Use of fluorodeoxyglucose–positron emission tomography for the differentiation of cerebral lesions in patients with acquired immune deficiency syndrome

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Intracranial mass lesions comprise approximately half of all acquired immune deficiency syndrome (AIDS)–related neurological complications. Although toxoplasmosis and lymphoma are the most common causes of these lesions, diagnosis and treatment can be delayed because computerized tomography and magnetic resonance imaging studies cannot accurately differentiate between them.

The authors retrospectively studied nine patients with AIDS in whom, after a 6-hour fast, [18F]-fluorodeoxyglucose (FDG)–positron emission tomography (PET) scanning demonstrated intracranial mass lesions. The FDG uptake within each lesion was classified as either increased or not increased. In six patients there was no increase in FDG uptake, which suggested a diagnosis of toxoplasmosis, and lymphoma was suggested in two patients in whom increased FDG uptake was demonstrated. In a patient with two lesions, one lesion was shown to have increased FDG uptake whereas the other was shown to have no increased FDG uptake. All patients in whom a diagnosis of toxoplasmosis was made were started on antimicrobial therapy. Two patients died of other AIDS-related complications before repeated neuroimaging could be performed to assess treatment response, one patient refused to undergo further treatment or follow up, and two patients responded well to treatment. One patient with toxoplasmosis did not respond to the drugs.

Analysis of a biopsy sample of the lesion confirmed the diagnosis; however, the patient died shortly thereafter. The two patients with FDG-PET–diagnosed lymphoma began corticosteroid therapy and improved considerably. In the patient in whom PET demonstrated two different FDG uptakes, a biopsy sample was obtained that confirmed the diagnosis of lymphoma; this patient was started on corticosteroid therapy and improved. A safe and reliable diagnostic tool, FDG-PET scanning can be used to differentiate causes of human immunodeficiency virus-related intracranial mass lesions. When available, this diagnostic study should be conducted before initiating empirical treatment or obtaining a stereotactically guided brain biopsy sample.

KEY WORDS • acquired immune deficiency syndrome • cerebral lesion • human immunodeficiency virus • positron emission tomography

Between 1997 and 1998, the number of patients living with AIDS in the United States increased 10%; at the same time, HIV-related deaths decreased 20%. Clinically relevant neurological disease is observed in up to two thirds of patients with HIV infection, and as many as half of these harbor an HIV-associated intracranial mass lesion. As the population of people living with AIDS increases, diagnosis and management of cerebral mass lesions will become a more frequently encountered problem for neurosurgeons.

The most common opportunistic infection of the CNS in patients with AIDS is toxoplasmosis. In 10 to 50% of HIV-related cerebral mass lesions, toxoplasmosis is the cause. The second most common opportunistic infections are primary CNS lymphoma and progressive multifocal leukoencephalopathy. The utility of CT or MR imaging for the differentiation of HIV-related intracranial masses is somewhat limited, because patients with toxoplasmosis or lymphoma, reveal contrast-enhancing lesions with mass effect. The current standard management of these intracranial masses is empirical pharmacological treatment for toxoplasmosis and careful clinical and neuroimaging monitoring for response to treatment. If the patient does not respond to treatment, a stereotactically guided biopsy procedure is performed to obtain histological diagnosis. Because the risk and cost of empirical treatment and/or brain biopsy procedures are important factors in the man-
agement of patients with AIDS, we propose the use of FDG-PET to differentiate between intracranial HIV-related masses.

**CLINICAL MATERIAL AND METHODS**

We retrospectively evaluated our institution's medical records and neuroimaging studies obtained in all patients with AIDS who were referred to the PET Imaging Center with a presumptive diagnosis of intracranial mass. Nine patients, all men, were examined. Their ages ranged from 27 to 48 years (mean 36.6 years). One patient received empirical toxoplasmosis treatment before the study. All patients underwent CT scanning to diagnose the mass, all but one underwent MR imaging, and one patient underwent a thallium-201 single-proton emission CT brain study. In two patients a stereotactic biopsy sample was obtained prior to the study, but the results were inconclusive. One patient began steroid treatment prior to the study. After a 6-hour fast, fingerstick blood glucose was determined using a commercially available method. The PET scans were obtained on a GE Advance scanner (GE Medical Systems, Milwaukee, WI) 1 hour after intravenous injection of a standard 10 to 15–mCi FDG.

