Single Photon Emission Computed Tomography in AIDS Dementia Complex

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Single photon emission computed tomography (SPECT) studies were performed in AIDS dementia complex using IMP in 12 patients (and HM-PAO in four of these same patients). In all patients, SPECT revealed either multiple or focal uptake defects, the latter corresponding with focal signs or symptoms in all but one case. Computerized tomography showed a diffuse cerebral atrophy in eight of 12 patients, magnetic resonance imaging exhibited changes like atrophy and/or leukoencephalopathy in two of five cases. Our data indicate that both disturbance of cerebral amine metabolism and alteration of local perfusion share in the pathogenesis of AIDS dementia complex. SPECT is an important aid in the diagnosis of AIDS dementia complex and contributes to the understanding of the pathophysiological mechanisms of this disorder.

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Subacute encephalopathy is a frequent neurologic manifestation of the acquired immunodeficiency syndrome (AIDS) (*1–4*). This encephalopathy characteristically manifests as a progressive dementia accompanied by motor dysfunction, and is only observed in HIV-1-(HTLV-III-) infected patients but not in those with other immunosuppressed states. A great number of investigations support the theory that this condition is caused by direct HIV-1 brain infection (*4–10*). Nevertheless, the pathogenesis of AIDS dementia complex is not fully understood, and metabolic and/or neurotransmitter disturbances are discussed as additional pathophysiological factors (*11–13*). Neuropathologic findings are cerebral atrophy, gray and white matter abnormalities, and vascular changes (*2,14,15*). The diagnosis is mainly based on clinical features and brain biopsy; computerized tomography (CT) and magnetic resonance imaging (MRI) may be of some diagnostic value (*16,17*). Recently, positron emission tomographic (PET) studies performed in a patient with AIDS dementia, showed an abnormal pattern of glucose metabolism, which recovered after treatment with 3′-azido-3′-deoxythymidine (AZT) (*18*).

SPECT represents a special method used to image radioactive distribution in three-dimensional direction and has gained special importance in the field of neuroimaging after the introduction of IMP (iodine-123-N-isopropyl-p-iodoamphetaminehydroacetate) and HM-PAO (technetium-99m-hexamethylpropyleneamine oxime). Recently, single photon emission computed tomography (SPECT) has been considered to be a useful method used in the differential diagnosis of dementia. (*19*). The purpose of this study was, therefore, to discuss observations made using SPECT in patients with AIDS dementia complex.

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Patients and Methods

SPECT studies of 12 HIV infected patients with subacute encephalopathy were reviewed. Of the 12 patients, there were seven homosexual men and five drug abusers (three males, two females) ranging in age from 26 to 46 yr (mean 38 yr). Three patients fit the criteria for AIDS established by the Centers for Disease Control, two of them were homosexual men suffering from Kaposi's sarcoma; one was a drug abuser with repeated opportunistic infections. Six patients were classified as ARC (AIDS-related complex), and three patients (including the two females) were seropositive without evidence of other than neurologic HIV-related disease. None of the patients suffered from other opportunistic or neoplastic diseases of the brain at the time of the SPECT examinations.

All patients underwent neurologic examination and psychiatric evaluation prior to CT, EEG, SPECT, and MRI. Follow-up examinations and repeated CT scans were carried out during a period between 2 and 6 mo. The degree of the mental changes was classified according to the criteria given by Navia et al. (*1*). A mild dementia was diagnosed, when complaints of cognitive impairment or deficits in at least one

cognitive area was present. A patient was considered as moderate demented if two or more cognitive areas were impaired but with preservation of the ability to perform simple activities of the daily life.

CT scans and EEG were performed in all patients; five patients underwent additional MRI examination. CT examinations were carried out on the DR 2 (Siemens Medical Systems, Inc., Iselin, NJ) using standard techniques; slice thickness was 8 mm, contrast material was administered intravenously in all patients before scanning (average amount of iodine injected: 21 g), double-dose contrast enhancement was not used. In suspicious cases other causes of meningitis or encephalitis were excluded by cerebrospinal fluid examinations.

MRI scans were performed on a Siemens Magnetom MR imager with a 0.5-T superconducting magnet using standard techniques. The T1 weighted scans were obtained with TR = 500 msec and TE = 30 msec, the T2 weighted images were performed with TR = 2,000 msec. and TE = 60 msec. The MR images were obtained in axial, sagittal and coronal planes.

