Demonstration of Focal Hyperemia in Acute Cerebral Infarction with Iodine-123 Iodoamphetamine

David L. Bushnell, Sudha Gupta, Anthony G. Mlcoch, Antonie Romyn, W. Earl Barnes, and Ervin Kaplan

Nuclear Medicine Service, Neurology Service, and Speech Pathology Service, Hines V.A. Hospital, Hines, Illinois

Focal hyperemia is known to occur in regions of acute cerebral infarction. Presented here are two cases in which SPECT images with ^{125}I-labeled iodoamphetamine demonstrated focal areas of increased tracer concentration associated with cerebral infarction. These results may have important implications regarding the physiology of iodoamphetamine in cerebral infarction and, in particular, whether the distribution of this tracer is related to regional blood flow in this setting. In addition, interpretation of iodoamphetamine images in cerebral infarction should include consideration of this finding.

J Nucl Med 28:1920–1923, 1987

Increased ("luxury") perfusion during acute stroke was first described by Lassen et al. as regional blood flow that is increased beyond the metabolic needs of the dysfunctional neurologic tissue being perfused (*1*). Recently, the lipophilic agent N-isopropyl-(^{123}I) p-iodoamphetamine (IMP) has been used with single photon emission computed tomography (SPECT) to evaluate regional cerebral blood flow (rCBF) in patients with cerebrovascular disease. Although this technique usually demonstrates photon deficient areas associated with cerebral infarction, several authors have reported an inability to identify regional hyperemias during acute stroke (*2–4*). As part of an ongoing study to evaluate language recovery in patients with ischemic infarction, we have noted two cases in which increased IMP concentration was present either adjacent to, or within, the margins of the cerebral infarction. The findings in these two cases suggest that, at least in certain instances, the SPECT/IMP technique will demonstrate reactive focal hyperemia in acute ischemic stroke.

MATERIALS AND METHODS

Two patients with acute ischemic cerebral infarction had SPECT/IMP imaging within several weeks of symptom onset. Both of these individuals had follow-up SPECT/IMP examinations ~1 mo later. Each had x-ray computed tomographic (CT) studies performed within 1 wk of the scintigraphic procedure.

SPECT/IMP brain images were obtained using a digital gamma camera with truncated head and medium-energy collimator. IMP was labeled with (p,2N) iodine-123 (^{123}I) having ~2-4% ^{124}I contaminant. The radius of rotation was 14–15 cm for each patient and data acquisition was performed with a 1.7 factor zoom on 64 × 64 matrix. Iodine-123 IMP (4–5 mCi) was administered i.v. in a secluded environment with the patients eyes closed and imaging was initiated 20 min later. Imaging was also performed 4-6 hr after injection of [^{123}I]IMP to assess the delayed distribution of this tracer. A Hanning filter was used for data reconstruction and cross-sectional images were created in transverse planes parallel to the canthomeatal line.

CASE REPORTS

Case 1

A 65-yr-old right-handed male presented with right hemiparesis and global aphasia. There was no history of previous neurologic disease. A SPECT/IMP study was performed 7 days post onset of symptoms that showed decreased tracer in the left frontal and temporal regions on the early images (Fig. 1A). Overall tracer activity was decreased 12% compared with the contralateral hemisphere in these regions. In addition, increased IMP activity was noted in the posterior parietal area adjacent and posterior-superior to the photopenic defect (Fig. 1B) having a 19% greater tracer concentration as compared to the opposite hemisphere. X-ray without contrast 2 days

Received Jan. 23, 1987; revision accepted July 8, 1987.

For reprints contact: David L. Bushnell, MD, Nuclear Medicine Service (115), Hines VA Hospital, Hines, IL 60141.

