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^{18}F-fluorodeoxyglucose-PET and ^{99m}Tc-bicisate-SPECT in Creutzfeldt-Jakob disease

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In a patient with the occipitoparietal form of Creutzfeldt-Jakob disease (CJD) (Heidenhain type) positron emission tomography (PET) demonstrated decreased glucose utilization in the occipital lobes and adjacent cortical regions. Single photon emission computed tomography (SPECT) with ^{99m}Tc-bicisate showed a "coupled" decrease in blood flow in identical cortical areas in this patient. In contrast, magnetic resonance imaging (MRI) was normal. In the early stage of CJD, when still no major morphological abnormalities can be observed, functional imaging is useful for differential diagnosis, particularly to exclude other causes of dementia or pathological EEG patterns.

Key words: PET, SPECT, Creutzfeldt-Jakob disease, bicisate, Neurolite, ECD

INTRODUCTION

THE ETIOLOGY of Creutzfeldt-Jakob disease (CJD), a subacute spongiform encephalopathy, is still not completely understood. A slow virus or prion infection is supposed to be the reason for the disease, which occurs during middle-age and leads to death within months or few years after onset.[1,2] On the basis of various EEG changes and a wide range of initial symptoms one assumes a focal beginning of functional deterioration in most cases.[3,4] According to the different clinical courses, several subtypes can be differentiated:[5] 1) corticospinal/frontopyramidal form 2) corticostriatal/dyskinetic form 3) occipitoparietal form (Heidenhain type) 4) borderline type with involvement of the cortex, basal ganglia, thalamus, cerebellum and spinal cord 5) atactic/cerebellar form (Brown-Oppenheimer type). In a patient suffering from CJD of the occipitoparietal type (Heidenhain), we could clearly demonstrate a regional decrease in glucose metabolism in the occipital lobes and adjacent cortical areas by means of ^{18}F-fluorodeoxyglucose-positron emission tomography (PET). Two sequential brain single photon emission computed tomography (SPECT) studies were performed in this patient. The first one was obtained one day after the PET study and the second two weeks later when epilepsy-like EEG changes occurred. Both studies revealed blood flow decrease in identical cortical areas, more pronounced in the second study.

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CASE REPORT

A 68-year-old woman was admitted to the Department of Neurology of the University Hospital because of visual loss. Initially, she complained of metamorphopsia. A few days later visual agnosia occurred. The patient was not able to recognize familiar objects in her environment. No further neurologic or psychiatric deficits could be observed, particularly the memory performance was not impaired and objects could be recognized well by touching.

At admission, serum parameters were completely normal. Lumbar puncture showed no major pathological results, the erythrocyte count had increased to 427/μl. The CSF and serum protein profile pointed to a slight impairment of the blood-brain-barrier function. Initially, the EEG showed an alpha-rhythm (10/sec) and frequent semiperiodic rhythmic sharp-slow-wave-complexes, partly bioccipital and partly generalized. After medication with diazepam the epilepsy-like EEG-alterations disappeared, but the clinical symptoms were unchanged. Cerebral magnetic resonance imaging (MRI) showed no

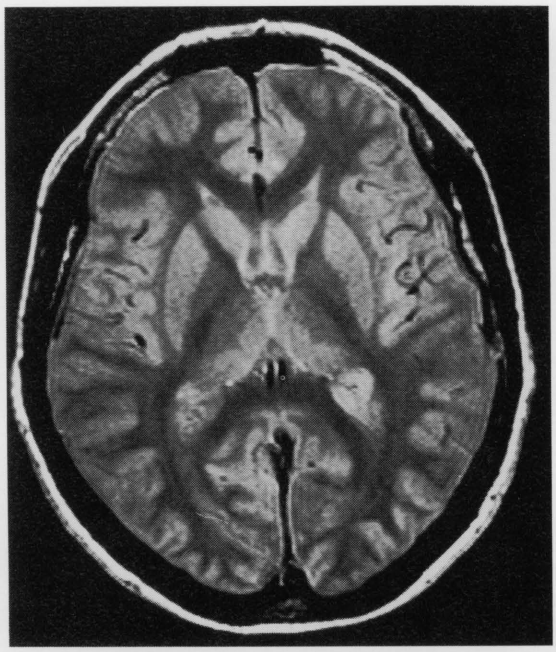

Fig. 1 The MRI scan (transaxial slice, parallel to the orbitomeatal line) in a patient with Creutzfeldt-Jakob disease (Heidenhain type) shows no abnormalities.