SPECT imaging was carried out with a conventional rotating gamma camera (Siemens Gammasonic) connected to a DEC PDP 11/34 computer for three-dimensional image reconstruction. Data were obtained from 64 projections into a 64 × 64 matrix using a high-resolution low-energy collimator. A dose of 185 MBq iodine-123 (^{123}I) amphetamine or technetium-99m HM-PAO ([^{99m}Tc]HM-PAO) were administered intravenously in a quiet room with dimmed lights. The patients were positioned supine; they were told to close their eyes, and their ears were plugged for 15–30 min. With the ^{123}I agent IMP data collection was started 20 minutes after the injection of the radiopharmaceutical. The total acquisition time was ~30 min during which time 2.5- 5 million counts were collected. From the 64 planar pictures around the patient's head tomographic slices in transverse, coronal and sagittal direction were reconstructed using a filtered backprojection algorithm. The data were examined by the staff of the department of nuclear medicine being unaware of the patient's clinical state.

RESULTS

Neurologic and Psychiatric Findings

The results are summarized in Table 1. At the time of the SPECT examination, seven patients suffered

TABLE 1
Characteristics and Findings in 12 Patients with AIDS Dementia Complex

Patient no.	Risk group*	Stage†	Neurologic signs	CT	MRI	SPECT	
						IMP	HM-PAO
1	h	AIDS	moderate dem. focal signs l parietal	atrophy	n.d.§	multiple	more pronounced
2	h	AIDS	moderate dem.	atrophy	n.d.	multiple	n.d.
3	h	ARC	moderate dem.	atrophy	n.d.	multiple	n.d.
4	h	ARC	mild dem. focal signs r frontal	normal	normal	r frontobasal	n.d.
5	h	ARC	moderate dem.	normal	leukoencephalopathy	multiple	additional lesions
6	h	ARC	mild dem.	atrophy	n.d.	multiple	n.d.
7	h	POS	mild dem. focal signs l frontal	normal	leukoencephalopathy	l frontobasal	additional
8	da	AIDS	mild dem. focal signs r frontotemporal	atrophy	atrophy	r frontotemporal	more pronounced
9	da	ARC	moderate dem.	atrophy	atrophy	multiple	n.d.
10	da	ARC	mild dem. l parietotemporal	atrophy	n.d.	l parietotemporal	n.d.
11	da	POS	mild dem. focal signs r frontobasal	atrophy	n.d.	r frontobasal	n.d.
12	da	POS	mild dem. l occipital	normal	n.d.	l occipital	n.d.

* h: homosexual; da: drug abuser.
† ARC: AIDS-related complex; POS: HIV-1-seropositive.
‡ dem: dementia; l: left; r: right.
§ n.d. - not done.

