CLINICAL NOTE

CEREBELLAR COGNITIVE AFFECTIVE SYNDROME IMPROVEMENT WITH SELECTIVE INHIBITOR OF SEROTONIN RECAPTATION

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ABSTRACT

Cerebellar cognitive affective syndrome (CCAS) is characterized by alterations at the cognitive level (dysexecutive syndrome, visuospatial deficit, language ...), associated with affective / emotional changes. Its pathophysiology is not well known and there is currently no specific treatment. We describe a 64-year-old man with a rare condition of cognitive-behavioral disorder after an infarction in the left middle cerebral artery, dominated by executive dysfunctions, predominantly oral apraxia, interrupted divided attention, disturbed visuospatial organization and affective abnormalities with great apathy, and whose symptoms improved with a selective serotonin reuptake inhibitor (SSRI). In absence of cerebellar structural damage, a perfusion brain single photon emission computed tomography using 99mTc-hexamethyl-propylene-aminoxime (SPECT-HMPAO) showed left frontotemporal and parietoccipital hypoperfusion of known vascular etiology, and hypoperfusion in the right cerebellar hemisphere compatible with the phenomenon of crossed diaschisis. We hypothesize that cognitive and affective deficits are aggravated by the functional disruption of the reciprocal cerebellar interconnections with areas of cerebral association and paralimbic cortex, altering the contribution of the cerebellum to cognitive and affective processing and modulation. In the case described, both the clinical situation and the functional control images improved after treatment with SSRI, which increases the possibility that there is connectivity of some serotonergic transmission projections between cerebellum and contralateral association cortices, and that said connectivity dysfunctional is involved in the pathophysiology of CCAS.

Keywords. Cerebellar cognitive affective syndrome, stroke, SPECT, cross hemispheric diaschisis, selective serotonin reuptake inhibitor.

To the editor,

Cerebellar cognitive affective syndrome (CCAS) is defined as a set of cognitive alterations characterized by alterations in executive functions (planning, flexibility, abstract reasoning, verbal fluency, sometimes to the point of mutism, working memory and thinking and/or persevering action), in spatial cognition (difficulties in organization and visuospatial memory) and in language production (dysprosody, agrammatism, and mild anomie), along with personality changes (flattening of affect or bizarre or impulsive actions and inappropriate or disinhibited behavior, and obsessive-compulsive traits)[1,2,3]. The pathophysiology of CCAS is not well understood and there is currently no specific treatment. We describe a patient with CCAS whose cognitive-affective dysfunction improved by using a selective serotonin reuptake inhibitor (SSRI) and whose functional brain imaging showed improvement in the contralateral association area.

CASE REPORT

A 71-year-old male, with well-controlled hypertension treated with amlodipine 5 mg as the only reported medical history, was admitted to the neurology ward due to sudden loss of strength in the right lower limb and mixed aphasia. Acute ischemic lesions in the territory of the left middle cerebral artery are detected in cranial MRI, and after Doppler ultrasound, occlusion of the ipsilateral internal carotid artery is observed. Given clinical stability, the patient is discharged with mixed aphasia with no other focality.

He required readmission one month later due to clinical worsening, mixed aphasia persists, associated cognitive impairment, gait pattern impairment and oropharyngeal dysphagia predominantly to liquids. In addition, he presented significant emotional lability that made adherence to speech therapy treatment difficult.

A neurological examination is performed in which, from the beginning, significant emotional lability is appreciated. Mixed aphasia with motor predominance. Normal cranial nerves. Oral cavity sensitivity is preserved; no alterations in lingual motility are appreciated, preserved gag reflex. No motor deficit. Apraxic gait. Assessed by the Nutrition Unit, a volume-viscosity clinical examination method (MECV-V)[4,5]

was performed, showing oropharyngeal dysphagia to both solids and liquids due to the absence of signs of efficacy and safety.

A neuropsychological assessment is performed (Table 1), which indicates that the patient has moderate cognitive impairment (executive impairment, spatial cognition, language processing, and praxis disorder) with significant functional repercussions, accompanied by behavioral symptoms (moderate apathy, depression, and anxiety).

In the absence of exploratory findings that justify the oropharyngeal dysphagia detected in the MECV-V test, and after performing the described neuropsychological examination, orofacial apraxia is suspected. It was decided to start nutrition through a nasogastric tube and orofacial practices for working in the room were explained to the patient and family.

MRI of the skull showed residual areas after previously described vascular lesions, with cortical laminar necrosis, with no other findings. A perfusion brain single photon emission computed tomography with 99mTc-hexamethyl-propylene-aminoxime (SPECT-HMPAO) is requested, in which there is no uptake of the radiotracer at the left frontotemporal, parieto-occipital and subcortical levels, compatible with a

