the role of irradiation induced inflammatory reaction and, finally, to identify tumor response to treatment at a very early stage.

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Thallium-201 Uptake in Cytomegalovirus Encephalitis

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A 36-yr-old man with AIDS exhibited intense ^{201}Tl uptake (lesion-to-brain uptake ratio 5.38) in a brain lesion previously detected by MRI and CT. The lesion was biopsied and found to contain cells with viral inclusions diagnostic of cytomegalovirus infection, not tumor as the thallium SPECT results suggested. Thallium-201 SPECT may be less specific than previously reported for differentiating neoplastic disease from opportunistic infections in AIDS patients.

Key Words: thallium-201; SPECT; AIDS; cytomegalovirus

J Nucl Med 1997; 38:1386–1388

Central nervous system (CNS) complications associated with Acquired Immune Deficiency Syndrome (AIDS) cause significant morbidity and mortality. Etiologies of CNS disease in AIDS include neoplasms and opportunistic infections. In one autopsy study, CNS lymphoma was found in 4% of AIDS patients (*1*). Autopsy incidence of 6.7%–34% has been reported for cerebral toxoplasmosis (*1*). Other common infections include: cytomegalovirus (CMV) (7.9%–33%), cryptococcosis (2.6–13.5%) and progressive multifocal leukoencephalopathy (0.8%–8%) (*1*).

Since CNS complications commonly occur in AIDS and the consequences are severe, rapid diagnosis leading to proper treatment might enhance the quality of life in these patients. Specific diagnosis of CNS complications is unreliable with MRI or CT since the imaging characteristics of lymphoma and opportunistic infections can be similar (*2,3*). The use of ^{201}Tl SPECT to differentiate between CNS lymphoma and infectious diseases in AIDS patients has been reported previously (*4–7*). In those studies, lymphomas showed increased thallium uptake, while infectious diseases generally did not. In this case, we report ^{201}Tl uptake in a biopsy and autopsy-confirmed case of CMV encephalitis.

Received Dec. 2, 1996; accepted Jan. 30, 1997.

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CASE REPORT

The patient, a 36-yr-old man with AIDS, was admitted with progressive neurological complaints, including left hemiparesis and an increased occurrence of falls. Past medical history included *Pneumocystis carinii* pneumonia and *Mycobacterium avium* infection. The patient was enrolled in an oral gancyclovir prophylaxis trial until the month of admission.

Neurological exam revealed mild psychomotor slowing, decreased facial sensation to pinprick and mild paresis of the lower extremity on the left side. Left upper extremity drift, mild graphesthesia and marked paresis were noted. Three months before admission, the patient was noted to have a "lazy left upper lip". A CT without contrast showed right thalamic and periventricular edema, mild hydrocephalus and mild atrophy. Based on these findings, the patient was started empirically on an anti-*Toxoplasma gondii* regimen (pyrimethamine tablets 25 mg bid, intravenous clindamycin 600 mg tid). MRI revealed a right basal ganglia lesion, extending inferiorly to the level of the right mid brain and superiorly to the level of the right corona radiata (Fig. 1). Three days after the initiation of anti-toxoplasma medication, ^{201}Tl SPECT brain imaging was performed. Thallium-201 uptake was shown in the right frontal/parietal region on both early and delayed acquisitions (Fig. 2). After 2 wk of anti-toxoplasma medication, an MRI with gadolinium showed a ring-enhancing lesion in the right basal ganglia unchanged from the previous study in size or mass effect. Because lymphoma was suspected, the patient underwent a stereotactic brain biopsy. The biopsy revealed cytomegalovirus encephalitis and subacute organizing infarction. To treat the CMV infection, the patient was started on intravenous gancyclovir 300 mg twice a day. After 1 wk without change in the patient's left hemiparesis and a decrease in platelet count, gancyclovir was discontinued and intravenous foscarnet 5 gm twice a day was initiated. A CT at this time showed no significant change in the lesion. After 3 days of foscarnet therapy, left side mobility had increased. Eight days after the initiation of foscarnet therapy, MRI with gadolinium showed, as

