

TO THE EDITOR

Cognitive and Mood Profile of Sturge-Weber Syndrome Affecting the Thalamus

Cerebrofacial venous metamerism syndrome (CVMS), previously known as Sturge-Weber Syndrome, is a neurocutaneous disease that is usually diagnosed in childhood. Males and females are equally affected¹. Familial cases are rare, and the disease is believed to be due to a somatic mutation as suggested by observations in monozygotic twins¹. Prevalence is one in 50,000 live births, although this does not include those with milder forms of the disease. Clinical presentation can vary in severity and can include facial port-wine stains, ocular abnormalities, and leptomeningeal angioma^{1,2}. Cerebrofacial venous metamerism syndrome is typically categorized into three main classes, segmented by their origin on the neural crest and mesoderm^{2,3}. Ramli and colleagues considered CVMS 1 as involving the medial prosencephalic group (including the hypothalamus and the nose); CVMS 2 involving the lateral

prosencephalic group (including the occipital lobe, thalamus, and maxilla) and CVMS 3 being a rhombencephalic lesion, involving the cerebellum, pons, and mandible. The most common type of CVMS involves full prosencephalic impairments, affecting the orbit and maxillofacial regions, classified as CVMS 1 + 2³. Cerebrofacial venous metamerism syndrome has been well described in children, where it is known to cause a spectrum of neurological and psychiatric deficits. Similarly, in adults a spectrum of disease exists, with patients demonstrating apparently normal abilities to severe retardation. Patients with apparently normal abilities suffer from mood disorders; however, the subjective and objective cognitive consequences of CVMS in adults have not been explored as they have been in the paediatric population. We present the case of an adult patient with a mild form of CVMS 1 + 2.

CASE REPORT

A 38-year-old married female presented with a long history of left-sided headaches, with aches and pains throughout her body,

