LETTERS TO THE EDITOR

Creutzfeldt-Jakob disease presenting as complex partial status epilepticus: a report of two cases

Creutzfeldt-Jakob disease is a transmissible human spongiform encephalopathy which may be familial, iatrogenic, or sporadic. The classic clinical features include a rapidly progressive dementia with the patient retaining clear consciousness until the terminal stages of the disease. We report on two patients presenting with a rapidly declining level of consciousness, in whom the clinical picture and EEG were suggestive of complex partial status epilepticus.

The first patient was a 58 year old woman who was admitted to a psychiatric unit with a short history of mood disturbance, confusion, and unsteadiness. A provisional diagnosis of agitated depression was made and she was started on lofepramine. She then became unsteady on her feet and required support when walking. She had had occasional complex partial seizures for 30 years but at presentation was not taking any anticonvulsant drugs.

On examination, she appeared perplexed, tearful, and agitated, and was unable to give a coherent history. She was intermittently confused and her gait was ataxic. There were no other cerebellar signs. The rest of the neurological examination was unremarkable although limited by poor cooperation.

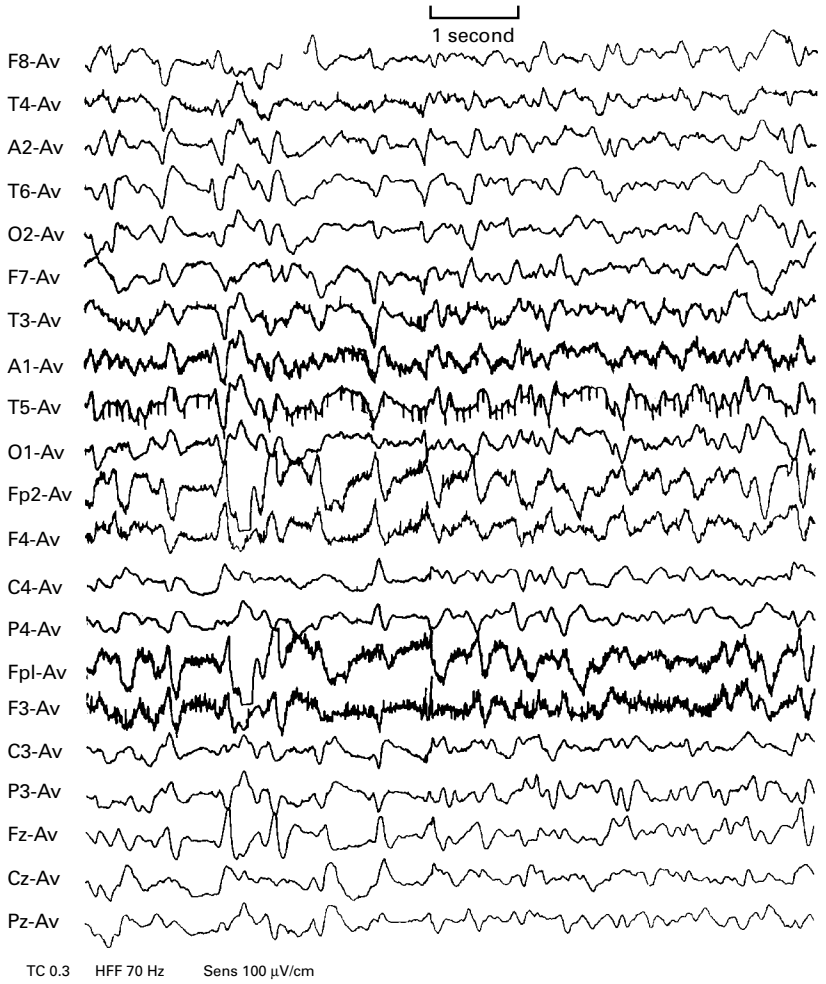
She became more withdrawn and uncommunicative with incontinence of urine. She would occasionally jump when sitting in a chair.