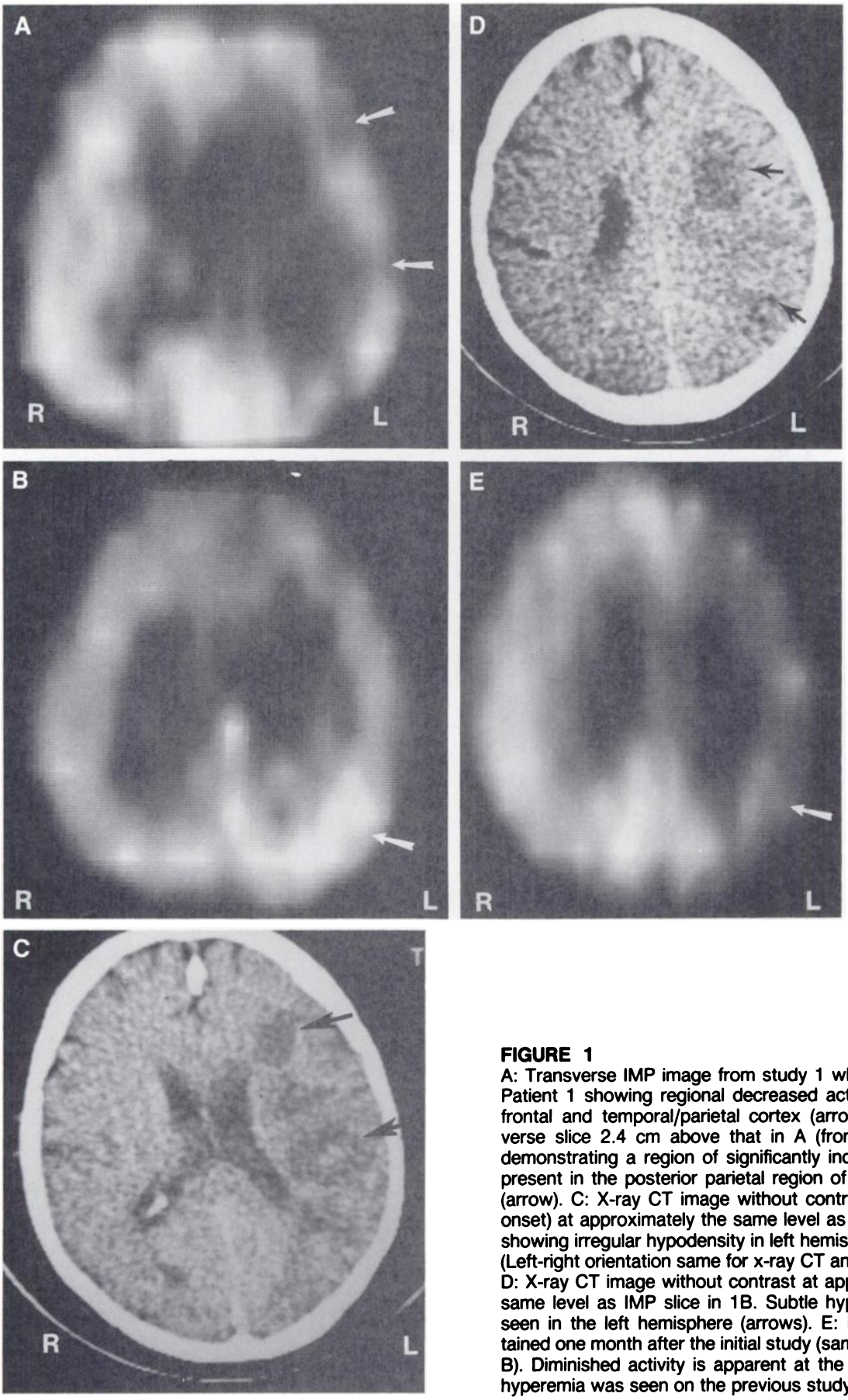

FIGURE 1
A: Transverse IMP image from study 1 wk post onset in Patient 1 showing regional decreased activity in the left frontal and temporal/parietal cortex (arrows). B: Transverse slice 2.4 cm above that in A (from same study) demonstrating a region of significantly increased activity present in the posterior parietal region of the left cortex (arrow). C: X-ray CT image without contrast (3 wk post onset) at approximately the same level as the image in A showing irregular hypodensity in left hemisphere (arrows). (Left-right orientation same for x-ray CT and IMP images). D: X-ray CT image without contrast at approximately the same level as IMP slice in 1B. Subtle hypodensities are seen in the left hemisphere (arrows). E: IMP image obtained one month after the initial study (same slice level as B). Diminished activity is apparent at the site where the hyperemia was seen on the previous study (arrow).

post onset demonstrated subtle hypodensities in the left frontal, temporal, and parietal regions which were much more apparent on a repeat CT exam 3 wk later (Fig. 1C, 1D). In addition, after contrast infusion, enhancement was seen on CT in the temporal and parietal regions of the infarct at this time.

The SPECT/IMP exam repeated 1 mo after the initial study continued to show the regional photopenia in the left cerebral hemisphere. Interestingly, in the site where the previous study had shown increased activity the new images revealed decreased IMP (Fig. 1E).