Acquisition time was 10 minutes in two-dimensional mode, and 35 slices were obtained with 4.25-mm thickness. The images were reconstructed using filtered-back projection, and planes were reformatted orthogonal to the orbitomeatal line. Fluorodeoxyglucose uptake in the lesion(s) was compared visually with average FDG uptake in cerebral cortical gray matter, and then it was compared with findings obtained from the previous neuroimaging studies.

The scans were reviewed and graded as 1) increased FDG uptake in the lesion or 2) no increased FDG uptake in the lesion. In patients with more than one lesion, each was evaluated separately.

**RESULTS**

In six patients no increased FDG uptake was demonstrated in the lesions, suggesting infection. In two patients increased FDG uptake was revealed, suggesting lymphoma. In the patient with two lesions one had increased FDG uptake and the other had no increased FDG uptake.

All patients diagnosed as having toxoplasmosis began antimicrobial therapy. Two of these patients subsequently died of other AIDS-related complications before repeated MR imaging could be undertaken. One patient left the hospital against medical advice and refused follow up. One patient did not respond to treatment; a stereotactic biopsy sample was obtained that revealed toxoplasmosis infection, and the patient died shortly thereafter. The other two patients with toxoplasmosis responded to treatment, as demonstrated on postoperative MR imaging and clinical examination, and continue to undergo follow up with their primary physicians.

In the patients in whom stereotactically guided biopsy samples were obtained prior to PET scanning, decreased FDG uptake, consistent with toxoplasmosis, was revealed. The two patients with increased FDG uptake were started on corticosteroid therapy, and their lesions were shown to have resolved on the follow-up MR imaging study. One of these had begun toxoplasmosis treatment prior to the study.

Analysis of a biopsy sample obtained in the patient in whom PET demonstrated two different FDG uptakes revealed lymphoma; he was started on corticosteroid therapy and his condition has improved clinically and radiologically, with resolution of both mass lesions (Table 1).

**ILLUSTRATIVE CASES**

**Case 1**

This 34-year-old man who had been HIV-positive for 7 years and had a history of multiple infections was admit-
ted with a 1-month history of mental status change, lethargy, and worsening constitutional symptoms. Magnetic resonance imaging revealed a contrast-enhancing lesion in the right frontal lobe involving the anterior basal ganglia (Fig. 1 left). Two days after undergoing the aforementioned study, PET scanning demonstrated intense FDG uptake in the lesion, suggesting CNS lymphoma (Fig. 1 right). He began corticosteroid therapy, and his symptoms improved. Fourteen days later, MR imaging revealed a decrease in the size of the intracranial lesion. The patient was discharged in fair condition.

Case 2

This 41-year-old man with a 4-year history of AIDS had developed progressive left-sided weakness, headache, and slurred speech during the 3 months prior to admission. On MR imaging a right basal ganglia contrast-enhancing lesion was revealed (Fig. 2 left). Four days later PET scanning demonstrated no increased FDG uptake, which was consistent with a diagnosis of toxoplasmosis (Fig. 2 right). Serum levels were elevated for toxoplasmosis titers, and the patient was started on pyrimethamine and sulfadiazine. His symptoms improved, and he was discharged to a nursing home. On follow-up examination 1 month later, MR imaging demonstrated a decrease in the lesion size.

DISCUSSION

Intracranial mass lesions are among the most common neurological consequences of HIV infection. Up to two thirds of patients infected with HIV will become neurologically compromised, and as many as half of these will develop intracranial mass lesions. Toxoplasma encephalitis is the most common cause of intracranial mass lesions in HIV-infected patients, occurring in 3 to 10% of cases in the United States and in up to 50% of cases in Europe and Africa. Primary CNS lymphoma is found in 2% of all patients with HIV-related intracranial mass lesions, and its incidence appears to be increasing, probably because of improved survival rates.

