Increased Technetium-99m-HMPAO Uptake in Grade II Astrocytoma

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Most brain tumors show decreased uptake of blood flow tracers in brain SPECT imaging and in some cases meningiomas show increased uptake, mainly associated with high regional blood flow values (*1–14*). A reason for regionally increased tracer uptake is partial epilepsy when a tracer is injected during the ictal phase (*15–17*). We present a case of a histologically proven Grade II astrocytoma in the mesial part of the left temporal lobe that caused complex partial seizures. After tracer injection during a phase without signs of clinical seizure, markedly increased uptake of ^{99m}Tc-hexamethylpropyleneamine oxime (^{99m}Tc-HMPAO) occurred, although the tumor was partially calcified.

Key Words: epilepsy; astrocytoma; HMPAO; single-photon emission computer tomography; magnetic resonance imaging

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CASE REPORT

A 33-yr-old man presented with a 10-yr history of medically intractable complex partial seizures. The seizure frequency was 20–40 per mo with occasional secondary generalization. Interictal and ictal EEG showed a left temporal focus. Neuropsychology testing revealed impairment of verbal and, to a lesser extent, nonverbal memory function. A Wada test of the left internal carotid artery resulted in complete transient aphasia. MRI was performed before and after injection of Gd-DTPA. In the mesial part of the left temporal lobe, a signal increase was observed, particularly in the T1- and T2-weighted sequences (Fig. 1). The lesion showed no significant contrast enhancement in the T1-weighted transaxial slices.

Interictal brain SPECT imaging was performed 30 min after injection of 740 MBq of ^{99m}Tc-HMPAO using an annular crystal CERASPECT system (Digital Scintigraphic Inc., Waltham, MA). The system works with three collimators rotating within a single crystal sodium iodide ring detector and acquires three views from three angles simultaneously. The spatial resolution of this system is about 8 mm in the center of rotation (*18*); the acquisition time was 30 min and 120 projections were acquired using a 512 × 64 matrix. Coronal, sagittal and transaxial (parallel to the orbitomeatal line) slices were calculated from the original transaxial slices and summed to obtain 6.68 mm (4 pixel) thick slices. Additionally, thin slices (1 pixel thick, parallel to the long-axis of the temporal lobes) were calculated for evaluation of the temporal lobes. Technetium-99m-HMPAO SPECT imaging revealed markedly increased tracer uptake in the mesial part of the left temporal lobe (partly involving the hippocampus) and slightly decreased uptake in the left temporal pole (Fig. 2). Semiquantitative analysis revealed an asymmetry index (left/right) of 1.70 for the temporomesial area and of 0.96 for the temporal pole.

The patient underwent selective left-sided amygdalo-hippocampectomy; pathology revealed an astrocytoma (WHO Grade II, diameter, 15 mm), which was partially calcified (Fig. 3). Three months following surgery, the patient was seizure-free with impaired verbal memory function. Nonverbal memory function remained unchanged compared with the preoperative situation.

DISCUSSION

MRI and brain SPECT imaging were used to evaluate epilepsy prior to surgery. Although mesial temporal sclerosis is the most common finding in temporal lobe epilepsy, brain tumors are detected in some patients (*19–21*). Since the patients studied in our department usually suffer from a long-lasting history of intractable complex partial seizures, detection of rapidly growing tumors is unusual. Low-grade tumors can occur concurrently with epilepsy or can be the origin of pathological discharges, particularly if they are associated with hippocampal structures (*21*).

Tumor perfusion may play an important role in the success of antineoplastic therapies such as radiotherapy and chemotherapy due to their dependence on adequate blood flow for oxygenation and drug transport (*1*). Perfusion of brain tumors has been extensively studied with SPECT using various radiopharmaceuticals (*2*). The uptake of N-isopropyl-p-(^{123}I)iodoamphetamine ([^{123}I]IMP) and ^{99m}Tc-HMPAO is proportional to blood flow in most cases (*3,4*). In addition, ^{99m}Tc-HMPAO uptake has been inversely correlated to [^{123}I]iodoazomycin arabinoside uptake, a marker for tumor hypoxia (*22*). Discrepancies, however, have been described, including high blood flow values (measured using ^{133}Xe inhalation methodology) and high ^{99m}Tc-HMPAO uptake, as well as a cold lesion in an [^{123}I]IMP SPECT image of a meningioma (*5*).

Therefore, due to different binding mechanisms, brain tumors can show increased as well as decreased uptake values in perfusion SPECT studies. For ^{99m}Tc-HMPAO, a correlation between glutathione content and tracer uptake has been demonstrated (*6*), suggesting glutathione involvment in the trapping mechanisms for ^{99m}Tc-HMPAO in brain tumors.