abnormalities (Fig. 1). Two weeks after admission, a 30-min static PET scan with a Siemens ECAT EXACT 921-47 PET scanner was performed after the injection of 370 MBq (10 mCi) ^{18}FDG (eyes closed). Cross sections were generated with filtered back projection (ramp 0.5) and corrected by means of a calculated attenuation matrix. The section images were added resulting in a final slice thickness of 6.74 mm. The PET study demonstrated a regional decrease in glucose metabolism bilaterally in the occipital cortex and adjacent parts of the parietal and temporal lobes (Fig. 2). Two sequential brain SPECT studies using ^{99m}Tc-bicisate (Neurolite) were performed in this patient. The first SPECT was obtained one day after the ^{18}FDG-PET study and the second two weeks later when the patient deteriorated clinically and epilepsy-like EEG changes were observed. Thirty minutes after the injection of 740 MBq (20 mCi) ^{99m}Tc-bicisate under resting conditions (eyes open), a brain SPECT study was performed by means of a high resolution CERASPECT system.[6] The acquisition time was 30 minutes. 120 projections were acquired with a 512 × 64 matrix (matrix of crystal for three simultaneous projections). Two pulse-height analyzer windows were used, one for the photopeak (126 to 154 keV), and one for the scatter correction (112 to 126 keV). Scatter correction and back projection with a Butterworth filter (cutoff frequency 0.9 cm) were performed. The transaxial slices (1.67 mm (1 pixel) thick) were attenuation corrected by Chang's method with an attenuation coefficient equal to 0.15 cm^{-1}. Coronal, sagittal and transaxial (parallel to the orbitomeatal line) slices were calculated from the original transaxial slices and summed in order to obtain 6.68 mm (4 pixel) thick slices. A distinct hypoperfusion was observed in the regions which showed decreased metabolism in the PET study (Fig. 3). Two weeks later, the SPECT study was repeated under the same conditions. In the second SPECT study the defects were enlarged (involving also bigger parts of the secondary and tertiary visual cortex) and more pronounced. No circumscribed hyperperfusions could be observed. In the second SPECT study, the left hemisphere was more affected than the right hemisphere. The final diagnosis was based on the characteristic clinical symptoms, the EEG pattern, the typical clinical course and the functional imaging studies.