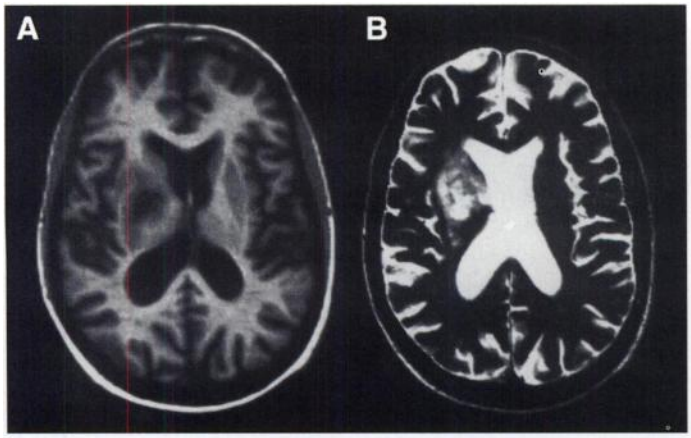

FIGURE 1. (A) An axial section of a magnetization prepared T1-weighted volume acquisition MRI without contrast. Abnormal decreased signal was apparent in the lesion located in the right basal ganglia with a rim of hyperintense signal surrounding this focus. (B) The center of the lesion increased in signal prominently on T2-weighted images.

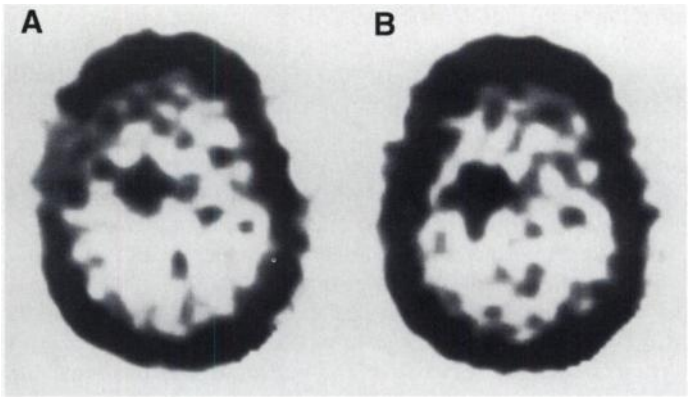

FIGURE 2. Thallium-201 SPECT studies were acquired at 20 min and approximately 2 hr after intravenous administration of 5 mCi ^{201}Tl-chloride. A 20% energy window was centered at the 80 keV photopeak of ^{201}Tl. Studies were reconstructed using a Butterworth filter with a 1.4 cyc/cm Nyquist frequency, a 0.6 cyc/cm high-cut frequency and an alpha of 3.0. Attenuation correction using Chang's algorithm was performed. Thallium uptake was shown in the right frontal/parietal region on both early and delayed acquisitions. Thallium uptake was quantified by dividing the average counts in a region of interest drawn around the lesion by the average counts in either the contralateral brain or scalp. (A) Twenty minutes after injection of ^{201}Tl. Lesion/contralateral brain ratio 5.38, lesion/contralateral scalp ratio 0.95. (B) Two hours after injection of ^{201}Tl. Lesion/contralateral brain ratio 5.39, lesion/contralateral scalp ratio 1.22.

compared to previous studies, diminished inferior extent of the enhancement within the lesion and an increase in the cephalad extent of the lesion within the perivascular spaces. The patient's clinical status continued to improve. He was discharged on foscarnet. Seven weeks later, the patient died following respiratory arrest precipitated by massive epistaxis.