Case 2

A 64-yr-old male, presented with a mixed aphasia characterized by dysfluent speech, agraphia, dyslexia, and moderate auditory comprehension problems suggesting involvement in the left frontal and parietal areas. There was no significant motor or sensory impairment. Initial SPECT/IMP images obtained 17 days post onset revealed a small region of minimally diminished IMP activity in a left frontal location representing a 10% decrease relative to the corresponding contralateral site. There was also a relatively large area of significantly increased IMP activity located in the left posterior parietal

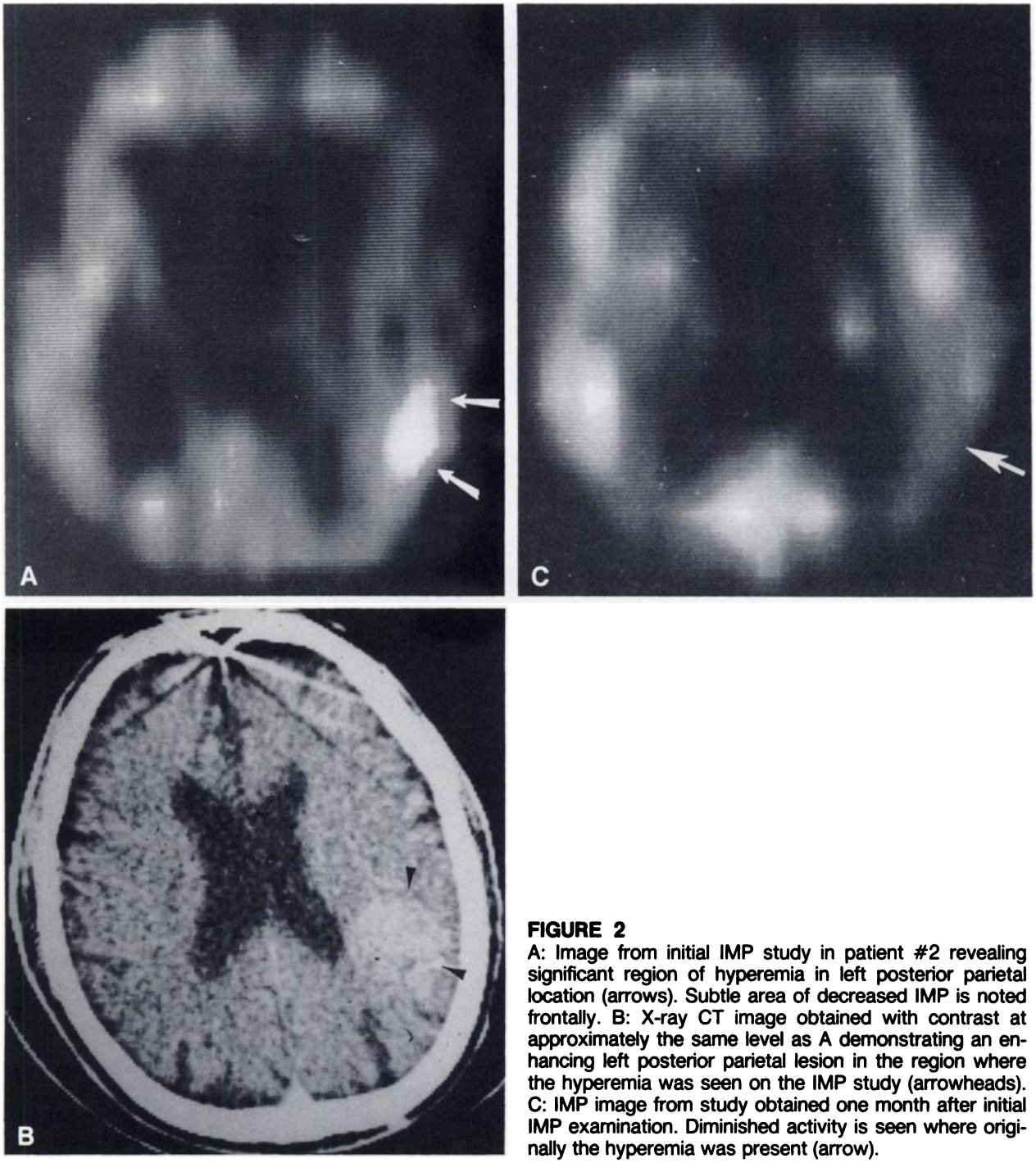

FIGURE 2
A: Image from initial IMP study in patient #2 revealing significant region of hyperemia in left posterior parietal location (arrows). Subtle area of decreased IMP is noted frontally. B: X-ray CT image obtained with contrast at approximately the same level as A demonstrating an enhancing left posterior parietal lesion in the region where the hyperemia was seen on the IMP study (arrowheads). C: IMP image from study obtained one month after initial IMP examination. Diminished activity is seen where originally the hyperemia was present (arrow).

region (Fig. 2A). Compared to the opposite hemisphere IMP activity was increased by 13% at this site. X-ray CT performed at this time demonstrated a hypodense lesion that showed enhancement with contrast agent present in the posterior parietal area corresponding anatomically to the location of the hyperemia seen on the IMP image (Fig. 2B). Repeat SPECT/IMP examination 1 mo later demonstrated decreased IMP at the site where the previous study had displayed the focal hyperemia and the x-ray CT without contrast had shown the hypodense lesion (Fig. 2C). In addition the small frontal defect seen on the initial scan was no longer identifiable.