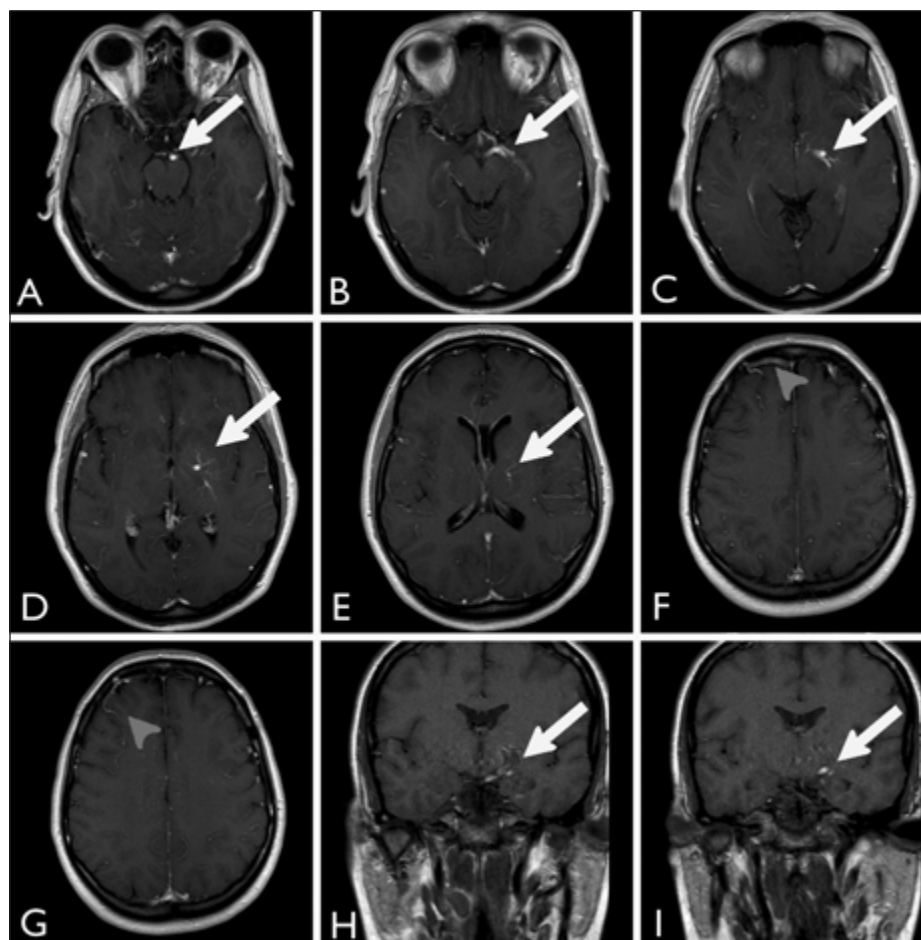


Figure: Gadolinium-enhanced MRI of the head. Panels A-E demonstrate the thalamic venous malformation in the axial plane (white arrow). Panels H and I demonstrate the thalamic venous malformation in the coronal plane (white arrow). Panels F and G demonstrate the frontal venous malformation (grey arrow head).

Table: Summary of objective and subjective cognitive assessments

Objective Cognitive Tests	
Montreal Cognitive Assessment (MoCA)	30 / max 30
Sustained Attention to Response Task (SART)	
Commission Errors	38
Omission Errors	8
Grooved Pegboard	
Right Hand Time (Drops)	68s (0)
Left Hand Time (Drops)	66s (0)
Phonemic Fluency	
Total Number of Words Correct	42
Number of Words Correct in First 15s	19
Number of Words Correct in Last 45s	23
Perseverative Errors	3
Semantic Fluency	
Total Number of Words Correct	18
Number of Words Correct in first 15s	10
Number of Words Correct in last 45s	8
Perseverative Errors	2
Subjective Questionnaires	
Cognitive Failures Questionnaire (CFQ)	50 / max 100
Frenchay Activities Index (FAI)	38 / max 45
Centre for Epidemiologic Studies Depression Scale (CES-D)	32 / max 60
Hospital Anxiety and Depression Scale –Depression (HADS- D)	13 / max 21
Hospital Anxiety and Depression Scale – Anxiety (HADS- A)	16 / max 21

Objective cognitive tests: MoCA, SART, grooved pegboard, and verbal fluency (phonemic fluency and semantic fluency). Subjective assessments: FAI, CFQ, CES-D, HADS-D and HADS-A. (max = maximum attainable score)

which were progressive over the past two years. Two vascular lesions were identified in the left eye: one lateral to the pupil and another inferior to the sclera. She had a deep, right-sided mass on her back and another on her left cheek. A pigmented nevus on her forehead was also identified. No neurological deficits were initially found. A family history of Ehlers-Danlos syndrome was noted, with an affected sibling; however, her joints were not found to be excessively hypermobile.

Magnetic resonance imaging revealed multiple intracranial developmental venous anomalies involving the left thalamus and the right frontal lobe with lesions in the orbits suggestive of cavernous malformations (Figure). She presented approximately eight months later with dizziness and blackouts with no apparent neurological cause and was subsequently referred to an otolaryngologist, although no interventions were undertaken.

A battery of neuropsychological tests was administered to assess multiple cognitive domains including global cognition, attention, visuo-motor ability, and language as well as subjective cognitive complaints, real-world functional ability and mood. (Table) Global cognitive testing revealed no abnormalities, with

a score of 30/30 on the Montreal Cognitive Assessment (MoCA). In addition visuo-motor deficits were not apparent on the grooved pegboard as the task was completed without any drops in 66 seconds and 68 seconds, with the left and right hands, respectively. However, the sustained attention to response task (SART) demonstrated a propensity to make a large number of commission errors (38 errors), and relatively fewer omission errors (eight errors). A commission error is a response to a target when instructed not to respond, while an omission error is the lack of response when instructed to do so. The low rate of omission error suggests she has no difficulties with sustaining attention over time. To contrast, patients with executive dysfunction after frontal lobe brain damage were found to have 24.8 and 30.6, commission and omission errors, respectively⁴. The results may be indicative of specific deficits in executive functioning, particularly difficulties with inhibition. The patient was aware of these errors and demonstrated post-error slowing of her responses, after both commission and omission errors. In the phonemic fluency task (F, A, S words) she produced 42 correct words and in the semantic fluency (animals) task she produced 18 correct words indicating spared language

production. However, perseverative errors were observed in both phonemic and semantic word generation tasks, which is suggestive of executive deficits and problems with inhibition.