DISCUSSION

The occipitoparietal type of CJD, described by Heidenhain[7] in 1929, occurs in about 20% of all cases of CJD. The appearance of morphological alterations in CJD, a disease of still unknown etiology and unclear pathogenesis, depends on the clinical subtype of the disease. In most cases alterations on CT or MRI cannot be detected in the early stage. Later on, cortical atrophy due to neuronal loss can be observed, whereas focal abnormalities are untypical.[8–10] Some reports on functional imaging with PET and SPECT suggest that these methods are sensitive in the detection of distinct hypometabolism and hypoperfusion when CT and MRI still do not show major abnormalities.[11–19] ^{18}FDG-PET studies revealed a decrease in glucose metabolism throughout the whole brain.[13,14,19] SPECT imaging in CJD has been performed with N-isopropyl-^{123}I-p-iodoamphetamine (^{123}I-IMP),[12] ^{123}I-N,N,N′-trimethyl-N-[2-hydroxy-3-methyl-5-iodobenzyl]-1,3-propanediamine (^{123}I-HIPDM),[11] and ^{99m}Tc-hexamethylpropylene amine oxime (^{99m}Tc-HMPAO).[15,18] In all case reports focal decreases in cerebral blood flow correlating to the clinical symptoms were described in patients with quite normal CT, MRI, and cerebral angiography results. Whereas a subtype of CJD is not described by Aharon-Peretz et al.,[18] Shih et al.[11] and Heye et al.,[15] Jibiki et al.[12] reported a case of Heidenhain type of CJD. In the patient described in the report by Jibiki et al.,[12] in whom visual loss was the first clinical symptom (like in the case described here), occipital hypoperfusions were also observed in the early stage when the CT was completely normal. Victoroff et al.[17] studied patients with "posterior cortical atrophy," caused by various underlying pathomechanisms. In CJD (in association with dysfunction of the posterior cortex classified as Heidenhain type) they found a generalized cortical hypometabolism by using ^{18}FDG-PET, most pronounced in the posterior cortex and in the left hemisphere. In the case presented here, glucose metabolism and ^{99m}Tc-bicisate uptake are decreased in the occipital lobes and adjacent cortex. Since ^{99m}Tc-bicisate can be regarded as a tracer for cerebral blood flow, a coupling of metabolism and blood flow seems to exist in this case in the affected cortical areas. A

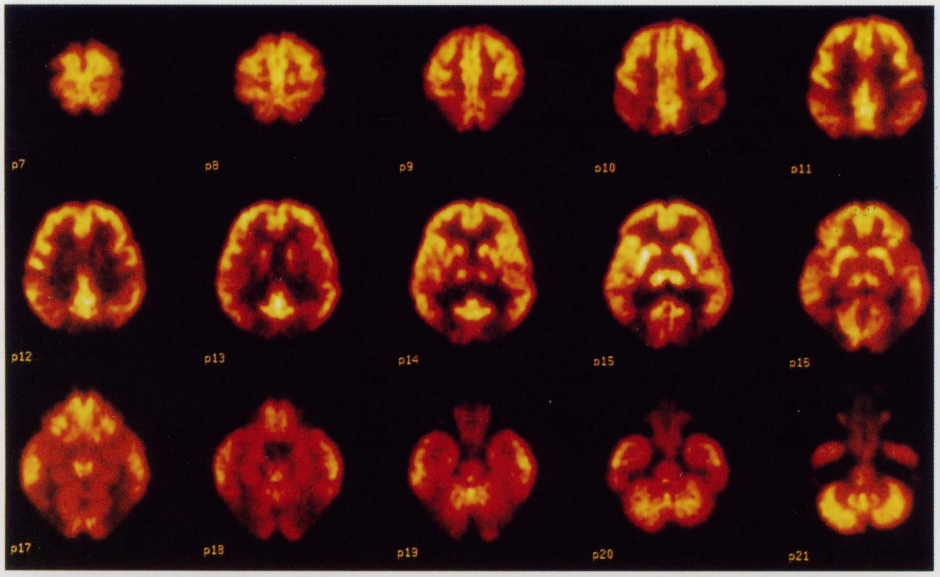

Fig. 2 In the ^{18}FDG-PET (transaxial slice, parallel to the orbitomeatal line) study a decreased glucose metabolism in the occipital cortex and adjacent parts of the parietal and temporal lobes was measured.