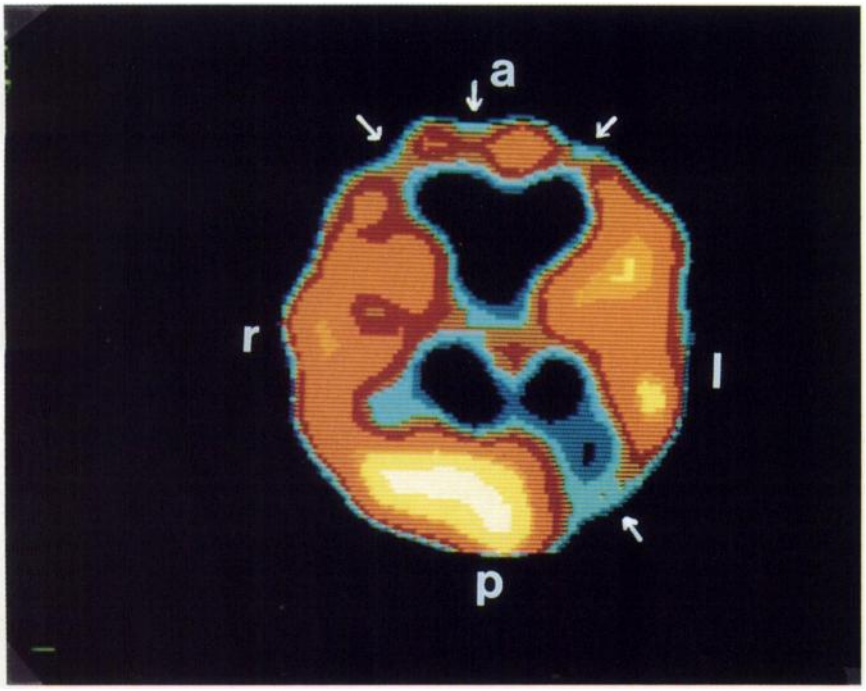

FIGURE 1
Multiple uptake defects (arrows) in Patient 9 (IMP-SPECT). One extended lesion is localized left occipital depicted by the color blue. Three minor lesions in the left and right frontal cortex are characterized by contour interruption and by color change (transversal section just above the basal ganglia and across the region of the lateral ventricles).

from a mild dementia and five patients were judged as moderate demented. During the follow-up period five of the seven mild demented patients developed a moderate degree of dementia, two of the prior moderate demented patients exhibited severe signs of mental impairment. In seven patients additional slight focal signs or symptoms could be found by neurologic examination; a peripheral neuropathy was present in ten patients.

Computerized Tomography and Magnetic Resonance Imaging

The computed tomographic (CT) scans showed evidence of diffuse cerebral atrophy in eight patients and were normal in four patients. In two patients magnetic resonance imaging (MRI) exhibited multiple white matter lesions, which were not apparent on CT images. In three other cases, MRI did not give additional informations.

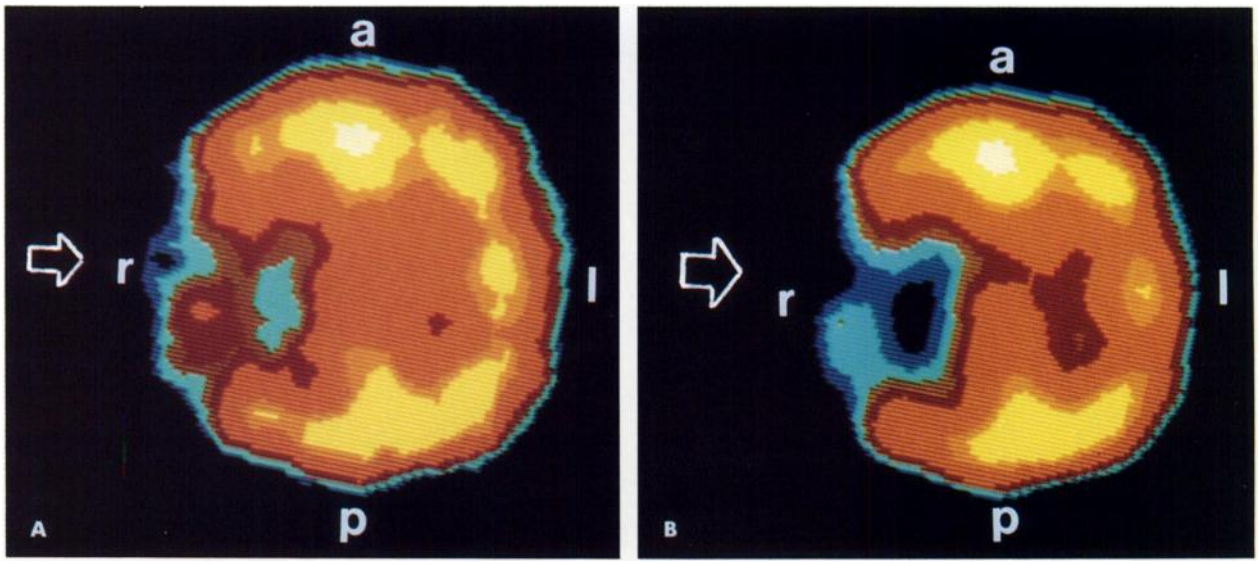

FIGURE 2
A: Unilateral uptake defect (IMP-SPECT) in Patient 10 (transversal section just above the central parts of the lateral ventricles). B: Increase of the uptake defect (IMP-SPECT) in Patient 10; or 3 wk later (transversal section just above the central parts of the lateral ventricles). (a: anterior; p: posterior; l: left; r: right).

EEG Findings

In three cases, EEG revealed mild to moderate abnormalities like diffuse slowing. In all other cases the EEG was normal.