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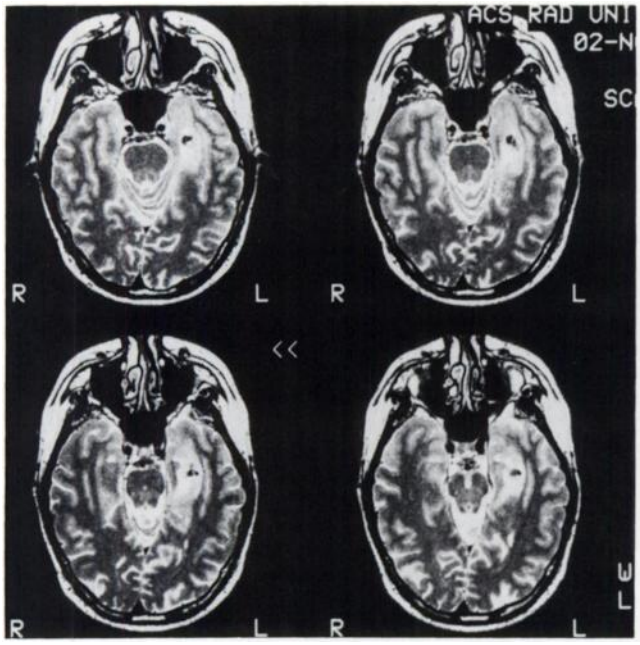

FIGURE 1. MRI scan (T2-weighted sequences, four transaxial slices, parallel to the long-axis of the temporal lobes, 2.0/0.2 mm thickness). A signal increase is detected in the mesial part of the left temporal lobe. A circumscribed signal decrease is visible in the ventral part of the lesion.

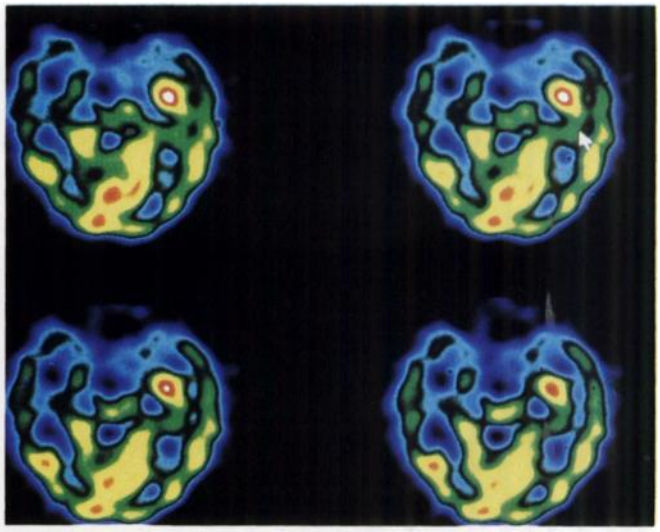

FIGURE 2. Technetium-99m-HMPAO-SPECT (four transaxial slices, parallel to the long-axis of the temporal lobes, 1.67 mm thickness). Markedly increased uptake is visible in the mesial part of the left temporal lobe (arrow). Uptake in the left temporal pole is slightly decreased.

Whereas most tumors present with decreased uptake, meningiomas more frequently show high tracer uptake values (*6–14*). Occasionally, other types of tumors have been reported to show increased tracer uptake (*8,10,23*). Following radiotherapy, increased as well as decreased tracer uptake values tend to return toward unity (*8*). No clearcut differentiation between malignant and benign gliomas can be derived from ^{99m}Tc-HMPAO SPECT studies (*9*), but ^{99m}Tc-HMPAO in combination with ^{201}Tl-chloride imaging might sensitize identification of tumor recurrence (moderate ^{201}Tl uptake and high ^{99m}Tc-HMPAO uptake) (*24*). Increased blood flow tracer uptake in astrocytomas is extremely rare, but has been described for both ^{99m}Tc-HMPAO (*25*) and [^{123}I]IMP (*26*).

In the case presented here, an astrocytoma revealed extreme increased ^{99m}Tc-HMPAO uptake (increased by 70% compared with the corresponding contralateral region). Since the tumor was partially calcified, an altered "trapping mechanism" is more likely responsible for the phenomenon than increased blood flow to the tumor. Transient hyperperfusion, which typically occurs ictally or postictally in temporal lobe epilepsy (*15–17*), must be considered, particularly because mesial hyperperfusion is combined with slight hypoperfusion of the left temporal pole. A similar pattern (mesial hyperperfusion and lateral hypoperfusion) has been described to be highly specific for the postictal state (*15*). No clinical seizure was observed during the ^{99m}Tc-HMPAO injection. Unfortunately, no EEG recording was performed during tracer administration. One argument against the theory that a "subclinical" seizure was responsible for the increased tracer uptake is