The patient was asked to evaluate her own cognitive abilities, functional abilities and mood (Table). The cognitive failures questionnaire (CFQ) demonstrated a relatively high degree of subjective cognitive complaints with a score of 50/100. Very few functional complaints were elicited on the Frenchay activities index (FAI), self and caregiver, scoring 38 and 41, respectively, out of 45 with higher scores indicative of fewer deficits. The patient scored a 32 on the Centre for Epidemiologic Studies Depression scale (CES-D), and 13 on the depression portion of the hospital anxiety and depression scale (HADS), which is suggestive of major depressive disorder. In addition, the patient was very anxious, scoring 16 on the anxiety portion of the HADS. Family history for any mood disorder was not reported.

DISCUSSION

The case presentation fits the criteria for a mild case of CVMS Class 1 + 2 (SWS), with no port-wine stain¹. The lack of a port-wine stain in this case suggests that the migrating neural crest cells to the distal destinations of the facial region did not result in an abnormal vascular network and formed the trigeminal dermatome normally³. The timing of the migration and transformational changes to the cells would alter the impact and multifocality of the disease. A previous theory of the etiology of leptomeningeal angiomas was the failure of development or thrombosis of superficial cortical veins causing a redirection of blood to the leptomeninges and deep venous system¹. However it has been suggested the etiology of the venous abnormalities is migrating neural crest cells which have an associated abnormality in the same cranial metameric distribution, making the thrombosis a secondary process rather than the primary (causative) event³.

The patient had experienced severe and diffuse pain progressive over two years, which may be central pain possibly associated with the left thalamic vascular abnormality observed on imaging. The pain was a diffuse right-sided pain that was not localized to the region of the thalamus affected by the vascular anomaly. The pain also was not dependent on cutaneous stimulation. The lack of hemiplegia, hemianaesthesia, hemiataxia, and astereognosis suggest that the patient does not suffer from thalamic pain syndrome.

Objective and subjective cognitive assessments of adult patients with CVMS have not previously been reported. Observations in children demonstrate that cognitive deficits can range from mild learning disabilities to severe retardation. Early onset of seizures is correlated with poor cognitive outcomes. It is estimated that 50%-60% of patients with CVMS present with mental retardation⁵. In addition, those with apparently normal intelligence may present with subtle findings, such as mood disorders⁵. The patient in the present case demonstrated frontal lobe dysfunction with decreased inhibitory control (large number of commission errors on the SART and perseverative errors on word generation tasks).

In addition, adult patients with normal intelligence are often depressed, and this is supported by the present case study⁵. In this case, depression may be a psychological sequelae of chronic

pain, as depression is a well-recognized co-morbidity in patients with chronic pain. Depression in intellectually normal CVMS patients was found in a previous study, however it was not significant enough to require treatment⁵. Headaches and low self-esteem due to cosmetic effects of CVMS have also been suggested to cause depression in some cases⁵.

It is important to recognize that patients presenting with mild disease can have many deficits, some obvious and others more subtle. As this case demonstrates, mild forms of CVMS can present with subtle or specific cognitive deficits, such as difficulties with inhibition. Currently, there are no recognized treatments to reverse executive dysfunction; however, a recent study has provided evidence for the efficacy of Goal Management Training in improving executive function in patients with frontal lobe damage⁴. In addition to cognitive deficits, CVMS has a considerable emotional burden that is appreciated through depressive symptoms; as such psychiatric care would be appropriate. Identifying and addressing these issues have the potential to improve the quality of life for such patients.

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