Brain CT and MRI were normal, as was her CSF. An EEG showed frequent, almost continuous variable amplitude sharp waves in all areas, although with a right sided emphasis, with a repetitive appearance up to 2 per second (figure). The record was thought to be in keeping with partial status epilepticus.

Her level of consciousness deteriorated despite intravenous valproate and phenytoin and she was transferred to the intensive care unit for continuous EEG monitoring. On arrival, she was deeply unconscious and despite aggressive management of her presumed complex partial status she died 3 weeks later. Histology of the brain was diagnostic of the sporadic form of Creutzfeldt-Jakob disease.

The second patient was a 68 year old man who was admitted with a short history of confusion and inappropriate behaviour. He appeared not to recognise his family. Initially he was dysphasic and obtunded. His conscious level then deteriorated and he became mute with evidence of right sided weakness.

All investigations including contrast enhanced brain CT and CSF examination were normal. An EEG was reported as showing frequent bilateral epileptiform activity, but there was no improvement in his clinical state after a loading dose of intravenous phenytoin. A repeat EEG was dominated by periodic lateralised epileptiform discharges (PLEDs), more marked on the left side. A third EEG 3 weeks later again showed frequent predominantly left sided epileptiform discharges, which were attenuated by a bolus of intravenous diazepam but without any improvement in his clinical condition.



Initial EEG at presentation in an acute confusional state, showing virtually continuous semirepetitive sharp waves with some right sided predominance. Although seizure-like evolution of discharges was not seen, the electrographic picture was considered to be in keeping with complex partial status.

He was transferred to this hospital for artificial ventilation because of the concern that he was in complex partial status. On admission he was mute, his eyes were closed, and he flexed to pain on the left side only. Intermittent twitching of both sides at a rate of between 1 Hz–2 Hz was seen. Reflexes were brisk and symmetric. His right plantar response was extensor, his left flexor.

A further EEG 5 days later showed generalised bisynchronous continuous periodic sharp waves occurring at a frequency of 1.3 Hz, at times in the form of biphasic or triphasic complexes. Myoclonic jerks occurred during the recording.

It was considered that overall these features were now consistent with a diagnosis of Creutzfeldt-Jakob disease. His condition continued to deteriorate and he died 2 weeks later. A request for a postmortem examination was refused.

These two cases illustrate a previously unrecognised presentation of Creutzfeldt-Jakob disease, namely presumed complex partial status.

In the first case, the interpretation of the EEG findings was made more difficult by the patient's depressed conscious level and the previous history of complex partial seizures, albeit mild. The initial psychiatric presentation, with mood and behaviour disturbance, as well as fluctuating confusion, was compatible with complex partial status. The initial EEG report, suggesting partial status epilepticus, prompted treatment, unsuccessfully, with anticonvulsant drugs and subsequent transfer for continuous EEG monitoring. This disclosed marked fluctuations, including discrete runs of rhythmic sharp waves that were considered to be electrographic seizures. Even after sustained burst suppression, the recording fluctuated between generalised periodic discharges and periods of relative inactivity within a matter of seconds.

In the second case, the patient developed focal seizures and PLEDs on the EEG. The initial recordings were suggestive of complex partial status, with asymmetric discharges abolished by diazepam but without any observable clinical change. Subsequent recordings were more characteristic of Creutzfeldt-Jakob disease, particularly as the patient had developed myoclonus. Although the electrographic changes were abolished by diazepam, suggesting seizure activity, the modification of both clinical and EEG activity in Creutzfeldt-Jakob disease by benzodiazepines has been reported[1] giving rise to further confusion with epileptiform sharp wave activity. The focal nature of the patient's signs and the lateralisation on the EEG is well recognised in Creutzfeldt-Jakob disease as are

periodic PLEDs, which are often associated with contralateral myoclonic jerks.[2]

The two cases described here illustrate that a diagnosis of Creutzfeldt-Jakob disease should be considered where a rapid decrease in consciousness is accompanied by EEG changes apparently compatible with complex partial status. When there is a clinical suspicion of Creutzfeldt-Jakob disease, the ideal method of monitoring such patients is with continuous EEG recording, allowing documentation of rapid fluctuations. The present cases are atypical in that the progression from presentation to death was rapid, but they underline the fact that minute to minute changes in EEG rhythm, asymmetry, and electrographic responsiveness to benzodiazepines can all be seen in Creutzfeldt-Jakob disease.

