J Neurol (2001) 248 : 1093–1095

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Crossed cerebellar diaschisis: a clue to the mechanism of ataxic hemiparesis in Creutzfeldt-Jakob disease?

Received: 29 December 2000
Received in revised form: 12 April 2001
Accepted: 5 June 2001

Sirs: In stroke patients, the presence of ipsilateral pyramidal and cerebellar signs (ataxic hemiparesis [1]) is difficult to explain with a single lesion; one of the current pathophysiological concepts is that crossing cerebro-cerebellar fibers, such as the cortico-ponto-cerebellar (CPC) tract, are disrupted in these patients [2–4]. In Creutzfeldt-Jakob disease (CJD), in contrast, the combination of pyramidal and cerebellar signs lies in the nature of this multiple system neurological disorder. However, we observed a discrepancy between functional imaging and neuropathological findings in a CJD patient with ataxic hemiparesis, which also suggested involvement of cerebro-cerebellar fibers.

A previously healthy 54-year-old man was admitted with a 2-week history of progressive diplopia, unsteady gait, clumsiness of right arm and leg, and impaired memory and speech. Besides bilateral dissociated, gaze-evoked, horizontal nystagmus, horizontal and vertical saccadic pursuit, and slowing of the horizontal and absence of the vertical optokinetic nystagmus, the patient had a pronator drift of the right arm and a right hemiataxia (intention tremor and bradydiadochokinesis of the right arm and ataxic gait with a drift to the right side). Tendon reflexes were normal and plantar responses were flexor bilaterally. The severity of the ataxia clearly exceeded that of the paresis. Sensibility was normal except for a decreased vibration sense in both legs.

T2-, fluid-attenuated inversion recovery (FLAIR), and diffusion-weighted magnetic resonance imaging (MRI) sequences showed an asymmetry of the basal ganglia with the left striatum appearing hyperintense (Fig. 1). Furthermore, there was an abnormal hyperintense signal in the cortex of the left superior and medial frontal gyrus on FLAIR and diffusion-weighted sequences (Fig. 1). ^{18}F-fluorodeoxyglucose positron emission tomography (FDG PET) revealed a decreased glucose utilization predominantly in the cortex and basal ganglia of the left cerebral hemisphere, the left pons, and the right cerebellar hemisphere (Figs. 1&2).

Eight weeks after onset, myoclonic jerks of the right arm and leg were present. The patient developed akinetic mutism and died 12 weeks after the onset of symptoms.

Neuropathological examination showed spongiform degeneration, astrocytic gliosis, and neuronal

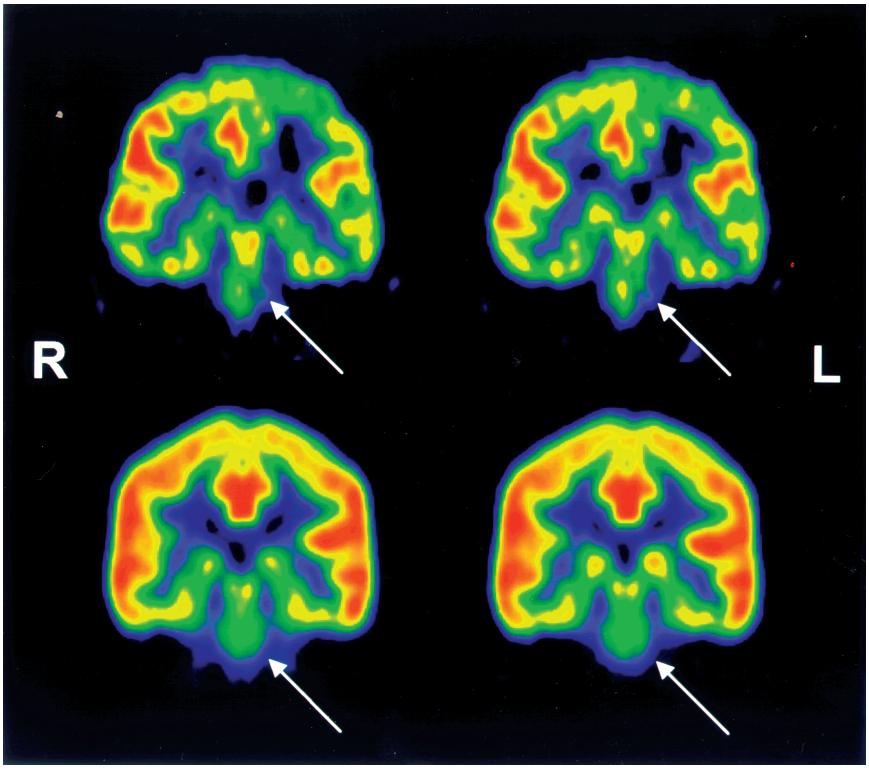

Fig. 1 Axial FLAIR sequences (left, 62 days before death) and diffusion-weighted images of cranial MRI (center, 54 days before death) show a hyperintense signal in the left striatum and left frontal cortex. Axial FDG-PET (right, 42 days before death) reveals decreased cerebral metabolic rates for glucose (cMRGl) predominantly in the cortex and basal ganglia of the left cerebral hemisphere and in the right cerebellar hemisphere. The cMRGl (μMol/min * 100 g) were 23.6 in the left and 34.4 in the right frontal cortex (upper panel). For a normal template created from ten healthy controls, the respective values were 57.3 and 59.7 (not shown). In the cerebellar cortex, the cMRGl were 34.8 on the left and 26.4 on the right side (lower panel). For the normal template, the respective values were 44.3 and 44.4 (not shown).