The current trend is to initiate empirical treatment for toxoplasmosis, except in cases in which a single intracranial mass lesion demonstrates negative toxoplasmosis serology. Patients treated presumptively for toxoplasmosis in whom there is no clinical and radiological improvement or patients with negative toxoplasmosis serology and a single intracranial mass should undergo a stereotactic brain biopsy procedure. The usually poor overall condition of these patients and the risk of causing medication- and surgery-related adverse effects make proper diagnosis prior to treatment essential.

Several attempts have been made to restrict further the differential diagnosis of HIV-related intracranial mass lesions. It is known that the similarity of neuroimaging findings in patients with toxoplasmosis and lymphoma prevent contrast-enhanced CT and MR imaging from differentiating these most common causes of intracranial mass lesions in patient with AIDS. Thallium-201 single-proton emission CT has been used, and when the results it obtains are positive, it appears to be highly specific for CNS lymphoma; however, it is not highly sensitive, particularly in the case of small or necrotic lesions.

Some authors have demonstrated the usefulness of PET scanning for the diagnosis and monitoring of primary CNS lymphoma, because the lesion is a hypermetabolic tumor with markedly elevated FDG uptake even when the patient is on steroid therapy; however, the patients included in these studies were not infected with HIV.

Hoffman, et al., have reported on a series of 11 HIV-positive patients who were treated empirically for toxoplasmosis and in whom therapy failed. In these cases, FDG-PET scanning was able to differentiate accurately nonmalignant from malignant causes of CNS lesions in all patients.

Villringer, et al., described 11 AIDS patients with intracranial mass lesions who underwent toxoplasmosis therapy at the time at which the PET session was conducted. This diagnostic study also was able to differentiate between cerebral infections (one patient was diagnosed with tuberculoma) and primary CNS lymphoma.

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In 1995, Pierce, et al., prospectively studied 20 patients with AIDS and contrast-enhancing lesions by performing FDG-PET scanning as well as toxoplasma serological testing. Diagnoses were confirmed by clinical response, autopsy findings, or brain biopsy results. They were clearly able to differentiate between toxoplasmosis and CNS lymphoma by examining the PET scans. The toxoplasma titer was positive in all patients in whom toxoplasmosis was confirmed, but it was also positive in half of the patients with confirmed lymphoma.

At our institution, nine patients with AIDS who presented with an intracranial mass lesion were evaluated using FDG-PET scanning. In contrast to previous series, only one patient received empirical toxoplasmosis treatment prior to the PET. The diagnosis of patients in whom results were suggestive of toxoplasmosis and who underwent follow-up testing was confirmed by response to treatment or examination of brain biopsy sample; the diagnosis of patients in whom PET findings were consistent with CNS lymphoma was confirmed by response to treatment.

Although the follow-up period in this series was limited, the results obtained in patients who did undergo follow-up review corroborate the usefulness of FDG-PET in HIV-related intracranial mass lesions that were suggested by previous studies. When available, FDG-PET should be considered before undertaking empirical treatment or before obtaining a stereotactic biopsy sample. If the PET scan reveals increased FDG uptake, the patient should receive treatment for lymphoma; if it reveals decreased FDG uptake, toxoplasmosis treatment should be initiated. Patients in whom high uptake and presumed lymphoma are demonstrated should be monitored closely. If corticosteroid therapy fails to resolve the disease, a different neoplastic diagnosis may be indicated. For example, at our institution, a patient with AIDS was recently diagnosed as having glioblastoma multiforme. Because the overall medical condition of AIDS patients who harbor an intracranial mass lesion is usually not optimal for surgery, stereotactic biopsy procedure should only be performed after FDG-PET-guided treatment has failed to provide conclusive results.

CONCLUSIONS

A safe and reliable diagnostic modality, FDG-PET can differentiate between the causes of HIV-related intracranial masses in most patients. If available, this diagnostic tool should be used prior to undertaking empirical treatment or performing a stereotactic brain biopsy procedure.

Once the results of the PET study are available, treatment can be initiated for the suggested diagnosis without the need to obtain further confirmation. A stereotactic brain biopsy should be performed only if treatment has failed.

References


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