

Case Report

Cognitive impairment and affective disorder: A rare presentation of cerebellar stroke

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ARTICLE INFO

Keywords:

Schmahmann syndrome
CCAS scale
Depression
Infarct
Cerebellum

ABSTRACT

The awareness of the “Cerebellar Cognitive Affective Syndrome” (CCAS) as a clinical entity is emerging. The CCAS is characterized by impaired executive functions, linguistic skills, visuospatial cognition and personality change. Here we report a 56-year-old, male teacher who developed acute psychomotor retardation, low energy level, infrequent speech, and mild cognitive decline. Two months before admission, he was initially diagnosed as depression, and later misdiagnosed as encephalitis, which misled him to receive high-dose intravenous steroids and antimicrobial drugs. The Brain MRI revealed multiple posterior cerebellar infarcts predominantly at the lobules VII and VIII. The standard neuropsychological tests were unremarkable; however, the CCAS Scale confirmed the diagnosis. The treatment of depression and secondary prevention of stroke was conducted. In cases that present with features of cognitive and affective disorders but with mild voluntary motor or without typical cerebellar features, the role of posterior cerebellar and vermal pathologies should be considered. The CCAS Scale is an appropriate screening tool to detect these patients and provides a framework for evidence-based treatment.

1. Introduction

Traditionally, the cerebellum has been viewed as an important regulatory center for the voluntary sensorimotor coordination; the maintenance of balance, gait, posture, rapid successive alternating movements, muscle tone, strength, fine motor movements, control of eye movements and the articulation of the speech. However, in the last two decades, accumulating evidence from patients with cerebellar lesions, neuroimaging and neuropsychological studies revealed the role of cerebellum in the cognitive, affective, autonomic and behavioral functions [1]. The “cerebellar cognitive affective syndrome (CCAS) /Schmahmann’s syndrome” is characterized by impairments of executive function (planning, set-shifting, abstract reasoning, verbal fluency, working memory), perseveration, distractibility or inattention; visual-spatial disorganization and memory; personality change with blunting of affect or disinhibited/ inappropriate behavior; and difficulties with language production including dysprosodia, agrammatism and mild anomia [2]. The CCAS may be associated with inherited neurodevelopmental diseases or acquired diseases/lesions involving the cerebellum and its various projections [3]. In a study of patients with cerebellar stroke examined 8.0 ± 6.0 days after the onset of stroke,

33.3% were reported to have normal motor functions, but their stroke in the posterior lobe of the cerebellum reported to produce the CCAS [4]. In a meta-analysis study including adult patients with isolated cerebellar lesions compared to the healthy controls, the cerebellar patients had significant cognitive deficits in the visuospatial, language and executive function domains [5].

2. Case report

A 56-year-old male teacher with history of coronary artery disease, hypertension, hyperlipidemia, and Type 2 diabetes mellitus was admitted to our clinic with history of acute onset of psychomotor retardation, emotional blunting, low energy level, disorder in decision making, inability to plan, prioritize or organize tasks, set and achieve goals successfully.

Our patient and his family had no previous medical history of psychiatric illness, dementia or inherited disease. Two months earlier, although the acute onset of these symptoms was reported, he was first examined by a psychiatrist and diagnosed with depression. Few weeks later, he was investigated by a neurologist with an initial diagnosis of encephalitis. The EEG was normal. The CSF examinations, serum