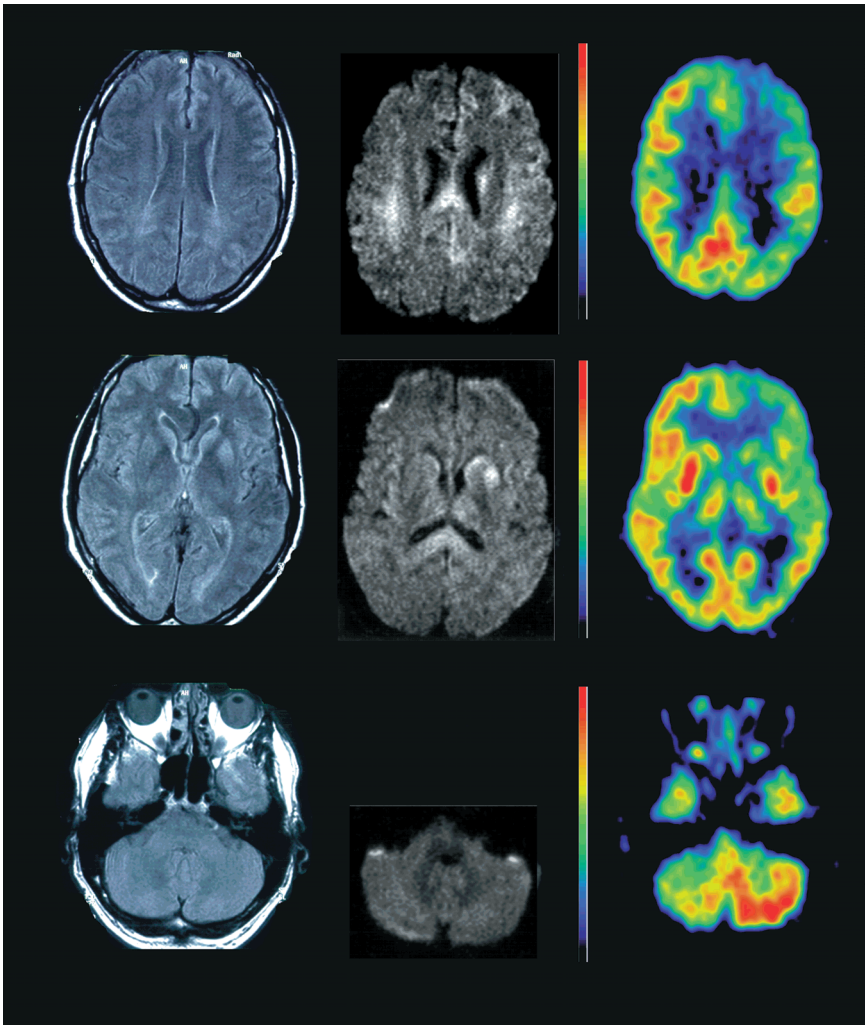

Fig. 2 Coronal FDG-PET of CJD patient (upper panel, 42 days before death) and a normal template created from ten healthy controls (lower panel) from caudal (right) to rostral (left) shows hypometabolism in the left pons of the CJD patient (arrow). The cMRGI (μMol/min * 100 g) were 23.8 in the left and 30.5 in the right pons of the CJD patient (upper panel) and 30.8 and 31.1 for the normal template (lower panel).

loss, as well as pathological prion protein (PrP) deposits (distributed symmetrically in a fine granular and perivacuolar fashion) in the cerebral neocortex, the basal ganglia, thalamus, and the cerebellum. Western Blot analysis detected PrP type 1. The neuropathological lesion profile and the deposition pattern of pathological prion protein were consistent with the picture of sporadic CJD. The paresis of the right arm and the MRI and FDG PET findings were reflected in severe neuropathological lesions in the left cerebral hemisphere (table). The right hemiataxia and the hypometabolism in the left pons and right cerebellum, however, contrasted with symmetrical neuropathological findings in these areas (table).

The observed pattern of regional hypometabolism correlates with the anatomy of the CPC pathway [5], which transmits information about planned movement to the cerebellum [4]. Its corticopontine portion is uncrossed and builds synapses on the pontine nuclei. Second order neurons then cross to the opposite cerebellar cortex via the middle cerebellar peduncle. Disruption of the CPC pathway will cause hypometabolism on the PET scan in the ipsilateral pons and the contralateral cerebellar cortex [5,6], resulting in crossed cerebellar diaschisis (reduced blood flow or metabolism in the cerebellum contralateral to a cerebral insult [7,8]). Disruption of the CPC tract may have contributed to cerebellar-like ataxia in our patient. Previous studies of CJD patients have reported that MRI or FDG PET, neuropathological, and clinical findings closely correlate [9–12]. Disruption of cerebro-cerebellar loops, resulting in crossed cerebellar diaschisis, is a novel finding that may provide a clue to the mechanism underlying ataxic hemiparesis in CJD.

Acknowledgements We thank Dr. M. Wick (Department of Clinical Chemistry), Dr. S. Arnold and Dr. A. Müller (Department of Neurology) for clinical cooperation. We also thank Ms. J. Benson for editing the manuscript.

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Table 1 Semiquantitative evaluation of neuropathological lesions on a scale of 0 (not found) to 3 (severe).

	Spongiosis	Gliosis	Neuronal loss
Caudate nucleus			
Left	3	2–3	1
Right	2	1	0–1
Putamen			
Left	3	2–3	2
Right	2	2	1
Medial frontal gyrus			
Left	2	2–3	2–3
Right	1–2	2	2
Superior temporal gyrus			
Left	1–2	2	2
Right	1	2	2
Cerebellar hemispheres			
Left	2–3	2	1
Right	2–3	1	1
Pontine nuclei			
Left	1	1	0
Right	1	1	0
Inferior olivary nuclei			
Left	0	2	1
Right	0	2	1

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