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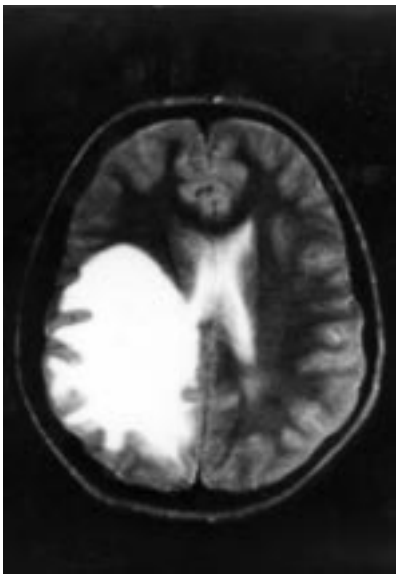
1 Elliott F, Gardner-Thorpe C, Barwick DD, *et al*. Jakob-Creutzfeldt disease. Modification of clinical and electro-encephalographic activity with methylphenidate and diazepam. *J Neurol Neurosurg Psychiatry* 1974;**37**:879–87.
2 Greenberg MK, McCarty GE. Periodic lateralised epileptiform discharges in Creutzfeldt-Jakob disease. *Neurology* 1981;**31**:362–3.

Childhood demyelinating diseases with a prolonged remitting course and their relation to Schilder's disease: report of two cases

Schilder's disease or myelinoclastic diffuse sclerosis is a rare acute or subacute demyelinating disorder which primarily affects children and young adults.[1 2] We report the clinical and neuroradiological follow up of two boys affected by a demyelinating disease with a prolonged relapsing-remitting course, response to corticosteroids, and relatively good long term prognosis.

The first patient presented at the age of 12 with a 2 month history of repeated episodes of headache and blurred vision followed by weakness in the left leg, lasting a few hours. Head CT and bilateral carotid angiography were normal. Two weeks later the left hemiparesis and headache recurred. T2 weighted images on brain MRI disclosed a hyperintense signal in the right parieto-occipital white matter of the centrum semiovale, without a mass effect. Flash visual evoked stimuli elicited a decreased potential on the left side. Motor and sensory nerve conduction were normal. Corticosteroid treatment (prednisone (1mg/kg/day)) reversed the clinical symptoms. At the age of 14, the boy began to have daily headaches. Brain MRI showed the previous white matter lesion, now extending to the parietal, temporal, and occipital areas, with a mass effect and contrast enhancement (figure). Light microscopy of a right parietal stereotactic biopsy disclosed perivascular cuffing with inflammatory cells and ultrastructural examination confirmed a loss of myelinated fibres. Immunohistochemical findings were negative. Five months later the patient had a third episode of left hemiparesis, this time with left sided focal motor and secondarily generalised seizures. Treatment with carbamazepine and cyclophosphamide improved the hemiparesis and controlled the seizures. Brain MRI showed that the mass effect had disappeared, leaving a right parietal, temporal, and occipital lesion. Follow up at the age of 19 showed that, except for a left visual field deficit, the patient had a normal neurological and mental status. He is now receiving azathioprine (75 mg/day).



Brain MRI of patient 1 at the age of 14.5 years. The T 2 weighted image (TR 2000/TE 50) shows a high intensive signal in the parieto-occipital white matter, involving the right centrum semiovale, with mass effect.