Table 1 Neuropsychological assessment

Cognitive test	Cognitive Domain	Total score
Cognitive Reserve Questionnaire	Education 1 point; Education of parents 0 points; Formation 0 points; Job occupation 1 point (construction professional); Musical training 0 points; Conversation 0 points (mother tongue only); Reading activity 0 points; Intellectual activity 0 points.	2 (cognitive reserve in very low range).
Montreal Cognitive Assessment	Visuospatial/executive: trace test 0/1, cube copy 0/1, clock 1/3; ID 1/3; Attention: number series 0/2, letter series 0/1, subtract 0/3; Language: repeat 0/2, fluency 0/1; Abstraction 0/2; Memory 1/5; Orientation 2/6.	5/30
(MoCA Screening)	Examination of sustained and alternating attention, visual tracking, and speed of information processing.	Part A, 75 seconds. Medium-low performance. Part B he is not capable and stops test. Poor performance.
Trail Making Test (TMT)	Examination of apraxias and visuospatial abilities, it allows evaluating aspects related to memory, executive functions, planning, comprehension, abstract thought, and attention.	He only makes a sphere (cart wheel). Positive test (total score less than 6, suggests cognitive impairment).
Clock-Drawing Test (CDT)	Examination of attention, concentration, fine coordination, visuospatial skills, non-verbal memory, strategic planning and organization.	Not capable, test stops after 3 minutes.
Rey–Osterrieth complex figure test (Copy)		He makes a symbolic gesture on command, imitates bilateral postures, correct in the use of non-face-to-face and real objects.
Manual Praxis	Blow 0; Tongue from right to left 2; Tongue up (rolled up) 1; Tongue between upper lip and teeth 2; Chew 1; Whistle 0; Engine sound 0; Sound of calling cat 1; Sound of disapproval 0; Tongue click 0.	7/20
Neuropsychological test Barcelona - Orophonatory praxis subtest	Evaluation of psychological and behavioral symptoms	Total frequency (6 points), total severity (4 points); The presence of moderate apathy, depression and anxiety is detected.
Neuropsychiatric Inventory (NPI)		Anxiety (4/9) and Depression (5/9)

known history of vascular lesions; there is also evidence of asymmetric hypo - uptake in the cerebellum at the expense of the right cerebellum, compatible with the clinical suspicion of a deafferentation phenomenon or diaschisis.

Given these neuropsychological and neuroimaging findings, a diagnosis of cerebellar cognitive affective syndrome secondary to crossed hemispheric-cerebellar diaschisis due to vascular injury was made.

Currently, the diagnosis of CCAS is based on detailed neuropsychological tests; Hoche et al. have recently validated a specific scale for CCAS that we have not used with our patient because it is not validated in Spanish6.

Treatment with a serotonin reuptake inhibitor (SSRI) is started; we chose citalopram due to its low risk of side effects and interactions with other drugs. It was administered in ascending dose, with an initial dose of 10 mg/day, and a progressive dose increase until reaching a maximum dose of 20 mg/day at four weeks, with a positive clinical evolution: emotional lability was decreased and we detected an improvement of oropharyngeal dysphagia, achieving the removal of the nasogastric tube and reintroduction of mashed diet and water with thickening nectar texture before hospital discharge.

A new assessment is performed on an outpatient basis one month after hospital discharge. Both he and his family report a subjective feeling of improvement. On examination: Euthymic. Mixed aphasia persists with slight improvement. Improvement in gait apraxia. The patient has been able to maintain oral nutrition (mashed diet and thickened liquids) without complications.

A new SPECT-HMPAO is performed, finding evidence of a decrease in hypo - uptake in cortical areas of frontal and parieto-temporal association, and in the cerebellum at the expense of the right hemisphere.

The MECV-V test was performed again, persisting oropharyngeal dysphagia to liquids (wet voice, slight oxygen desaturation), but not to solids, so it was decided to modify the diet from crushed to easy chewing.

Neuropsychological assessment was performed again with improvement in executive function, spatial cognition, language processing and praxis disorder, with functional and also behavioral improvement (apathy, depression and anxiety).

DISCUSSION

The cerebellum is organized into a primary sensorimotor region in the anterior lobe and adjacent part of lobe VI, and a secondary sensorimotor region in lobe VIII. Current evidence indicates that cognitive and limbic regions are located in the posterior lobe (lobe VI, lobe VIIA including Crus I and Crus II, and lobe VIIB); lobe IX may also be part of this network. Cognitively relevant areas are located more laterally in these lobes, while the limbic cerebellum is represented in the posterior vermis. The cerebellum presents rich bidirectional connections with cerebral cortical and subcortical areas, both with those responsible for motor functioning and with those responsible for processes related to cognition and emotion1. Through these connections, the cerebellum acts as a processing center that integrates information from the associative cortex, and in the same way that it regulates the rhythm, force, and precision of movements, it is also involved in the regulation of speed, consistency and adequacy of cognitive processes. The functional interruption of these pathways, either by the cerebellar lesion itself or by the deprivation of connections with the corresponding brain areas, reflects the interruption of reciprocal cerebellar interconnections with cerebral association areas and paralimbic cortices, altering the contribution of the cerebellum to processing, and cognitive and affective modulation. The constellation of deficits in CCAS suggests disruption of neural circuits linking the prefrontal, posterior parietal, superior temporal, and limbic cortices with the cognitive and limbic areas of the cerebellum[1,3].

In our patient, the areas where the SSRI restored focal cerebral blood flow were mainly the frontal and parieto-temporal association cortices. Although it is well known that there is a complex dysfunction of the serotonergic system in other types of cognitive pathologies such as Alzheimer's disease[7], the alteration of serotonergic function is not well known in CCAS. Our patient showed marked improvements in his symptoms clinical and radiological findings with the SSRI, suggesting that serotonergic function is dysregulated in CCAS.

Although the prevalence of CCAS is high, no effective treatment has yet been identified. In the case we described, some improvements have been detected during the neuropsychological tests after treatment with an SSRI (citalopram); in this case the changes observed in tests coincide with the cognitive-behavioral improvement reported by both the patient and the his family. In addition, SPECT-HMPAO showed that SSRIs successfully improved focal cerebral blood flow reduction, so it's possible that SSRIs could be an effective treatment for your higher brain dysfunction.

In conclusion, there may be some projections with serotonergic transmission between the cerebellum and the contralateral association cortices. Although more studies are required to confirm our findings, it seems that SSRIs are worth considering for the treatment of some patients with CCAS.

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None.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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