SPECT

IMP-SPECT showed pathologic findings in all patients. Multiple focal lesions (Fig. 1) in the cerebral cortex were detected in six patients. Of the remaining patients, three had isolated unilateral lesions in the left and three in the right hemisphere (Fig. 2A), which were in accordance to the focal signs found by neurologic examination. One patient with focal signs and symptoms exhibited multiple uptake defects. In two patients follow-up studies performed 3–5 wk later showed significant deteriorations of the prior scan findings (Fig. 2B).

In Patient 5 (Table 1) the first SPECT examination, which was performed three months before onset of demential symptoms, revealed a normal distribution. The second examination, performed 5 wk after the presentation of demential complaints, showed multiple uptake defects.

HM-PAO-SPECT was additionally performed in four of the 12 patients with an interval of 4 to 7 days after the IMP scans. Two patients exhibited IMP and HM-PAO uptake defects in identical regions, while in the two other patients additional areas of reduced HM-PAO uptake could be observed.

DISCUSSION

Central nervous system manifestations often complicate AIDS. Among these, subacute encephalopathy is one of the most striking events, clinically presenting as a progressive dementia. The precise incidence of this complication is uncertain, but it seems to afflict at least half of the AIDS patients. In over one-third the dementia is present either at the time of diagnosis of AIDS or prior to other manifestations (*1*). The most frequent neuropathologic findings in AIDS dementia complex are diffuse astrocytosis of the white matter and fibrillary gliosis of the gray matter structures in the cerebral hemispheres (*2,4,14*). Vascular changes are of two types—calcific and inflammatory (*15*). The cause of the AIDS encephalopathy is still under discussion. Several investigations (e.g., in-situ hybridization, virus isolation from and identification of HIV-1 antigen in the brain, transmission studies) suggest a direct HIV-1 infection of brain tissue (*4–10*). However, the lack of a clear correlation between clinical severity and the degree of neuropathologic changes indicate that additional factors could be involved in the pathogenesis of the AIDS dementia complex (*2*). Some preliminary studies on metabolic and neurotransmitter disturbances have been carried out, but the results are inconclusive (*11–13*).

While CT and MRI are suitable for detecting space-occupying lesions within the brain in patients with AIDS (*20*), the diagnosis of subacute AIDS encephalopathy is mainly based on clinical findings which allow for the separation of different stages and degrees of AIDS dementia complex. CT findings are nonspecific; they often show evidence of diffuse cerebral atrophy, and—in advanced disease—may exhibit widening of the frontal horn and bilateral low density of the adjacent white matter (*16,17*). MRI seems to be superior to CT in the imaging of AIDS dementia (*17*), because it is more sensitive than CT in evaluation of white matter lesions which are typical for HIV-associated subacute encephalitis. However, in three out of five cases of our study MRI findings did not exceed the data gained by CT. In contrast, IMP- and HM-PAO-SPECT displayed pathologic results in all patients. In all but one patient with focal neurologic signs, SPECT revealed focal lesions in identical localizations. No differences in the SPECT patterns could be detected between the group of homosexual patients and the group of drug abusers. Follow-up examinations in two patients revealed an increase of uptake defects in parallel to the increase of clinical symptoms. In a third case, a prior normal SPECT pattern changed to abnormal 5 wk after the patient developed demential symptoms. In this patient, CT and MRI confirmed the diagnosis of a leukoencephalopathy only in a later stage of the disease.

HM-PAO is degradated into a hydrophilic complex after blood-brain-barrier passage and fixed in brain tissue proportional to regional cerebral blood flow (*21*). IMP reflects local perfusion too, and furthermore interacts relative unspecifically with synaptosomal amine binding sites (*22*). Thus, the radiopharmaceuticals have different mechanisms of intracerebral retention and therefore probably point out different forms of brain tissue alteration. The uptake defects of IMP and HM-PAO reflect the above mentioned vascular changes in brain autopsy studies, although altered perfusion itself cannot be regarded as the primary pathogen event. In addition, reduced uptake of IMP supports the preliminary studies on metabolic and neurotransmitter disturbances in AIDS dementia complex.

The findings of IMP- and HM-PAO-SPECT are not specific for AIDS encephalopathy and a variety of other conditions produce similar uptake defects, but the method very sensitively shows pathophysiological changes at early stages of the disease. Thus, besides the diagnostic value, the method may also contribute to the understanding of the pathophysiological mechanisms generating AIDS dementia complex. Since SPECT is more readily available than PET, it may be beneficial in diagnosis and evaluation of this disorder.

