxoplasmosis or tuberculosis, suggesting that an ¹⁸F-FDG PET/CT scan may not be useful in the diagnosis of CNS histoplasma lesions, contrary to what has been reported in the literature thus far.

**LEARNING POINTS**

1. CNS histoplasmosis is difficult to diagnose on conventional imaging modalities such as CT or MRI.
2. The literature suggests a possible role for ¹⁸F-FDG PET/CT scan in the diagnosis of CNS histoplasmosis.
3. CNS histoplasma lesions in HIV-positive patients, similar to toxoplasmosis or tuberculosis, can be hypometabolic on ¹⁸F-FDG PET/CT scan compared with

**Figure 1.** (a) Transaxial CT, (b) PET, (c) PET/CT fusion and (d) MRI T₁ weighted post-gadolinium images. The intensely enhancing cerebral lesions seen on MRI appear hypometabolic on the PET/CT images when compared with normal grey matter. PET, positron emission tomography.

**Figure 2.** (a) Coronal CT, (b) positron emission tomography, (c) positron emission tomography/CT fusion and (d) MRI T₁ weighted post-gadolinium images. The largest single lesion in the right temporal lobe measured 2.4 × 1.9 cm in the coronal plane.

**Figure 3.** A follow-up MRI performed 2 years later with (a) transaxial and (b) coronal T₁ weighted post-gadolinium images showed complete resolution of the right temporal lobe Histoplasma capsulatum lesions.
the grey matter of the brain, suggesting that PET/CT scan likely does not have a role in the diagnostic work-up of these lesions.

CONSENT
Informed consent to publish this case (including images and data) was obtained and is held on record.

REFERENCES

1. Knapp S, Turnherr M, Dekan G, Willinger B, Stingl G, Rieger A. A case of HIV-associated cerebral histoplasmosis successfully treated with fluconazole. *Eur J Clin Microbiol Infect Dis* 1999; **18**: 658–61. doi: http://dx.doi.org/10.1007/s100960050368

2. Sarosi GA, Johnson PC. Disseminated histoplasmosis in patients infected with human immunodeficiency virus. *Clin Infect Dis* 1992; **14**: S60–S67. doi: http://dx.doi.org/10.1093/clinids/14.Supplement_1.S60

3. Goodwin RA, Shapiro JL, Thurman GH, Thurman SS, Dse Prez RM. Disseminated histoplasmosis: clinical and pathologic correlations. *Medicine* 1980; **59**: 1–33. doi: http://dx.doi.org/10.1097/00005792-198001000-00001

4. Wheat LJ, Connolly-Stringfield PA, Baker RL, Cufman MF, Eads ME, Israel KS, et al. Disseminated histoplasmosis in the acquired immune deficiency syndrome: clinical findings, diagnosis and treatment, and review of the literature. *Medicine* 1990; **69**: 361–74. doi: http://dx.doi.org/10.1097/00005792-199001100-00004

5. Wheat LJ, Batteiger BE, Sathapatayavongs B. Histoplasma capsulatum infections of the central nervous system. A clinical review. *Medicine* 1990; **69**: 244–60. doi: http://dx.doi.org/10.1097/00005792-199007000-00006

6. Ciricillo SF, Rosenblum ML. Use of CT and MR imaging to distinguish intracranial lesions and to define the need for biopsy in AIDS patients. *J Neurosurg* 1990; **73**: 720–4. doi: http://dx.doi.org/10.3171/jns.1990.73.5.0720

7. Joseph Wheat L. Current diagnosis of histoplasmosis. *Trends Microbiol* 2003; **11**: 488–94. doi: http://dx.doi.org/10.1016/j.tim.2003.08.007

8. Azizirad O, Clifford DB, Groger RK, Prelutsky D, Schmidt RE. Histoplasmosa: isolated central nervous system infection with *Histoplasma capsulatum* in a patient with AIDS. Case report and brief review of the literature. *Clin Neurol Neurosurg* 2007; **109**: 176–81. doi: http://dx.doi.org/10.1016/j.clineuro.2006.04.010

9. Livas IC, Nechay PS, Nauseef WM. Clinical evidence of spinal and cerebral histoplasmosis twenty years after renal transplantation. *Clin Infect Dis* 1995; **20**: 692–5. doi: http://dx.doi.org/10.1093/clinids/20.3.692

10. Klein CJ, Dinapoli RP, Temesgen Z, Meyer FB. Central nervous system histoplasmosis mimicking a brain tumor: difficulties in diagnosis and treatment. *Mayo Clin Proc* 1999; **74**: 803–7. doi: http://dx.doi.org/10.4065/74.8.803

11. Lewitschnig S, Gedela K, Toby M, Kulasegaram R, Nelson M, O’Doherty M, et al. 18F-FDG PET/CT in HIV-related central nervous system pathology. *Eur J Nucl Med Mol Imaging* 2013; **40**: 1420–7. doi: http://dx.doi.org/10.1007/s00259-013-2448-1

12. Westwood TD, Hogan C, Julyan PJ, Coutts G, Bonington S, Carrington B, et al. Utility of FDG-PETCT and magnetic resonance spectroscopy in differentiating between cerebral lymphoma and non-malignant CNS lesions in HIV-infected patients. *Eur J Radiol* 2013; **82**: e374–e379. doi: http://dx.doi.org/10.1016/j.ejrad.2013.03.008