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# Central Nervous System Lymphoma Not Detectable on Single-Photon Emission CT with Thallium 201

Dale C. Fisher, David P. Chason, Dana Mathews, Dennis K. Burns, and James L. Fleckenstein

**Summary:** A 33-year-old man with acquired immunodeficiency syndrome had an erosive supraglottic mass visible on CT scans of the neck; biopsy was postponed because of the patient's debilitated condition. Two weeks later, he was admitted with altered mental status; an MR image of the brain obtained at that time showed multiple bilateral mass lesions, the largest of which was 5 cm. Findings on a thallium-201 single-photon emission CT (SPECT) scan of the brain were normal. Ten days later, the patient died and autopsy showed both the neck and the brain lesions to be large-cell lymphoma. This case is counterevidence to the reported 100% sensitivity of thallium-201 brain SPECT for demonstrating lymphoma of the central nervous system.

**Index terms:** Acquired immunodeficiency syndrome (AIDS); Lymphoma; Single-photon emission computed tomography

The use of thallos chloride Tl 201 (thallium-201) brain single-photon emission computed tomography (SPECT) is currently advocated for differentiating central nervous system (CNS) lymphoma from toxoplasmosis in patients with acquired immunodeficiency syndrome (AIDS). Despite two recent series reporting 100% diagnostic sensitivity of thallium-201 SPECT for CNS lymphoma (1, 2), we encountered a patient with autopsy-proved CNS lymphoma that was not detectable by this imaging technique.

## Case Report

A 33-year-old man with AIDS had a 3-month history of difficult and painful swallowing accompanied by a 13.5-kg weight loss. He was admitted to the hospital and treated for esophagitis. Endoscopy revealed a normal esophagus and stomach. Laryngoscopy and computed tomography (CT) of the neck showed an erosive supraglottic mass. The patient was sent home to be readmitted 1 week later for panendoscopy and biopsy of the mass. When he returned, he was too debilitated to undergo the procedure and it was rescheduled for the following week.

The next week, the patient was admitted for dehydration, lethargy, and altered mental status. The biopsy was further postponed and magnetic resonance (MR) imaging of the brain was performed, which revealed multiple, bilateral intracranial mass lesions, the largest of which measured approximately 5 cm (Fig 1A–C). A thallium-201 SPECT study of the brain showed no abnormal tracer activity (Fig 1D). The family opted for conservative management of the patient's illness and aggressive comfort care. He died 10 days later. The biopsy was never performed, and the patient did not receive corticosteroids, radiation, or empiric treatment for toxoplasmosis. At autopsy, both the supraglottic mass and brain lesions were proved to be large-cell lymphoma (Fig 1E and F).

## Discussion

Toxoplasmosis and lymphoma are the leading causes of CNS mass lesions in patients with AIDS (1–6). In general, CT and MR imaging have failed to provide specific distinguishing characteristics to differentiate CNS lymphoma from toxoplasmosis, and it is difficult to differentiate these entities clinically; thus, biopsy is often required to make the distinction. Hyperattenuation on noncontrast CT scans, low signal intensity on T2-weighted MR sequences, and periventricular location with subependymal spread are features that tend to favor lymphoma. It is important to make the correct diagnosis expeditiously, since the two diseases require markedly different treatments and have different prognoses.

At present, patients with AIDS who have CNS mass lesions are frequently treated empirically for toxoplasmosis and monitored clinically and by CT or MR imaging. Those who do not respond to treatment often have a biopsy performed for definitive diagnosis. Patients with toxoplasmosis usually improve within 1 to 3