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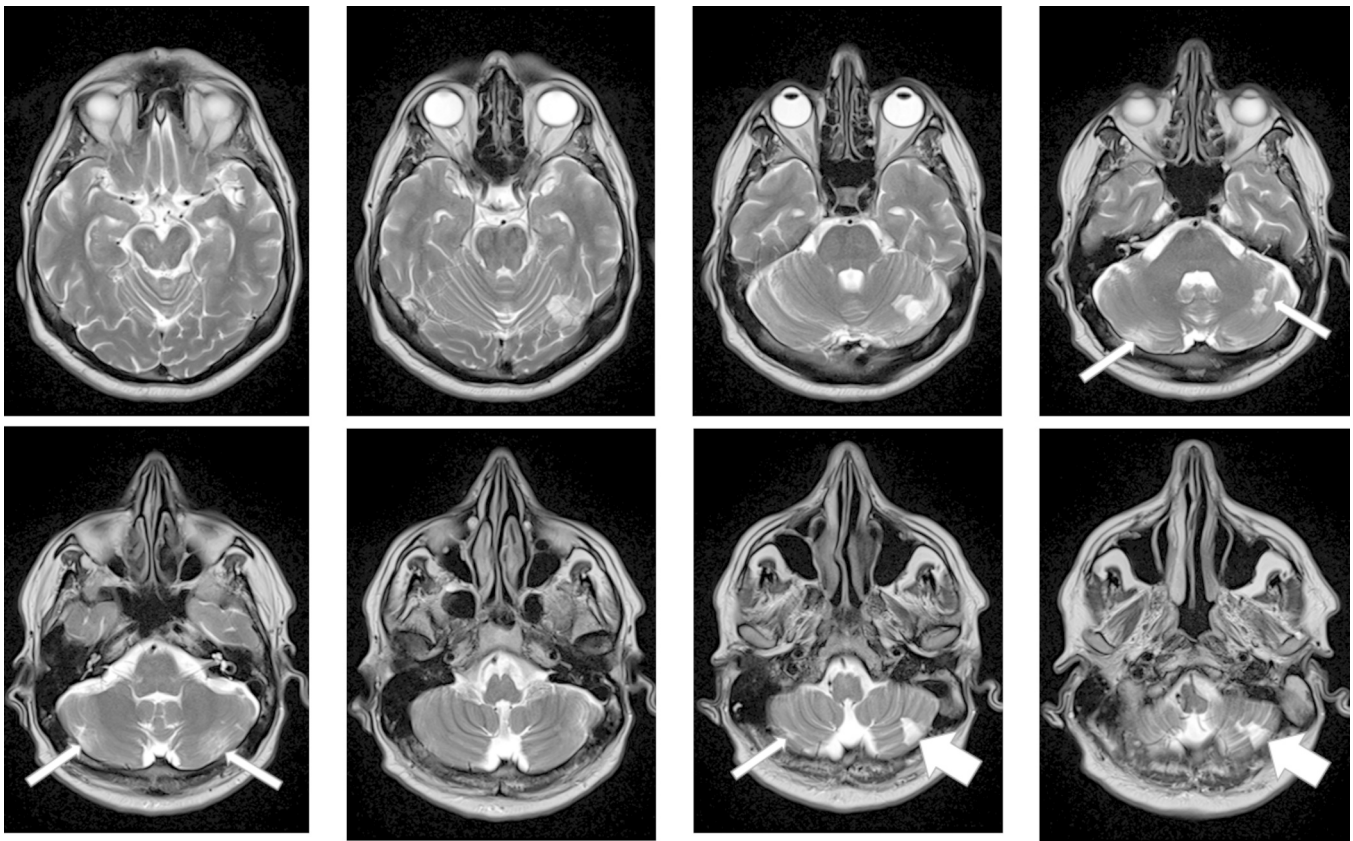


Fig. 1. Brain MRI images. Eight sequential axial T2-weighted images, from superior to inferior cerebellar slices (thickness 5 mm) demonstrating multiple chronic infarcts in the bilateral cerebellar hemispheres (thin arrows) and a predominant wedge shaped chronic infarct on the left cerebellar VII and VIII lobules (thick arrow).

autoimmune antibody panel and tumor markers were reported to be negative. On Brain MRI non-specific, white matter lesions in the cerebral hemisphere and bilateral subacute cerebellar infarcts were detected. Although the diagnosis of encephalitis was not confirmed, he was treated with intravenous methylprednisolone 1 g daily for 10 days accompanied by empirical monotherapy with intravenous ceftriaxone 2 g bid for 10 days. Two months after the acute onset of his symptoms, the patient was admitted to our university hospital. On neurologic examination, he had psychomotor retardation, but no signs of meningeal irritation, cranial nerve deficits, pyramidal/extrapyramidal signs or definite voluntary sensorimotor coordination deficit. The Mini-Mental State Examination (MMSE) score was 24 out of 30 (orientation: 10/10, registration: 3/3, attention and calculation: 1/5, recall: 1/3, language: 9/9). On standard neuropsychological assessment, mild impairment was reported in attention and executive functions. The Beck Depression Inventory revealed an intermediate degree of intensity of depression. The Brain MRI revealed multiple, non-specific, cerebral white matter hyperintensities and bilateral posterior cerebellar infarcts predominantly involving the left cerebellar lobules VII and VIII (Fig. 1). To confirm the diagnosis we performed CCAS/ Schmahmann Scale test [6]. On CCAS-Scale, among the 10 items; he passed in semantic fluency (18/26), phonemic fluency (10/19), category switching (10/15), digital span backward (4/6), cube draw (15/15), similarities (8/8) and go no-go (1/2) items. However he failed in digital span forward (5/8), verbal recall (7/15) and affect (3/6) items. His total raw score was 91/120. On CCAS scale, our patient failed in three items and the diagnosis of “definite CCAS” was made. The antidepressant treatment and secondary prevention of stroke was conducted for his long-term follow-up.