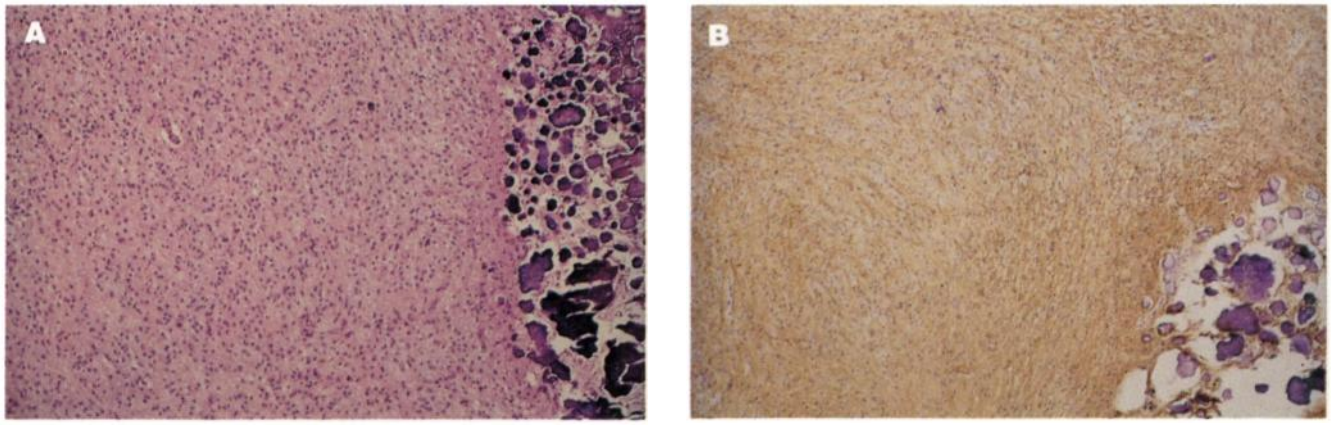

FIGURE 3. Histology of the temporal lesion shows a low-grade astrocytoma with areas of extensive calcification. (A) Hematoxylin-eosin staining. (B) Immunostaining with anti-glial fibrillary acidic protein antibodies.

that simultaneous EEG video monitoring was extensively performed on this patient during the presurgical evaluation. All typical EEG discharges were accompanied by clinical symptoms in this patient. Nevertheless, it remains undetermined whether increased ^{99m}Tc-HMPAO uptake is due to a specific tumor-associated process or subclinical epileptic activity. Pathological discharges between tracer injection and acquisition cannot be responsible for the increased uptake since ^{99m}Tc-HMPAO allows rapid freezing of the cerebral perfusion pattern (*27*) and shows no redistribution. The slightly decreased tracer uptake in the left temporal pole is not related to a morphological alteration, but can be explained by a functional deficit commonly observed in interictal ^{99m}Tc-HMPAO-SPECT studies in temporal lobe epilepsy (*28,29*).