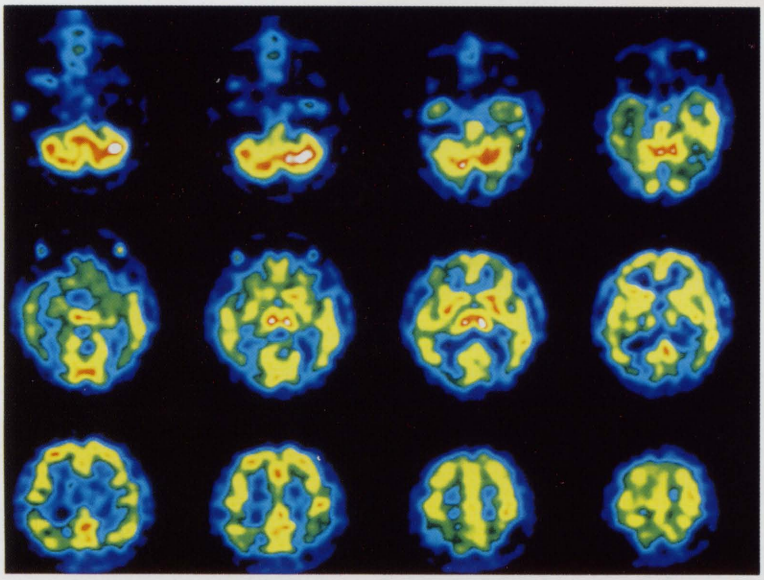

Fig. 3 The initial ^{99m}Tc-bicisate (Neurolite)-SPECT (transaxial slice, parallel to the orbitomeatal line) study shows areas of decreased blood flow corresponding to the PET result.

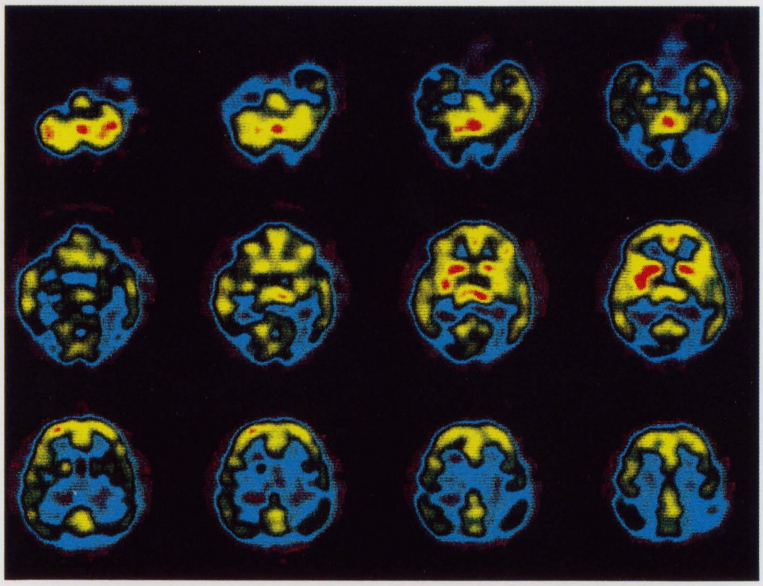

Fig. 4 The second ^{99m}Tc-bicisate (Neurolite)-SPECT (transaxial slice, parallel to the orbitomeatal line) study shows enlarged areas of decreased blood flow, compared with the initial SPECT. In addition, the defects are more pronounced than in the first study.

lesion with unchanged morphology but reduced function can be assumed, associated with the underlying pathomechanisms leading to neuronal loss in the further clinical course of CJD. Nevertheless, since no absolute quantification of glucose metabolism was obtained in this case, a general decrease in cortical glucose utilization cannot definitely be ruled out.

In the initial stage of CJD, PET and SPECT may be useful for differential diagnosis. Whereas in the patient reported by Aharon-Peretz et al.[18] the initial clinical syndrome resembled dementia of the Alzheimer-type, in the case presented here a syndrome associated with epilepsy could not be ruled out during the first stay in our hospital because of the epileptiform EEG changes. Focal hyperperfusion, known to be present with a high frequency in ictal brain SPECT studies,[20] could not be observed in this patient. Silverman et al.[21] studied seven patients with cortical visual loss. In one of these patients the symptom was caused by a status epilepticus. In the ictal ^{99m}Tc-HMPAO-SPECT study occipital/parietal hyperperfusion was observed in this patient.

The PET and SPECT results therefore proved to be helpful for differential diagnosis in the case described in this report.

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