3. Discussion

Here we report an active male teacher with acute onset of affective disorder and mild cognitive impairment, initially misdiagnosed as depression and encephalitis, and received high dose intravenous steroids and antimicrobial drugs. The CCAS may be due to acquired or inherited conditions such as post-infectious cerebellitis, cerebellar infarction, trauma, toxic insults, neoplasia or cerebellar cortical atrophy [3]. In most cases with cerebellar infarcts, the main complaint of the patient may be a sudden onset of vertigo, ataxia, dysarthria, dizziness, nausea and vomiting [7,8]. However in CCAS the major symptom is impaired cognition and altered affective modulation [4].

The proposed mechanism of the CCAS relates to the disruption of the neural circuits that link prefrontal, posterior parietal, superior temporal and limbic cortices with the cerebellum [2]. Considering the clinical consequences of cerebellar topographic injury, the anterior lobe (lobules I-V) damage was reported to be characterized by motor syndromes, the posterior lobe (Lobules VI, VII and IX) with cognitive and affective syndrome, whereas the vermis and fastigial nuclei constitute the limbic cerebellum associated with pronounced affective presentations [4,9]. In a fMRI study, functional connections of the posterior cerebellum with the right frontal lobe, left hippocampus and right cingulate gyrus were found to be decreased in cases of cerebellar infarction with respect to healthy population [10]. The cognitive impairment occurs as a result of impaired corticocerebellar connections. Apart from cerebellar infarction; CCAS can be due to posterior fossa tumors [11], ataxia - telangiectasia (especially AT-3) [12], congenital cerebellar malformations [13], spinocerebellar ataxias [14], post-infectious cerebellitis [2,15] and paraneoplastic cerebellar degeneration [16]. Nevertheless, in these complex diseases, cognitive and psychiatric problems accompany motor symptoms and other neurological symptoms. The isolated and acute/subacute onset CCAS cases are frequently associated with cerebellar

infarcts. The strategic infarcts of the hippocampus, fronto-cingulate cortex, insular cortex, angular gyrus, thalamus, caudate nucleus, diffuse subcortical white matter lesions, cortical laminar necrosis and typically any disorder affecting the cholinergic pathways, the regions/networks essential for cognition, memory and behavior may be associated with vascular cognitive impairment and vascular dementia [17]. The brain MRI findings and acute onset of cognitive and affective symptoms in our patient were also consistent with CCAS. The diagnosis of CCAS relies on neuropsychological testing. The Mini-Mental State Examination (MMSE) test [18] or the Montreal Cognitive Assessment (MoCA) test [19], are reported to be insensitive to detect the CCAS patients [6]. Recently, the CCAS/Schmahmann scale has been developed, which can be applied at bedside and provides a detailed evaluation of executive, visual-spatial, linguistic regions and affect domains of the CCAS cases [6]. The CCAS-Scale is a 10-item scale with a sensitivity of 94% and a specificity of 78%. Based on pass/fail criteria it determines “possible CCAS” (one item failed), “probable CCAS” (two items failed) and “definite CCAS” (three or more items failed) [6]. The current status for CCAS scale usage is in an expedited manner. In Friedreich ataxia patients, significant positive correlation between severity of ataxia progression and cognitive deficits assessed by CCAS-Scale is reported [20]. In a cohort study of spinocerebellar ataxia type 3 (SCA3) patients, the CCAS-S is reported to differentiate the SCA3 patients from healthy controls, detect neuropsychological deficits early in the disease course, and correlate with ataxia severity measures [21].

To conclude, the awareness of the CCAS as a clinical entity is emerging. The role of posterior cerebellar and vermal pathologies should be considered in the differential diagnosis of patients with cognitive and affective disorders. The standard neuropsychological test are reported to be insensitive to detect the CCAS patients. The CCAS Scale is a good screening tool to determine patients accurately and provides a framework for the evidence-based treatment. We hope, this manuscript to foster and encourage communications between all related physicians and experts by adding to their knowledge and alerting them to this clinical entity which may affect their practice of medicine.

Funding

N/A.

Conflicts of interest

The authors declare no conflicts of interest.

