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Hatred of the hemiparetic limbs (misoplegia) in a 10 year old child

Injury to the right parietal region in adults may cause disorders of visuospatial ability in drawing and construction, neglect of the left side of space, denial of left hemiparesis (anosognosia), and sometimes an active hatred of the paralysed limb (misoplegia), occasionally associated with a personification of a limb (calling it "the nuisance"), or attempting to injure the paralysed left limbs.¹⁻³ Although misoplegia is reputed to be fairly common,³ it seems not to have been reported in adults since the classic work of Critchley.²

These neuropsychological signs have been far less often reported in children. There have been reports of left neglect and extinction in children,^{4,5} together with reports of a general tendency in children with head injury to deny their deficit. However, there seem to be no previous reports of anosognosia proper, or misoplegia, in children in relation to the classic pattern of right parietal neuropsychological deficits.

A 10 year old right handed boy, with no previous neurological history of note, had an episode of acute loss of consciousness (Glasgow Coma Scale score 6) after a spontaneous intracerebral haemorrhage. Brain CT showed a lesion in the deep white matter and basal ganglia of the right temporoparietal region (figure).

He had a dense left hemiparesis with reduced sensation, hemianopia, and a tendency to ignore things on the left side (for example, failing to dress his left limbs). His mother reported that he seemed to have regressed emotionally (for example, he had episodes of swearing, tantrums, and impulsive behaviour). He had become more self centred, often feeling that he had been "left out". His physiotherapist and occupational therapist reported that it was impossible to please him, as he found their treatment "wrong" or "faulty". This was dramatically different from his premorbid state, where he was described as a normal and emotionally stable child. Corroborating accounts of his change in behaviour were reported by his school teachers, although they noted no decline in his general intellectual abilities,

and he returned to his old class at school.

His mother reported that everything was "a laugh", and that you could not hold a serious conversation with him (although his serious side "came back" when he was "in trouble"). His physiotherapist reported that he avoided conversations about his hemiparesis, "as if it wasn't there", and instead talked excessively about other things. In an early physiotherapy session he insisted that he could run, but soon tripped and fell as a result of his hemiparesis. He had been a member of a football team and maintained that he would be able to return to the team, but he was clearly unable to play and was not selected. He then asserted that the team was inferior, and promised to find a better team. Both his physiotherapist and occupational therapist reported that it was difficult to gain his cooperation in therapy because of his denial of deficit. However, apart from anosognosia, he showed no other delusional beliefs.

In sharp contrast with this denial of deficit, his family, physiotherapist, and occupational therapist also reported that he held some unusual attitudes towards his left side. He was angry about his left limbs, often "hated" them, blamed them, and wanted to get rid of them. In the acute period in hospital he once actually threw himself out of his bed, on to his left side, in an attempt to injure his left arm and leg. He would often bend the fingers of his left hand backwards, attempting to break them. Both his mother and his physiotherapist reported him as saying that he "would rather destroy it, if he couldn't use it". They also reported that he expressed a desire that his left side might be replaced, with that of his mother.

He was assessed by us three months after the cerebrovascular accident, at which stage the left hemianopia and hemiparesis were still present, although the paresis had improved slightly so that he could now walk (with typical circumduction in gait). His left arm had recovered proximal movement, but he still had very poor control over his hand and finger movements. During our assessment his speech was entirely normal, as was his recent memory and recognition of well known faces. However, he performed poorly on drawing and constructional tasks (the block design subtest of the WISC-III, scaled score 5), showing some features of constructional dyspraxia, as well as occasionally



Brain CT of patient.

omitting components on the left. He showed further features of hemispatial neglect—missing some words on the left in reading, bisecting lines well to the right of true centre (mean line length 9.7cm, mean bisection position 59.7% from the left) and omitting items on the left in a figure cancellation task (Bell test, 11 of 16 targets identified in the left hemispace, 17 of 17 in the right).

At this stage he was anosognosic for his hemiparesis and neglect, but was aware that his drawing and constructional abilities seemed poor. Although he agreed that his left arm was "not the same" as before the injury, he denied that it caused him any disability. Asked directly to judge whether he might be able to use his arm to open a door, he said that this would not be a problem. When challenged to do this, he found it impossible, and solved the problem by using his right (good) hand to wrap the fingers of the left hand around the handle, and then pulled the door open using his body.

