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Rapid cognitive decline: not always Creutzfeldt-Jakob disease

[1]A Randall, [2]R Ellis, [2]B Hywel, [3]RR Davies, [3]SH Alusi, [3]AJ Larner
[1]*Core medical trainee year 2,* [2]*SpR in Neurology,* [3]*Consultant Neurologist, Walton Centre for Neurology and Neurosurgery, Liverpool, UK*

ABSTRACT A patient with rapidly progressive cognitive decline over an approximately four month period was suspected to have sporadic Creutzfeldt-Jakob disease. Features thought to support this diagnosis included psychiatric symptoms (anxiety and depression), visual hallucinations and a visual field defect. However, the finding of papilloedema broadened the differential diagnosis. Although standard brain imaging and electroencephalography had shown only non-specific abnormalities, subsequent cerebral angiography disclosed an intracranial dural arteriovenous fistula. Following embolisation, the patient made a good functional recovery. Intracranial dural arteriovenous fistula merits consideration in any patient with subacute cognitive decline, and should be included in the differential diagnosis of sporadic Creutzfeldt-Jakob disease.

***Correspondence to** AJ Larner*
Cognitive Function Clinic
Walton Centre for Neurology and Neurosurgery
Lower Lane
Fazakerley
Liverpool L9 7LJ
UK

e-mail ***a.larner@thewaltoncentre.nhs.uk***

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INTRODUCTION

Rapidly progressive cognitive decline in an older person is an extremely worrying clinical presentation which often prompts consideration of the diagnosis of sporadic Creutzfeldt-Jakob disease (sCJD). However, other causes of subacute cognitive decline also need to be considered in the differential diagnosis, some of which may have scope for partial reversal, as illustrated by the following case.

CASE

A 67-year-old woman was referred to the neurology clinic with a progressive history of anxiety, depression, cognitive decline and visual hallucinations over a period of approximately four months. Four years previously she had an episode of cranial herpes zoster infection complicated by severe post herpetic neuralgia which had been treated with increasing doses of analgesics, including paracetamol, tramadol, diazepam, amitriptyline, pregabalin, and fentanyl patches. In an attempt to rationalise her polypharmacy, her general practitioner had withdrawn pregabalin as she was having episodes of drowsiness, impaired concentration and lassitude. After withdrawal of pregabalin, her post herpetic neuralgia worsened and she developed low mood, anxiety, insomnia, and general loss of confidence. Her husband noted that the patient suffered from episodes of mild confusion, was indecisive and appeared unable to complete routine tasks such as setting the table. At times her limb movements were 'jerky', and he observed twitching movements when she was sleeping. She had occasional visual hallucinations in which she reported seeing absent family members in the house.

An initial neurology opinion noted pronounced anxiety and hesitancy of movement but no other neurological signs, and the presentation was thought to be in keeping with a primary anxiety/mood disorder. She was subsequently admitted to a psychiatric unit where a diagnosis of agitated depression was made and treatment commenced with mirtazapine, but there was no improvement in mood or anxiety; increasing drowsiness was noted.

She then developed transient visual loss in the right eye. An ophthalmology opinion noted right-sided disc oedema, extensive bilateral visual field defects, and deranged colour vision in both eyes despite relatively preserved visual acuity (R 6/9; L 6/12) with no relative afferent pupillary defect. Magnetic resonance imaging (MRI) of the brain showed diffusely increased signal in the occipital lobe white matter (R>L) with restricted diffusion in these areas; the appearance was reported as being suggestive of ischaemic change. These imaging appearances and her continued clinical deterioration triggered admission to her local hospital, and thereafter transfer to the neurology unit.

On admission to the neurology unit her Glasgow Coma Scale score was 13/15 (E4V3M6). She was orientated in person but not in time or place. She was unable to follow a one-step command. Speech was dysphonic but not aphasic. Cranial nerves were otherwise intact. Tone