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REFERENCES

1. Babich JW. Technetium-99m-HMPAO retention and the role of glutathione: the debate continues. *J Nucl Med* 1991;32:1681–1683.
2. Biersack HJ, Grünwald F, Kropp J. Single photon emission computed tomography imaging of brain tumors. *Semin Nucl Med* 1991;21:2–10.
3. Ohnishi T, Hoshi H, Watanabe K, et al. Dynamic SPECT using Tc-99m hexamethylpropyleneamine oxime in the patients with intracranial mass lesions—a comparison with Xe-133 and IMP. *Jpn J Nucl Med* 1988;25:431–439.
4. Langen KJ, Herzog C, Kuwert T, et al. Tomographic studies of rCBF with ^{99m}Tc-HM-PAO SPECT in patients with brain tumor: comparison with $C^{15}O_2$ continuous inhalation technique and PET. *J Cereb Blood Flow Metab* 1988;8:S90–S94.
5. Hoshi H, Jinnouchi S, Watanabe K, et al. Mismatch between iodine-123 IMP and technetium-99m HM-PAO brain perfusion imaging in a patient with meningioma. *Clin Nucl Med* 1987;12:737–740.
6. Suess E, Malessa S, Ungersböck K, et al. Technetium-99m-d,l-hexamethylpropyleneamine oxime (HMPAO) uptake and glutathione content in brain tumors. *J Nucl Med* 1991;32:1675–1681.
7. Lindegaard MW, Skretting A, Hager B, et al. Cerebral and cerebellar uptake of ^{99m}Tc-(d,l)-hexamethyl-propyleneamine oxime (HM-PAO) in patients with brain tumor studied by single photon emission computerized tomography. *Eur J Nucl Med* 1986;12:417–420.
8. Babich JW, Keeling F, Flower MA, et al. Initial experience with Tc-99m-HM-PAO in the study of brain tumors. *Eur J Nucl Med* 1988;14:39–44.
9. Langen KJ, Roosen N, Herzog H, et al. Investigations of brain tumors with Tc-99m-HM-PAO SPECT. *Nucl Med Commun* 1989;10:325–334.
10. Ell PJ, Jarritt H, Costa C, et al. Functional imaging of the brain. *Semin Nucl Med* 1987;17:214–229.
11. Moretti JL, Askienazy S, Raynaud C, et al. Iodine-123-p-iodo-isopropyl amphetamine for brain tumor diagnosis. In: Biersack HJ, Winkler C, eds. *Amphetamines and pH-shift agents for brain imaging: basic research and clinical results*. New York: de Gruyter; 1986:167–170.
12. Schober O, Meyer GJ, Creuzig H, et al. IMP-SPECT and amino acid-PET in brain tumors. In: Biersack HJ, Winkler C, eds. *Amphetamines and pH-shift agents for brain imaging: basic research and clinical results*. New York: de Gruyter; 1986:157–164.
13. McVeigh MC, Merchut MP, Karesh SM, Ghobrial MW, Dillehay GL. Intracranial tumors: unexpected uptake of I-123 HIPDM. *Radiology* 1986; 161:409–411.
14. Zhang JJ, Park CH, Kim SM, Ayyangar KM, Haghbin M. Dual isotope SPECT in the evaluation of recurrent brain tumor. *Clin Nucl Med* 1992;17: 663–664.
15. Rowe CC, Berkovic SF, Sia STB, et al. Localization of epileptic foci with postictal single photon emission computed tomography. *Ann Neurol* 1989; 26:660–668.
16. Stefan H, Bauer J, Feistel H, et al. Regional cerebral blood flow during focal seizures of temporal and frontocentral onset. *Ann Neurol* 1990;27:162–166.
17. Grünwald F, Menzel C, Pavics L, et al. Ictal and interictal brain SPECT imaging in epilepsy using technetium-99m-ECD. *J Nucl Med* 1994;35:1896–1901.
18. Holman BL, Carvalho PA, Zimmermann RE, et al. Brain perfusion SPECT using an annular single crystal camera: initial clinical experience. *J Nucl Med* 1990;31:1456–1461.
19. Gates JR, Cruz-Rodriguez R. Mesial temporal sclerosis: pathogenesis, diagnosis, and management. *Epilepsia* 1990;31 (suppl 3):S55–S66.
20. Meldrum BS. Epilepsy octet; anatomy, physiology and pathology of epilepsy. *Lancet* 1990;336:231–234.
21. Theodore WH, Katz D, Kufta C, et al. Pathology of temporal lobe foci: correlation with CT, MRI and PET. *Neurology* 1990;40:797–803.
22. Groshar D, McEwan AJB, Parliament MB, et al. Imaging tumor hypoxia and tumor perfusion. *J Nucl Med* 1993;34:885–888.
23. Maeda H, Kobayashi H, Hayashi M, Ishii Y. Unusual accumulation of I-123 IMP and Tc-99m HMPAO in glioblastoma multiforme. *Jpn J Nucl Med* 1988;25:655–658.
24. Schwartz RB, Carvalho PA, Alexander III E, Loeffler JS, Folkerth R, Holman BL. Radiation necrosis vs high-grade recurrent glioma: differentiation by using dual-isotope SPECT with ^{201}Tl and ^{99m}Tc-HMPAO. *AJNR* 1991;12:1187–1192.
25. Ono S, Fukunaga M, Otsuka N, et al. Single photon emission computed tomography (SPECT) using ^{99m}Tc-hexamethylpropyleneamine oxime in brain tumor: comparison of N-isopropyl-^{123}I-p-iodoamphetamine and ^{99m}Tc-DTPA SPECT. *Jpn J Nucl Med* 1988;25:1371–1379.
26. Ishihara M, Yui N, Togawa T, et al. Blood flow measurement of brain tumor by ^{123}I-IMP using three-heads rotating gamma camera (SPECT). *Kaku Igaku* 1991;28:1503–1507.
27. Reichmann K, Biersack HJ, Basso L, et al. A comparative study of brain uptake and early kinetics of ^{99m}Tc-HMPAO and other PnAO derivates in baboons. *J Nucl Med* 1986;25:134–137.
28. Holman BL, Devous MD. Functional brain SPECT: the emergence of a powerful clinical method. *J Nucl Med* 1992;33:1888–1904.
29. Grünwald F, Durwen HF, Bockisch A, et al. Technetium-99m-HMPAO brain SPECT in medically intractable temporal lobe epilepsy: a postoperative evaluation. *J Nucl Med* 1991;32:388–394.