DISCUSSION

Under normal conditions cerebral blood flow is closely coupled to the degree of local metabolic activity. However, in certain pathologic states such as acute cerebral infarction metabolic control of rCBF is lost and cerebral perfusion may exceed tissue requirements. In particular, autoregulation in the region of infarction may be absent for several weeks after the event with the consequence that local blood flow becomes coupled to changes in perfusion pressure. Using positron emission tomography, Kuhl et al. (*5*) were able to directly identify the depressed areas of glucose metabolism associated with the increased blood flow (luxury perfusion) in patients with acute cerebral infarction.

The pathophysiology of acute hyperemia in association with cerebral infarction is not well defined. It has been suggested that vasodilitation in response to diminished pH created by local elevation in lactic acid may result in regional hyperemia (*6*). Related observations include the occasional loss of autoregulation (as noted above) and vascular reactivity to CO_2 in regions of acute cerebral ischemia. Recanalization of the occluded artery may also be important in the genesis of reactive hyperemias (*7*).

While most focal hyperemias in acute stroke have been identified during the first several days post onset, recent PET data have determined that luxury perfusion also occurs as late as several weeks after the initial ischemic event (*5*, *8*). Our results are consistent with these findings since focal hyperemias were identified in the patients presented here at 8 and 17 days post onset of symptoms. Importantly, these later onset hyperemias may result from distinctly different physiologic phenomena than the early hyperemias.

There is good evidence to indicate a direct relationship between rCBF and IMP uptake in normal brain tissue (*9*, *10*). However, in acute cerebral ischemia or infarction the distribution of IMP in the region of pathology may not reflect rCBF alone, but may in fact be determined by a variety of local metabolic changes (*11*). Therefore, whether IMP imaging is capable of identifying focal hyperemia in acute stroke has important implications. As noted previously other authors have not identified areas of cerebral hyperemia in acute cerebral infarction using IMP (*3*, *4*).

The findings presented indicate that, in some cases, luxury perfusion associated with acute cerebral infarction can be identified with IMP. Further investigation will be required to determine the factors which lead to visualization of regional hyperemias with IMP and whether these phenomena have clinical relevance.

REFERENCES

1. Lassen NA. The luxury perfusion syndrome and its possible relation to acute metabolic acidosis localized within the brain. *Lancet* 1966; 2:1113–1115.
2. Ackerman RH, Alpert NM, Correia JA, et al. Positron emission tomography in cerebrovascular disease. In: Magistretti, ed. Functional radionuclide imaging of the brain. New York: Raven Press, 1983: 277–280.
3. Yonekura S, Tanada M, Senda H, et al. Regional distribution of N-isopropyl-p-iodoamphetamine in cerebrovascular disease compared with regional cerebral blood flow and oxygen metabolism. [Abstract]. *J Nucl Med* 1985; 26:235.
4. O'Leary DH, Hill TC, Lee RG, et al. The use of 123I iodoamphetamine and single-photon emission computed tomography to assess local cerebral blood flow. *AJNR* 1983; 4:547–549.
5. Kuhl DE, Phelps ME, Kawell AP, et al. Effects of stroke on local cerebral metabolism and perfusion: Mapping by emission computed tomography of ^{18}FDG and ^{13}NH3. *Ann Neurol* 1980; 8:47–60.
6. Holman BL. Radionuclide imaging of the brain. New York: Churchill Livingstone, Inc., 1985; 1–26.
7. Olsen T, Larsen B, Skriver E, et al. Focal cerebral hyperemia in acute stroke: incidence, pathophysiology and clinical significance. *Stroke* 1981; 12:598–606.
8. Ackerman RH, Correia JA, Alpert NM, et al. Positron imaging in ischemic stroke disease using compounds labeled with oxygen 15: initial results of clinicophysiologic correlations. *Arch Neurol* 1981; 38:537–543.
9. Winchell HS, Horst WD, Braun L, et al. N-isopropyl-(123I) p-iodoamphetamine; single pass brain uptake and washout; binding to brain synaptosomes; and localization in dog and monkey brain. *J Nucl Med* 1980; 21:947–952.
10. Kuhl DE, Barrio R, Huang SC, et al. Quantifying local cerebral blood flow by n-isopropyl-p-(123I) iodoamphetamine (IMP) tomography. *J Nucl Med* 1983; 23:196–203.
11. Ackerman RH. Of cerebral blood flow, stroke and SPECT. *Stroke* 1984; 15:1–3.