References

- [1] F. Bodranghien, A. Bastian, C. Casali, M. Hallett, E.D. Louis, M. Manto, P. Marien, D.A. Nowak, J.D. Schmahmann, M. Serrao, K.M. Steiner, M. Strupp, C. Tilikete,

- D. Timmann, D.K. van, Consensus paper: revisiting the symptoms and signs of cerebellar syndrome, *Cerebellum* 15 (2016) 369–391.
- [2] J.D. Schmahmann, J.C. Sherman, The cerebellar cognitive affective syndrome, *Brain* 121 (Pt 4) (1998) 561–579.
- [3] G.P.D. Argyropoulos, D.K. van, M. Adamaszek, M. Leggio, M. Manto, M. Masciullo, M. Molinari, C.J. Stoodley, O.F. Van, R.B. Ivry, J.D. Schmahmann, The cerebellar cognitive affective/Schmahmann syndrome: a task force paper, *Cerebellum* 19 (2020) 102–125.
- [4] J.D. Schmahmann, J. MacMore, M. Vangel, Cerebellar stroke without motor deficit: clinical evidence for motor and non-motor domains within the human cerebellum, *Neuroscience* 162 (2009) 852–861.
- [5] N. Ahmadian, B.K. van, Z.M. van, P.A. Robe, The cerebellar cognitive affective syndrome—a meta-analysis, *Cerebellum* 18 (2019) 941–950.
- [6] F. Hoche, X. Guell, M.G. Vangel, J.C. Sherman, J.D. Schmahmann, The cerebellar cognitive affective/Schmahmann syndrome scale, *Brain* 141 (2018) 248–270.
- [7] L.R. Caplan, Cerebellar infarcts: key features, *Rev. Neurol. Dis.* 2 (2005) 51–60.
- [8] M. Venti, Cerebellar infarcts and hemorrhages, *Front. Neurol. Neurosci.* 30 (2012) 171–175.
- [9] C.J. Stoodley, J.P. MacMore, N. Makris, J.C. Sherman, J.D. Schmahmann, Location of lesion determines motor vs. cognitive consequences in patients with cerebellar stroke, *Neuroimage Clin.* 12 (2016) 765–775.
- [10] L. Fan, J. Hu, W. Ma, D. Wang, Q. Yao, J. Shi, Altered baseline activity and connectivity associated with cognitive impairment following acute cerebellar infarction: a resting-state fMRI study, *Neurosci. Lett.* 692 (2019) 199–203.
- [11] D. Omar, T. Ryan, A. Carson, T.H. Bak, L. Torrens, I. Whittle, Clinical and methodological confounders in assessing the cerebellar cognitive affective syndrome in adult patients with posterior fossa tumours, *Br. J. Neurosurg.* 28 (2014) 755–764.
- [12] F. Hoche, M.P. Daly, Y.K. Chutake, E. Valera, J.C. Sherman, J.D. Schmahmann, The cerebellar cognitive affective syndrome in Ataxia-Telangiectasia, *Cerebellum* 18 (2019) 225–244.
- [13] A. Tavano, R. Grasso, C. Gagliardi, F. Triulzi, N. Bresolin, F. Fabbro, R. Borgatti, Disorders of cognitive and affective development in cerebellar malformations, *Brain* 130 (2007) 2646–2660.
- [14] L. Orsi, F. D’Agata, P. Caroppo, A. Franco, M.M. Caglio, F. Avidano, C. Manzone, P. Mortara, Neuropsychological picture of 33 spinocerebellar ataxia cases, *J. Clin. Exp. Neuropsychol.* 33 (2011) 315–325.
- [15] A. Rosinski, M. Goldman, O. Cameron, A case of cerebellar psychopathology, *Psychosomatics* 51 (2010) 171–175.
- [16] M.M. Le, S. Dent, Anti-Yo antibody-mediated paraneoplastic cerebellar degeneration associated with cognitive affective syndrome in a patient with breast cancer: a case report and literature review, *Curr. Oncol.* 25 (2018) e585–e591.
- [17] M.B. Paradise, P.S. Sachdev, Vascular cognitive disorder, *Semin Neurol.* 39 (2019) 241–250.
- [18] M.F. Folstein, S.E. Folstein, P.R. McHugh, “Mini-mental state”. A practical method for grading the cognitive state of patients for the clinician, *J. Psychiatr. Res.* 12 (1975) 189–198.
- [19] Z.S. Nasreddine, N.A. Phillips, V. Bedirian, S. Charbonneau, V. Whitehead, I. Collin, J.L. Cummings, H. Chertkow, The montreal cognitive assessment, MoCA: a brief screening tool for mild cognitive impairment, *J. Am. Geriatr. Soc.* 53 (2005) 695–699.
- [20] G. Naeije, M. Rai, N. Allaerts, M. Sjogard, T. De, M. X, Pandolfo, Cerebellar cognitive disorder parallels cerebellar motor symptoms in Friedreich ataxia, *Ann. Clin. Transl. Neurol.* 7 (2020) 1050–1054.
- [21] R.P.P.W. Maas, S. Killaars, B.P.C. van de Warrenburg, D.J.L.G. Schutter, The cerebellar cognitive affective syndrome scale reveals early neuropsychological deficits in SCA3 patients, *J. Neurol.* (2021).