An autopsy showed pulmonary invasive aspergillosis, CMV pneumonitis and CMV adrenalitis. Macroscopic examination of the brain revealed a 1.7 × 1.2 × 1.1 cm multicystic, necrotizing lesion within the right basal ganglia (Fig. 3A). Microscopically, the right basal ganglia exhibited a necrotizing process where several cells contained intranuclear and intracytoplasmic eosinophilic inclusions diagnostic of CMV infection (Fig. 3B). Infiltrating histiocytes (Fig. 3C) were primarily distributed around blood vessels. Sections from the cerebral cortex showed

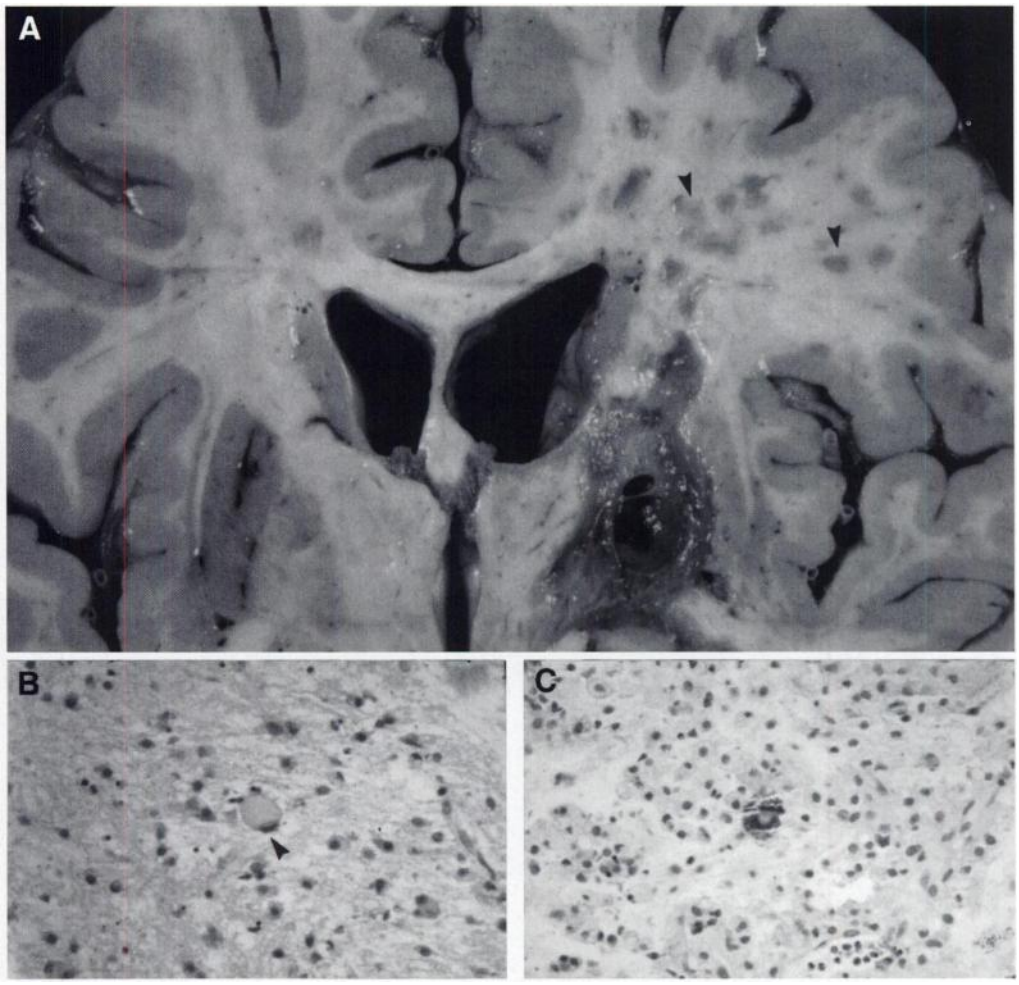

FIGURE 3. (A) Coronal section of the brain with a necrotic, cavitated lesion at the level of the right basal ganglia. Several discolored and irregular "plaques" (arrowheads) are diffusely present in the white matter. (B) Diagnostic CMV inclusions (arrowhead) were seen in several cells (H&E, ×100). (C) Infiltrating histiocytes were primarily visible around blood vessels (H&E, ×50).

moderately thickened, focally fibrotic meninges infiltrated by chronic inflammatory cells, predominantly histiocytes and a few lymphocytes. Many of the histiocytes exhibited both intranuclear and intracytoplasmic inclusions diagnostic of CMV infections. Both the ependymal and subependymal periventricular tissue were extensively infiltrated with histiocytes laden with CMV inclusion bodies. Microglial nodules, although present, were rare. The white matter of the right frontal lobe contained numerous histiocytes and gitter cells and exhibited mild-to-moderate gliosis and neovascularization. The center of the lesions exhibited severe myelin breakdown with marked axonolysis seen on silver staining. Necrotizing CMV lesions were also seen in the right cerebral peduncle, area postrema and pons.