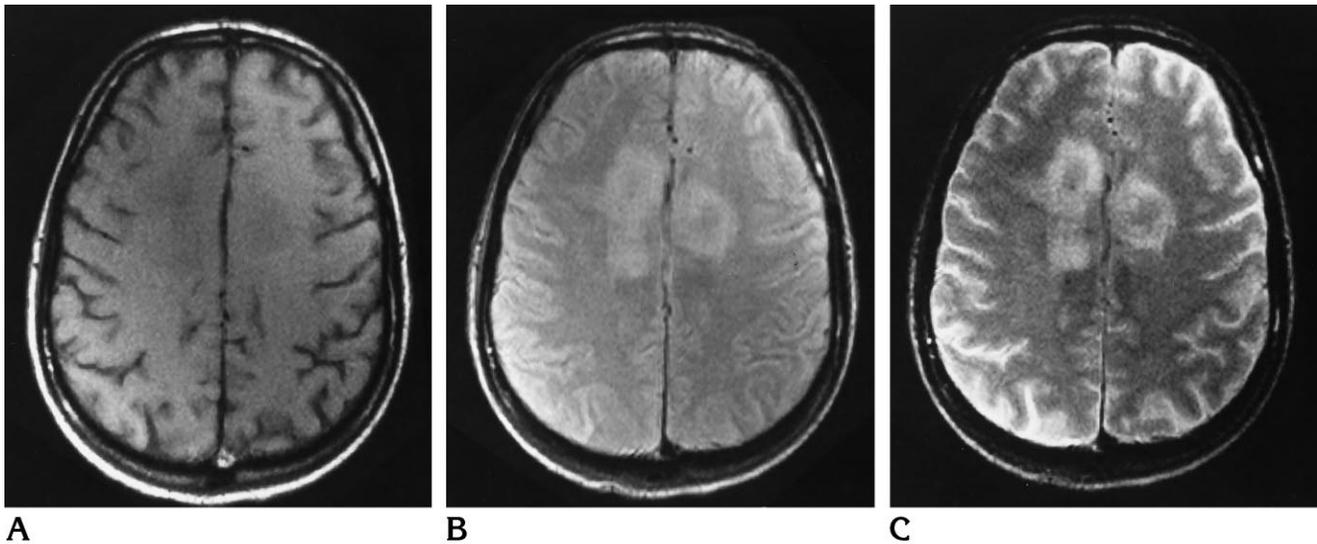
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From the Departments of Radiology (D.C.F., D.P.C., D.M., J.L.F.) and Pathology (D.K.B.), University of Texas Southwestern Medical Center, Dallas.

Address reprint requests to James L. Fleckenstein, MD, Department of Radiology, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd, Dallas, TX 75235.

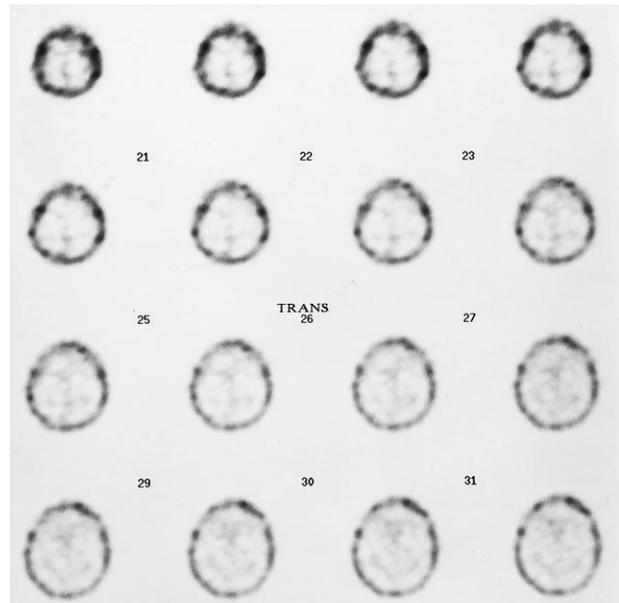
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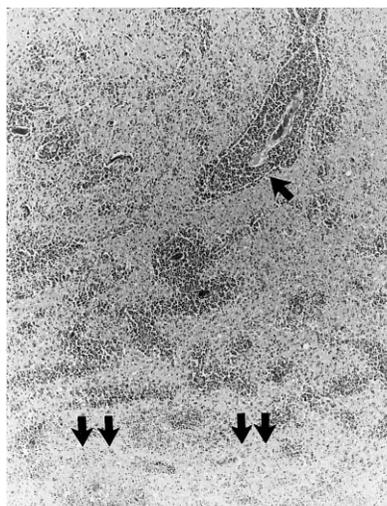
**Fig 1.** CNS lymphoma in 33-year-old man with AIDS. **A**, Axial T1-weighted (525/15), **B**, spin density-weighted (2550/30), and **C**, T2-weighted (2550/80) spin-echo MR images of the brain. The right-sided lesion measured approximately  $4.5 \times 2.5 \times 3$  cm; the left-sided lesion measured approximately  $3 \times 2 \times 5$  cm. Note slight hypointensity on T1-weighted sequences with low to intermediate signal centrally and high signal peripherally on T2-weighted sequences.