The second patient was admitted at the age of 4 because of the sudden onset of headache and vomiting with ataxia and drowsiness followed by generalised clonic seizures. Clinical examination on admission showed left hemiparesis, anisocoria (left>right), and dysarthria. Ocular funduscopy was normal. Head CT disclosed a reduced right lateral ventricle and subarachnoid spaces and, 1 week later, a small hypodense area in the right periventricular white matter. A carotid angiogram was normal. At the age of 5 the child had a second episode characterised by high fever, vomiting, sixth nerve bilateral paresis, dysarthria, truncal ataxia, and stupor. Treatment with corticotrophin (35 units daily for 5 days, then every 48 hours for 20 days) induced a rapid clinical improvement. From the ages of 5 to 14 the child had yearly relapses characterised by the sudden onset of left hemiparesis with variable involvement of the cranial nerves and impairment of consciousness associated with inconsistent alteration of white matter on brain CT (widespread hypodensity in the right centrum semiovale with a mass effect on the right ventricle). These attacks regressed spontaneously or after corticosteroid treatment. The last episode, at the age of 14, consisted of right sided paraesthesias of the face and hand, right hemiparesis, dysarthria, and drowsiness. T2 weighted sequences on MRI disclosed multiple focal abnormalities in supratentorial white matter. Corticosteroid treatment induced marked clinical improvement. Follow up at the age of 18 detected only a bilateral paretic nystagmus and hypometric saccades. Mental development was normal. Brain MRI showed that the white matter lesions had partly regressed.

In both patients the following investigations during and between attacks yielded normal findings: CSF examination (absence of oligoclonal bands), CSF lactate and pyruvate; extensive serological and CSF immune screen; extensive viral, bacterial, and parasitic serological and CSF tests; blood lactate and pyruvate, blood ammonia, amino acids in plasma, urine and CSF, gas chromatography-mass spectrometer analysis of organic acid in urine, adrenal function, plasma C26/C22 fatty acid ratio, serum copper, plasma ceruloplasmin, pyruvate dehydrogenase complex and cytochrome *c* oxidase activity in skin fibroblasts; arylsulphatase A, β-galactosidase, β-glucosidase, and galactocerebroside-β-galactosidase activities in leucocytes.

In both cases the overall findings raise the question of myelinoclastic diffuse sclerosis.[1 2] A prerequisite for the diagnosis is a normal very long chain fatty acid plasma concentration. Clinical signs include an intracranial hypertension syndrome, mental deterioration, hemiplegia, and visual field defects. The disease has either a monophasic course, rarely rapid and fatal, or a relapsing-remitting course.[3] Most patients have neurological sequelae during follow up and few patients fully recover.[3 4] Histological studies typically show a demyelinating process similar to that of multiple sclerosis, with an inflammatory perivascular infiltrate, and in severe cases, cystic lesions. Neuroimaging findings tend to parallel the clinical course. Corticosteroids may improve the outcome of the single relapse and possibly of the disease, as they did in our patients. Some patients respond to immunosuppressive therapy.

In both the patients described the association of headache, signs of diffuse and focal brain dysfunction, a relapsing course, and the response to corticosteroids also raise the possibility of an isolated CNS angiitis, a condition primarily affecting middle aged and elderly people. But neither cerebral angiography nor histological examination disclosed a primary vascular disorder. In addition, the early onset and the sporadic occurrence of the disorder rule out another recently described vasculopathy often associated with familial hemiplegic migraine.[5]

In conclusion, although demyelinating diseases that do not fulfil the classic definition of multiple sclerosis or encephalomyelitis remain difficult to label in children, the two cases we report here seem to fit Schilder's description of myelinoclastic diffuse sclerosis. Owing to the current lack of knowledge on the causes of this disease strict diagnostic criteria cannot be applied. Some presentations may warrant brain biopsy. The differing clinical and neuroimaging features seen in these patients may help in delineating Schilder's disease subtypes.

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