DISCUSSION

While CT and MRI cannot reliably distinguish between neoplasm and opportunistic infection, uptake of ^{201}Tl has been reported to be specific for neoplastic diseases such as lymphoma. Ruiz et al. (*6*) reported ^{201}Tl uptake in 12 of 12 lymphoma patients but no uptake in 26 of 26 patients with infectious disease (specificity = 100%, sensitivity = 100%). Berry et al. (*7*) reported ^{201}Tl uptake in 4 of 5 lymphoma patients, but no uptake in one markedly necrotic lymphoma or in one patient with toxoplasmosis (specificity = 100%, sensitivity = 80%. O'Malley et al. (*5*) reported ^{201}Tl uptake in 6 of 6 lymphoma patients, but no uptake in 6 of 7 patients with other diseases (specificity = 86%, sensitivity = 100%). The false-positive result was found in a patient with a toxoplasmosis abscess, surrounded by CMV and scattered *Mycobacterium tuberculosis* foci (*5*). Lorberboym et al. (*4*) reported ^{201}Tl uptake in eight patients with lymphoma, in one patient with adenocarcinoma, and in one patient with probable toxoplasmosis but no uptake in nine other patients with benign etiologies (specificity = 90%, sensitivity = 100%).

In this case report, we describe ^{201}Tl uptake in the brain of an AIDS patient with CMV encephalitis and no neoplasm. Thallium uptake in infectious disease has been previously reported in the lung with CMV pneumonitis (*8*), actinomycosis (*9*) and *Pneumocystis carinii* pneumonia (*10*). In cerebral infection, ^{201}Tl uptake is unusual but has been reported in candidiasis (*11*) in a bacterial abscess (*12*), concurrent *Toxoplasma gondii*, *Mycobacterium tuberculosis* and CMV infection (*5*) and in a case of probable toxoplasmosis (*4*).

The exact mechanism of ^{201}Tl uptake in brain lesions is unclear. Mechanisms involved on the cellular level include active transport via sodium-potassium pumps (*13*) and passive transport depending on membrane permeability and charge (*14*). In addition, blood flow (*15*), neovascularization (*12,16*) and reactive processes such as gliosis (*12*) may influence thallium uptake. It is possible, but unproven, that infiltrating, metabolically active macrophages might also accumulate ^{201}Tl. Although uptake of ^{18}F-fluorodeoxyglucose in tumor infiltrating macrophages has been shown with PET (*17,18*), the role of macrophages in thallium uptake has not been elucidated. In our case, neovascularization and macrophage infiltration were both prominent and may have contributed to the ^{201}Tl uptake.

Semiquantitative analysis such as lesion-to-contralateral brain uptake ratio (*5*) or the retention index (*4*) has been proposed to improve the diagnostic accuracy of ^{201}Tl SPECT in this application. However, uptake in a case of candidiasis (lesion-to-brain at 15 min = 3.3, at 3 hr = 3.5) (*11*) and our report of CMV encephalitis (lesion-to-brain ratio at 30 min = 5.38, at 2 hr = 5.39) are in the range reported for neoplasms (*19*). The retention index calculated by Lorberboym et al. (*4*) for their lymphoma cases (1.35 ± .16) was higher than the retention index in this case (1.00), but direct comparison may be misleading since the scans were acquired at different times after ^{201}Tl injection (10 min and 3 hr versus 15 min and 2 hr).

CONCLUSION

Using ^{201}Tl uptake to differentiate between lymphoma and infection, even when a semiquantitative index is calculated, may be less specific than previously reported. Larger studies are needed to further characterize the sensitivity and specificity of thallium SPECT in diagnosing AIDS-associated brain lesions.

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