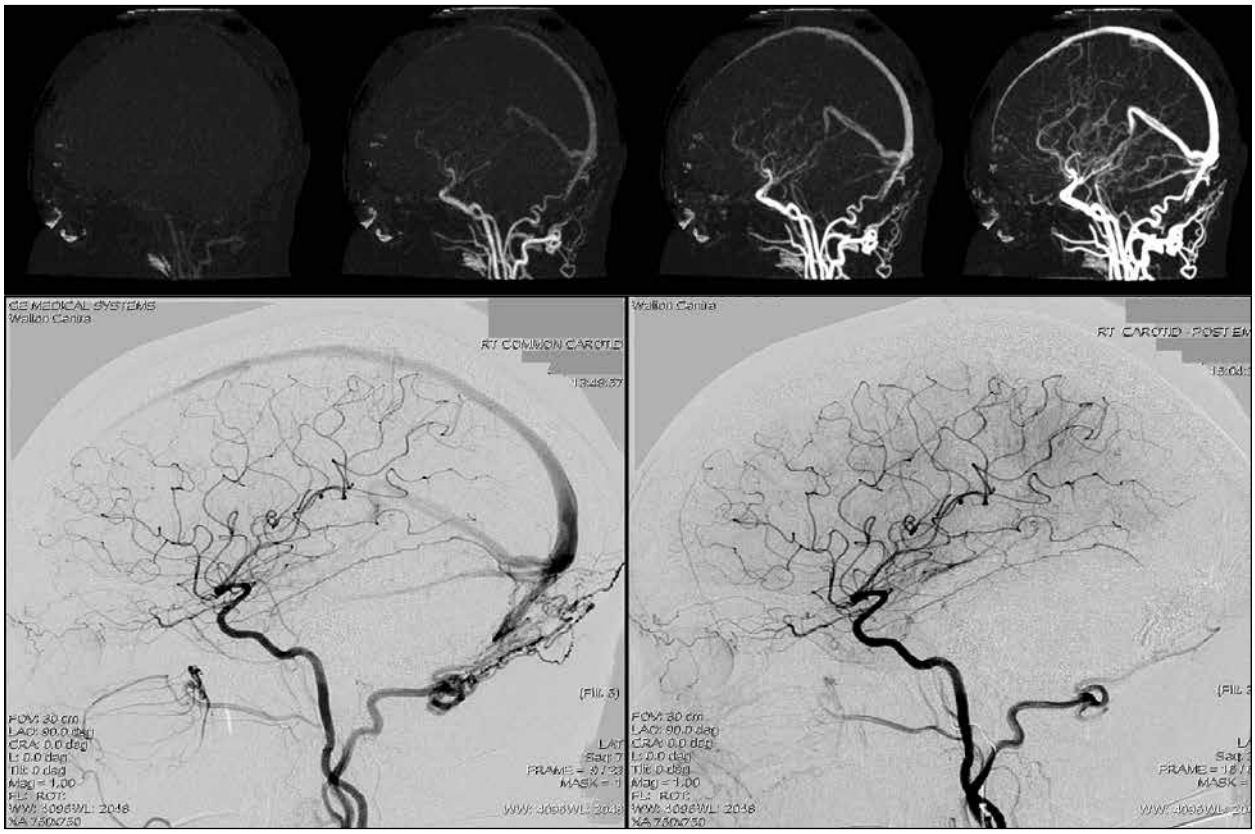

FIGURE 1 Top images: 4D computed tomography angiography showing sequential images with simultaneous contrast filling of the intracranial arteries and the sagittal and transverse sinuses, suggestive of an arteriovenous connection.

Bottom images: Digital subtraction angiography showing (left) the occipital dural AVF and confirming the early filling of the sagittal and transverse sinuses seen on computed tomography angiography, with (right) obliteration of the dAVF following embolisation with Onyx, and absence of early filling of the sinuses.

was increased globally with cogwheel rigidity (both R>L). Muscle power, co-ordination and sensation were difficult to assess due to cognitive impairment, but grip strength appeared good bilaterally. Tendon reflexes were brisk. Plantar responses were withdrawal. No involuntary movements were observed. Investigations showed normal cerebrospinal fluid (CSF) cell count, protein, and glucose ratio with serum. An electroencephalogram showed diffuse slowing over both hemispheres, consistent with encephalopathy, but there were no periodic complexes or sharp-wave discharges.

In light of the patient's rapid cognitive decline, psychiatric features, history of visual hallucinations and possible history of myoclonus, with evidence of visual field defect, a diagnosis of possible sCJD was suspected.

Within 24 hours the patient's clinical condition deteriorated further. She became increasingly drowsy with incomprehensible speech. Because of this acute deterioration, which would not be an expected feature of sCJD, a vascular process was considered. Since repeat CT brain imaging showed no haemorrhage or acute infarct, urgent CT angiography was undertaken to look for vasculitis or vascular malformation. This showed a large intracranial dural arteriovenous fistula (dAVF) with early filling of the sagittal sinus (Figure: top 4 images), findings which were confirmed on subsequent digital subtraction angiography (Figure: bottom left). This was defined as a Type 3 tentorial dAVF, fed by the occipital artery, left middle meningeal artery and left accessory artery from the ophthalmic artery, with reflux into the cortical veins, superior sagittal and straight sinus.