As regards the misoplegia, he said that he hated his arm and leg because he couldn't use them, and that he wanted to break them. He believed that, if the bones were broken, "the muscles might grow back together again", and he would be miraculously healed. Concerning his wish to have the left side replaced with that of his mother he confirmed that he had, quite naturally, asked her to do this.

This patient therefore showed the classic pattern of neuropsychological deficits seen after right parietal lesion in adults: misoplegia, anosognosia, left hemispatial neglect, and constructional apraxia.¹⁻³ The case seems to be the first in which misoplegia has been reported in a child. It has been suggested that signs of denial of deficit are common in all children after brain injury, but it is of clinical relevance to be able to differentiate between different forms of denial of illness. A pattern of neuropsychological deficit known to be associated with anosognosia, involving signs such as left neglect, visuospatial errors, and constructional apraxia, would be a suitable marker in making a distinction between anosognosia as part of a right parietal syndrome, and denial of deficit for other reasons (for example, as part of a frontal syndrome, or as a purely psychogenic defence mechanism).

The nature of the misoplegia in this case seems to be largely the same as that found in adults,¹⁻³ in that it involved a hatred for the left limbs, and a desire to injure them. In one respect, however, his attitude was different from that of misoplegic adults, in that he expressed a desire for the limbs to be "replaced", and it is surprising that his mother was chosen as the source of the exchanged body parts.

Another interesting feature of the case is the finding that anosognosia and misoplegia coexisted in one patient. This is surprising given that they reflect polar opposites in attitude to the disabled limbs. However, we noted during our assessment that the anosognosia and misoplegia were never present *simultaneously*. Rather he often switched between hating the left limb and denying his hemiparesis.

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Valproate induced encephalopathy treated with carnitine in an adult

Hepatotoxicity due to valproate often necessitates discontinuation of the drug. We report a patient with unstable epilepsy in whom valproate was an irreplaceable component of anticonvulsant treatment. Hepatic encephalopathy was reversed and remained controlled by combining carnitine supplementation with an essentially unchanged valproate schedule.

A 35 year old previously healthy woman developed status epilepticus secondary to viral encephalitis initially requiring mechanical ventilation and phenobarbitone concentrations of over 100 mg/l with phenytoin to maintain seizure control. Phenytoin was discontinued due to rash and replaced by carbamazepine, which was subsequently withdrawn due to abnormal liver function tests and sedation. Valproate was initiated in combination with phenobarbitone. Isolated generalised breakthrough seizures sometimes associated with urinary tract infections continued during a period of rehabilitation.

Thirteen months after her initial illness, she was again admitted after three days of increasing confusion, drowsiness, and tremulousness without seizure activity. On examination, delirium with asterixis raised the clinical suspicion of hepatic encephalopathy. Routine blood tests including white blood count and liver function tests were normal, and anticonvulsant concentrations were therapeutic (phenobarbitone 34.2 mg/l, valproate 83 mg/l). Serum ammonia on admission was 43 $\mu\text{mol/l}$ (normal < 33 $\mu\text{mol/l}$), rising to 215 $\mu\text{mol/l}$ by the next morning. Serum free carnitine was 7.6 $\mu\text{mol/l}$ (normal 19.0-60.0 $\mu\text{mol/l}$) and total carnitine 15.4 $\mu\text{mol/l}$ (normal 30.0-73.0 $\mu\text{mol/l}$). Phenobarbitone was maintained and valproate decreased from 3 g to 2.75 g a day with supplemental L-carnitine added (330 mg four times daily). The delirium and asterixis resolved over the next three days permitting discharge on the fourth hospital day with normal serum ammonia (25 $\mu\text{mol/l}$) and therapeutic valproate concentrations (93 mg/l).

Valproate has been shown to cause reduced serum carnitine concentrations and hyperammonaemia in certain children when compared with the administration of other antiepileptic drugs.¹ However, not all valproate induced hepatotoxicity is carnitine related. Children at greatest risk are those

receiving a multidrug anticonvulsant regimen. The condition usually develops within a few months of starting valproate.

