Iodine-123 HIPDM Brain Imaging Findings in Subacute Spongiform Encephalopathy (Creutzfeldt-Jakob Disease)


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Decreased perfusion of the left frontal and left temporoparietal cortex has been shown in [123I] HIPDM planar and single photon emission computed tomographic images of a patient with Creutzfeldt-Jakob disease (CJD) that was proven by brain biopsy and subsequent autopsy. An EEG showed diffuse, periodic discharges most prominent to the left hemisphere. Concurrent head computed tomography (CT), nuclear magnetic resonance (NMR), and cerebral angiographic studies were negative. Abnormalities demonstrated by [123I]HIPDM imaging and by EEG may represent changes in neurophysiological and neurochemical status while cerebral angiography, CT, and possibly NMR register only anatomic or structural lesions. Premortem diagnosis of CJD depends on brain biopsy; the availability of the [123I] HIPDM study may provide regional cerebral neurochemical and neurophysiological information, guiding or avoiding brain biopsy in the appropriate clinical setting.


Subacute spongiform encephalopathy, or Creutzfeldt-Jakob disease (CJD), is a rapidly progressive, fatal central nervous system disease. It almost always occurs during middle-age and is, as a rule, fatal within several months to several years after onset. It has been proposed that the etiology of the disease is a slow viral infection (3). The clinical triad of CJD includes dementia, akinetic mutism, myoclonus, and periodic synchronous discharges in the EEG (4). Premortem diagnosis depends only on a brain biopsy revealing spongiform changes and astrocytic proliferation of the cerebral gray matter (3,5). Head computed tomography (CT) has been evaluated for CJD (6–15) and most studies have reported normal CT (6–10). We present a patient whose brain biopsy revealed spongiform degeneration, also found at subsequent autopsy.

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CASE REPORT

A 68-yr-old man was admitted with 2 mo history of progressive aphasia and changes in mental status. Two years earlier he experienced unexplained right arm weakness that persisted for ~1 hr without subsequent residual. Six weeks prior to the latest admission he complained of headaches and blurred vision and was observed to have mild personality changes. Physical examination revealed a lethargic patient, but one who was responsive to noise and pain. The patient demonstrated a jargon aphasia; his speech was disorganized, words were used inappropriately regarding meaning and relationship to each other, and he seemed unaware of the incoherence of his own speech. An electroencephalogram (EEG) revealed severe generalized slowing with periodic epi-leptiform discharge from the left hemisphere.

X-ray computed tomography (CT) and nuclear magnetic resonance (NMR) of the head were negative (Fig. 1) and a cerebral arteriogram demonstrated only slowing of the vascular circulation. An HIPDM brain imaging study showed decreased radioactivity in the left frontal and the left parieto-temporal region (Fig. 2). Based on this finding, biopsy of the left temporal lobe was performed demonstrating spongiform changes suggestive of Creutzfeldt-Jakob Disease. A repeat EEG with intermittent photic stimulation demonstrated diffuse periodic discharges suggestive of CJD.

During his hospitalization, the patient’s condition progres-
sively deteriorated with decerebrate posturing and myoclonic jerking of all four extremities. He died on the 41st hospital day. An autopsy confirmed subacute spongiform encephalopathy; the distribution of the pathological findings of spongiform changes and astrocytosis was scattered. The sites of severe pathological findings found were in the left temporal cortex (biopsy site) and left inferofrontal area (Fig. 3).

DISCUSSION

The results of cerebral angiography in CJD not, to the best of our knowledge, been documented, however, CT and NMR findings in the disease have been reported. Although the CT studies were normal in the majority of cases (6-9), several authors have reported cerebral atrophy. Galvez et al. found that the CT was abnormal in 20% (three of 15 patients) (9) that included dilatation of the ventricles and extension of the sulci, or brain atrophy (9-12). Serial CTs may demonstrate atrophic process of the brain, that results from neuron loss characteristic of spongiform encephalopathy (13,14). Three patients with CJD studied by NMR also showed signs of cortical atrophy, however, the changes observed by NMR were more prominent than those
noted by CT (14). No focal cerebral lesion was demonstrated by CT or NMR images (14). Based on these findings, it appears that the contribution of NMR and CT in the diagnosis of CJD is the demonstration of cortical atrophy and the exclusion of focal cerebral lesions (14).

Iodine-123 HIPDM, a lipophilic amine analog, normally passes through the blood–brain barrier (BBB) and localizes in the brain tissue in a manner dependent on the distribution of the regional blood flow (15,16). The exact mechanism of the $^{[123]}\text{I}$HIPDM localization in brain is unknown but probably is related to binding to nonspecific receptors or metabolism to nonlipophilic compounds (16).

An absence or decrease in cerebral perfusion usually indicates cerebral infarction, transient ischemia attack, or severe carotid stenosis (17–22). In patients with a cerebral infarct, there is frequently discordance between the $^{[123]}\text{I}$HIPDM or $^{[123]}\text{I}$odoamphetamine and the CT studies (19). Images obtained by CT may be normal for several days following the onset of symptoms, while the absence of perfusion shown by $^{[123]}\text{I}$HIPDM will be apparent immediately after the onset of the stroke (19). Similarly patients with Alzheimer’s disease (AD) have been described who demonstrated specific areas of absent perfusion (23–26) by $^{[123]}\text{I}$HIPDM study although no observable changes in brain tissue density was shown by CT study. Although the exact mechanism of absent perfusion in AD has not been elucidated, a neuronal metabolic alteration in AD patients is apparently responsible for the absent perfusion. It has been proposed that there is a decrease in protein synthesis, a neuronal metabolic change, in AD without BBB changes. Thus the discrepancy between CT and the $^{[123]}\text{I}$HIPDM study is not surprising.

Clinically this patient had a rapidly progressive dementing disorder; the interval between the diagnosis and death was <3 mo. The results of CT, NMR, and angiography were not helpful. Iodine-123 HIPDM brain single photon emission computed tomographic images showed abnormalities in the left frontal and left temporoparietal regions. A temporal lobe brain biopsy showed spongiform changes suggestive of subacute spongiform encephalopathy. The autopsy results confirmed CJD and also indicated that cerebral involvement of CJD is nonhomogenous, compatible with the finding of $^{[123]}\text{I}$HIPDM brain imaging. Apparently the morphological change in this disease is preceded by a long period of neuronal metabolic alteration. The BBB may remain intact resulting in no cerebral parenchymal changes and that may explain the normal CT, NMR, and cerebral angiographic studies. The mechanism of HIPDM uptake is not clear; however, a normal HIPDM uptake in the brain requires an intact cerebral blood flow and cerebral neuronal function. Focal absence or decrease of $^{[123]}\text{I}$HIPDM localization represents either interruption of blood flow or alteration of the functional status of the brain. For the latter, it is presumably loss of the neuronal capabilities to metabolize the HIPDM to nonlipophilic compounds, or a change in the status of nonspecific receptors.

In a recent case report of Creutzfeld-Jakob disease, CT was normal while positron emission tomography (PET) using fluorine-18-2-fluoro-deoxyglucose showed temporal lobe hypometabolism with hemispheric asymmetry similar to the finding described on AD (27). This points to neurophysiological and neurochemical aberrations in CJD demonstrated by decreased regional cerebral metabolism by PET while anatomic/structural changes are not evident by CT or NMR. Similarly in our case, $^{[123]}\text{I}$HIPDM images demonstrated regional absence or decrease in perfusion, while the lack of abnormal findings by angiography, CT and MRI indicates that these diagnostic modalities detect only ana-
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