In light of this definitive diagnosis, embolisation of the fistula was undertaken at digital subtraction angiography (Figure, bottom right image). The patient was left with some mild right-sided weakness and right hemineglect but overall made a good functional improvement following a period of neurorehabilitation. Subsequently available results confirmed the absence of CSF 14-3-3 protein, which is typically found in sCJD.

DISCUSSION

Intracranial dural arteriovenous fistula may present clinically in a number of ways, either due to haemorrhage, or due to venous hypertension with shunting of arterial blood into the cerebral venous system.[1] Within the latter category, presentation with progressive cognitive

TABLE 1 Classification of dAVF (based on Cognard et al.[5])

Type	Venous drainage	Flow pattern in sinus	Cortical venous drainage
'Benign'			
I	Dural sinus	Anterograde	No
IIa	Dural sinus	Retrograde	No
'Aggressive'			
IIb	Dural sinus	Anterograde	Yes
IIa+b	Dural sinus	Retrograde	Yes
III	Cortical vein	-	Yes
IV	Cortical vein	-	Yes + venous ectasia
V	Cortical vein with spinal perimedullary drainage	-	-

decline, sometimes mimicking dementia, may occur, as attested to by a number of case reports and small case series[2,3] published over the last 20 years. Parkinsonism, pulsatile tinnitus, encephalopathy, and epileptic seizures may also occur.[1]

Different types of dAVF are recognised. The angiography-based classification systems of Borden et al.[4] and Cognard et al.[5] (Table 1) broadly divide them according to prognosis into 'benign' or 'aggressive' subtypes, based on the characteristics of venous drainage, flow pattern in the sinuses, and cortical venous drainage.

The presentation of dAVF with subacute cognitive decline may overlap with other causes of rapidly progressive dementia, such as autoimmune encephalitides, cerebral vasculitis and, as was the clinical concern in this case, sCJD. Factors initially thought to be in favour of the latter diagnosis in our patient included the history of cognitive decline, psychiatric symptoms including visual hallucinations, possible myoclonus ('jerky' movements and twitching during sleep), and evidence of a visual field defect.

Psychiatric symptoms may be an early and prominent symptom of sCJD, and may be mistaken for a primary psychiatric disorder and thus delay reaching the correct diagnosis.[6] Visual hallucinations may support a suspected diagnosis of sCJD, although these are usually elemental rather than formed hallucinations; failure to differentiate the specific type of visual hallucination may lead to incorrect diagnosis, causing particular misdiagnosis with dementia with Lewy bodies.[7] Visual field defects may be a presenting or early feature of sCJD,[8] which may sometimes be reported to simulate a vascular disorder.[9] Based on the clinical findings of cognitive decline and visual signs, our patient would have qualified for a diagnosis of 'possible sCJD' based on suggested diagnostic criteria.[10] However, papilloedema is not a recognised finding in sCJD. The original brain MRI finding of ischaemic change was non-specific; typical findings in sCJD are of hyperintensities in the basal ganglia and thalamus, together with cortical signal increase on diffusion weighted imaging.

The cognitive impairment encountered with dAVF is typified by cognitive slowing, reflecting slowed cerebral vascular transit time due to venous hypertension.[2] Intracranial dural arteriovenous fistula presenting with a clinical picture mimicking sCJD has, to our knowledge, only once been previously reported.[11]

The cognitive deficits associated with dAVF may be reversible, at least in part. Although some case reports describe 'reversible dementia', following interventional neuroradiology and fistula embolisation, residual cognitive deficits may nevertheless be apparent on formal testing.[2] Persistent cognitive deficits may be related to irreversible structural brain changes, such as complete or partial venous infarction of tissues which have been subject to chronic venous hypertension. Hence it is important to consider the possible diagnosis of dAVF in the clinical context of rapid and otherwise unexplained cognitive decline. In retrospect, it is clear that the finding of disc oedema in our patient, suggesting raised intracranial pressure, was a significant clue to the correct diagnosis.

CONCLUSION

Subacute cognitive decline may be due to intracranial venous hypertension associated with dAVF. Although infrequently reported, this diagnosis should be considered in any patient with rapid cognitive decline, in particular if there is evidence of papilloedema, as the symptoms may be partially or totally reversible with early occlusion of the fistula.

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