Carnitine supplementation has been used to prevent hepatotoxicity in children considered at increased risk due to suspected mitochondrial disorder, malnutrition, mental retardation, high dose valproate treatment, or a history of hepatotoxicity to the valproate.² Treatment with oral carnitine has also been reported to reverse this hepatotoxicity in children despite continued valproate.³

Less is known about the relation between valproate induced hepatotoxicity and carnitine deficiency in adults. Reduced free carnitine concentrations have been reported in 76.5% of adults receiving anticonvulsant drug regimens including valproate compared with 21.5% of adults on schedules without valproate.⁴ Coma from valproate induced carnitine deficiency in adults is reported to respond rapidly to discontinuation of the drug.⁵

This case shows that certain adults receiving valproate are, like children, at risk for carnitine deficiency and hyperammonaemia with its clinical accompaniment. The incidence among encephalopathic adults on valproate is unknown. This patient further illustrates that identification and correction of a drug induced deficiency may allow continuation of treatment without disturbing control of an unstable seizure disorder. Much as folate is used in chronic phenytoin administration, supplemental carnitine should be considered in adult patients with epilepsy at risk for hyperammonaemia.

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Increased serum neopterin concentrations in a patient with Creutzfeldt-Jakob disease

Spongiform encephalopathies or prion diseases affect both human beings and animals. The human transmissible spongiform encephalopathies include Kuru, Creutzfeldt-Jakob disease, and the Gerstmann-Sträussler-Scheinker syndrome (GSS), and fatal familial insomnia; all these diseases are associated with the accumulation of β -pleated amyloid protein in the brain.¹

Besides genetic abnormalities, epidemiological studies disclosed that a transmissible agent is involved in the spread of Creutzfeldt-Jakob disease,¹ and small virus-like structures in brains from sporadic and familial Creutzfeldt-Jakob disease and GSS have been described.² More recently the possible association between bovine spongiform encephalopathies and Creutzfeldt-Jakob disease received much attention.

In a study comprising patients with neurodegenerative disorders we had the opportunity to examine a 67 year old woman who was clinically suspected of having Creutzfeldt-Jakob disease. She had shown rapidly progressive dementia, typical EEG patterns, and myoclonus; intercurrent illness was apparent. The woman died five months after the onset of clinical symptoms. At necropsy, performed by one of us (KJ), diffuse spongiform changes were found in the cerebral cortex, thalamus, striatum, and cerebellum associated with neuronal loss and astroglial proliferation, confirming the diagnosis of Creutzfeldt-Jakob disease. Blood specimens were obtained two months and one month before death. Among other routine laboratory tests, neopterin concentrations were measured by enzyme linked immunosorbent assay (ELISA; BRAHMS-Diagnostica, Berlin, Germany). Neopterin concentrations were 16.3 nmol/l (first occasion) and 12.4 nmol/l (second occasion), clearly raised compared with the serum neopterin concentrations in healthy controls (mean (SD) 5.4 (2.3) nmol/l).³

Increased neopterin concentrations are indicative of activation of cell mediated immunity in humans, because large amounts of neopterin are released from human monocytes and macrophages on stimulation with interferon- γ .⁴ Similarly, increased neopterin concentrations are often found in body fluids of patients with infections, autoimmune disorders, or certain types of malignancies, usually correlating with the extent and the activity of the diseases and giving prognostic information.^{3,4} Also in various infections of the CNS increased neopterin concentrations, preferentially in the CSF, have been reported.⁵ Thus increased serum neopterin is by no means specific for Creutzfeldt-Jakob disease but provides a hint that the cell mediated immune system was chronically activated in our patient with late stage Creutzfeldt-Jakob disease. This is surprising as there is no evidence so far that prion diseases are associated with abnormal cellular immunity. We are unable to deduce at which stage of disease immune deterioration may start in Creutzfeldt-Jakob disease, when an increase of serum neopterin may begin, and whether the presence of any transmissible agent was the cause of increased neopterin in the patient. Further studies involving larger numbers of patients are required to answer these questions.

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