REFERENCES

1. Navia BA, Jordan BD, Price RW. The AIDS dementia complex. I. Clinical features. *Ann Neurol* 1986; 19:517–524.
2. Navia BA, Cho E-S, Petito CK, et al. The AIDS dementia complex. II. Neuropathology. *Ann Neurol* 1986; 19:525–535.
3. Price RW, Navia BA, Cho E-S. AIDS encephalopathy. *Neurol Clin* 1986; 4:285–301.
4. de la Monte SM, Ho DD, Schooley RT, et al. Subacute encephalomyelitis of AIDS and its relation to HTLV-III infection. *Neurology* 1987; 37:562–569.
5. Shaw GM, Harper ME, Hahn BH, et al. HTLV-III infection in brains of children and adults with AIDS encephalopathy. *Science* 1985; 227:177–182.
6. Gajdusek DL, Aureyx HL, Gibbs CJ, et al. Infection of chimpanzees by human T-lymphotropic retroviruses in brain and other tissues from AIDS patients. *Lancet* 1985; 1:55–56.
7. Gyorkey F, Melnick JL, Gyorkey P. Human immunodeficiency virus in brain biopsies of patients with AIDS and progressive encephalopathy. *J Infect Dis* 1987; 155:870–876.
8. Gartner S, Markovits P, Merkovitz DM, et al. Virus isolation from and identification of HTLV-III/LAV-producing cells in brain tissue from a patient with AIDS. *JAMA* 1986; 256:2365–2371.
9. Stoler MH, Eskin TA, Benn S, et al. Human T-cell lymphotropic virus type III infection of the central nervous system. A preliminary in situ analysis. *JAMA* 1986; 256:2360–2364.
10. Pumarola-Sune T, Navia BA, Cordon-Cardo C, et al. HIV antigen in the brains of patients with the AIDS dementia complex. *Ann Neurol* 1987; 21:490–496.
11. Kairam R, Rudelli R, Patel P, et al. Further observations on the AIDS encephalopathy - the role of iron-metabolism. *Ann Neurol* 1986; 20:443.
12. Navia BA, Khan A, Pumarola-Sune T, et al. Cholinesterase-acetyltransferase activity is reduced in the AIDS dementia complex. *Ann Neurol* 1986; 20:142.
13. Navia BA, Rottenberg DA, Sidtis J, et al. Regional cerebral glucose metabolism in acquired immune deficiency syndrome dementia. *Neurology* 1985; 35 (suppl 1):233–234.
14. Nielsen SL, Petito CK, Urmacher CD, et al. Subacute encephalitis in acquired immune deficiency syndrome. A postmortem study. *Am J Clin Pathol* 1984; 82:678–682.
15. Sharer LR, Epstein LG, Cho E-S, et al. Pathologic features of AIDS encephalopathy in children. Evidence for LAV/HTLV-III infection of brain. *Human Pathol* 1986; 17:271–284.
16. Levy RM, Rosenblum S, Perrett LV. Neuroradiologic findings in AIDS. A review of 200 cases. *Am J Radiol* 1986; 147:977–983.
17. Post MJD, Sheldon JJ, Hensley GT, et al. Central nervous system disease in acquired immunodeficiency syndrome. Prospective correlation using CT, MR imaging, and pathologic studies. *Radiology* 1986; 158:141–148.
18. Yarchoan R, Browers P, Spitzer AR, et al. Response of human-immunodeficiency-virus-associated neurological disease to 3′-azido-3′-deoxythymidine. *Lancet* 1987; I:132–135.
19. Jagust WJ, Budinger TF, Reed BR. The diagnosis of dementia with single photon emission computed tomography. *Arch Neurol* 1987; 44:258–262.
20. Gill PS, Graham RA, Boswell W, et al. A comparison of imaging, clinical, and pathologic aspects of space-occupying lesions within the brain in patients with acquired immune deficiency syndrome. *Am J Physiol Imaging* 1986; 1:134–141.
21. Sharp PF, Smith FW, Gemmel HG, et al. Technetium-99m HM-PAO stereoisomers as potential agents for imaging regional cerebral blood flow: human volunteer studies. *J Nucl Med* 1986; 27:171–177.
22. Winchell HS, Horst WD, Braun L, et al. N-isopropyl-(123 I) 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.