**D**, Findings on thallium-201 SPECT axial scans of the brain are normal.

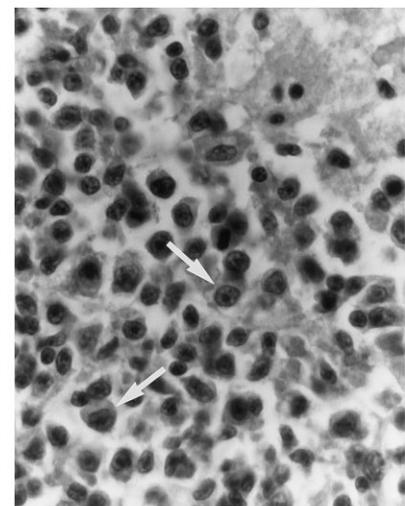
**E** and **F**, Photomicrographs of lymphoma within the neostriatum. Low-magnification photomicrograph (**E**) shows well-developed angiocentric growth (*single arrow*) and necrosis (*double arrows*) (hematoxylin-eosin, original magnification  $\times 10$ ). Higher-magnification photomicrograph (**F**) shows atypical lymphoid cells with large nuclei and distinct nucleoli (*arrows*) infiltrating and expanding the vascular walls (hematoxylin-eosin, original magnification  $\times 60$ ).



**D**



**E**



**F**

weeks after the initiation of treatment, with median survival times of 10 to 16 months (4–6). Patients with AIDS and CNS lymphoma tend to respond to therapy with increased longevity, although prognosis remains poor (2, 4, 7–10). The mean time of survival for patients with CNS lymphoma after the appearance of symptoms is 134 days for those who undergo radiation therapy and 42 days for those not treated (10). Thallium-201 SPECT is currently advocated for the purpose of differentiating CNS lymphoma from toxoplasmosis (1, 2). Thallium is a potassium analogue with a high affinity for sodium- and potassium-activated adenosine triphosphatase and a slow washout from cells. Although the precise mechanism for thallium uptake in the brain is unknown, factors that may play a role include blood flow, tissue viability, disruption of the blood-brain barrier, cell membrane potential and permeability, and metabolic activity of the tumor (11–15).

Two recent reports described the results of the use of thallium-201 SPECT in differentiating CNS lymphoma from toxoplasmosis (1, 2). A total of 50 patients with AIDS and CNS mass lesions were examined. Eighteen patients with lymphoma all showed intensely increased thallium-201 tracer activity. One false-positive finding occurred in a patient with three concurrent CNS infections. In retrospect, this finding was discounted by the authors because they discovered insufficient tracer activity to diagnose lymphoma. Of the patients with no abnormal thallium-201 uptake, 28 had toxoplasmosis, one had progressive multifocal leukoencephalopathy, one had a mycobacterium tuberculosis abscess, and one had a venous angioma. Importantly, there were no false-negative findings for lymphoma. The authors did acknowledge that potential false-negative findings could arise in specific situations. These included small lesions beyond the resolution of SPECT (ie, less than 8 mm), lesions near the skull base (because of intense normal activity within the adjacent soft tissues), and subtle subependymal and nonfocal leptomeningeal deposits of lymphoma.

The fact that small lesions could escape detection with thallium-201 SPECT was suggested by Kosuda et al (16), who reported a case of CNS lymphoma in which two separate brain lesions were seen on MR images, but only one showed increased activity on thallium-201 SPECT scans. The smaller of these lesions (size

not reported) went undetected by SPECT. Our case of CNS lymphoma showed large bilateral masses that exhibited no abnormal thallium-201 activity.

Histopathology revealed a well-developed angiocentric growth pattern accompanied by mitotic activity and large areas of necrosis, all typical features of AIDS-associated CNS lymphomas. The histologic appearance of the neoplasm provides no clear morphologic explanation for the lack of thallium-201 uptake. One explanation that has been proposed for the lack of uptake in some neoplasms is an intact blood-brain barrier, the presence of which would exclude tracer accumulation within the lesion. That the blood-brain barrier may occasionally be intact in CNS lymphoma is supported by the literature for both AIDS (3) and non-AIDS patients (17, 18). However, in view of the extensive angiocentric growth and necrosis seen in our case, an intact blood-brain barrier would be unlikely. Although factors other than blood-brain barrier integrity play a role in thallium-201 uptake in tumors, it remains unclear why our case of CNS lymphoma failed to show the characteristic intense uptake that has been documented in previous reports (1, 2, 16).

Thallium-201 brain SPECT will undoubtedly continue to play a role in differentiating CNS toxoplasmosis from lymphoma; however, further work is needed to ascertain the accuracy and predictive power of this technique.

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