Pearls & Oy-sters: Cognitive and Affective Dysfunction Caused by a Small Cerebellar Hemangioblastoma

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Abstract

The primary function of the cerebellum is the coordination and regulation of movement; therefore, cerebellar tumors usually present with ataxia, dysarthria, and vertigo. Large tumors also cause elevated intracranial pressure that may lead to a disturbance of consciousness. Furthermore, it has become increasingly evident that the cerebellum plays a substantial role in cognitive and affective processing. A 44-year-old female patient presented with a 1-month history of depression and flat affect. She had no cerebellar symptoms including no coordination dysfunction or dysarthria. Cognitive function tests revealed impairments in attention, execution, and processing speed. Hamilton Depression Scale and Hospital Anxiety Depression Scale indicated moderate-to-severe depression. Magnetic resonance (MR) imaging revealed a 7-mm enhancing lesion in the culmen of the cerebellar vermis with surrounding edema. Technetium-99m ethyl cysteinate dimer single-photon emission tomography (SPECT) showed hypoperfusion in the left frontal lobe. Although she was initially treated with corticosteroids for presumed sero-negative autoimmune encephalitis, her symptoms persisted. She then underwent cerebellar lesion resection. The histologic diagnosis was hemangioblastoma. The patient’s symptoms dramatically improved within 1 week of resection, including improved batteries for cognitive function and depression. Complete regression of cerebellar edema and left frontal lobe hypoperfusion was observed on MR and SPECT images, respectively. This case reiterates the crucial influence of the cerebellum on cognitive and affective function. Moreover, cognitive dysfunction may be masked in cases with focal cerebellar symptoms or elevated intracranial pressure and, consequently, not adequately evaluated.

Pearls

• Research increasingly highlights a substantial role for the cerebellum in cognitive and affective processing.
• Cerebellar tumors can cause cerebellar cognitive affective syndrome (CCAS).

Oy-sters

• Cognitive affective dysfunction may be inconspicuous due to more prominent cerebellar symptoms or elevated intracranial pressure leading to inadequate evaluation.
• Patients with cerebellar tumors should be carefully screened for cognitive affective dysfunction as it can be reversed with appropriate treatment.
• Although diagnosing CCAS poses a clinical challenge, decreased cerebral blood flow may be of diagnostic value.

Case Report

A 44-year-old woman with no medical history was referred to our hospital for 1 month of depression with flat affect and concentration difficulties. On examination, she exhibited slow responses and flat facial expressions. Her cognitive function was impaired based on a Mini-Mental State Examination (MMSE) score of 23/30. Detailed cognitive function tests revealed...
impaired in attention, execution, and processing speeds. Her Hamilton Depression Scale (HAM-D) score was 14/63, indicating moderate depression. The Hospital Anxiety Depression Scale (HADS) score was 13 for anxiety and 16 for depression, consistent with moderate anxiety and severe depression. The patient had no motor paresis, coordination dysfunction, or dyasthria. On screening, her blood test results ruled out inflammatory diseases (white blood cell count: 6,600/μL [normal range, 3,500–8,600], C-reactive protein 0.02 mg/dL [0.00–0.14], erythrocyte sedimentation rate 3 mm/h [3–15]), hypothyroidism (free triiodothyronine 2.61 pg/mL [2.30–4.30], free thyroxine 1.23 ng/dL [1.00–1.80], thyroid stimulating hormone 1.15 μU/mL [0.50–5.00]), and metabolic diseases (vitamin B1 26 ng/mL [24–66], vitamin B12 283 pg/mL [233–914], and ammonia 33 μg/dL [12–66]). Magnetic resonance (MR) imaging showed a 7-mm nodular enhancing lesion in the culmen of the cerebellar vermis (lobule IV) with surrounding edema in the superior vermis (lobules III–V) (Figure 1, A and B). The CSF test revealed a slightly elevated protein level (56 mg/dL) and a positive oligoclonal band, with normal white blood cell count (1/μL) and glucose level (60 mg/dL). Autoantibodies observed in autoimmune encephalitis, such as anti-N-methyl-D-aspartate antibody or anti–voltage-gated potassium channel antibody, were all negative. The patient was treated with steroid pulse therapy (intravenous methylprednisolone 1 g/d for 5 days with an oral prednisone taper) for a tentative diagnosis of autoimmune encephalitis. She temporarily responded to treatment with improved executive function only, but the improvement subsided within 4 weeks after the steroid pulse therapy. Technetium-99m ethyl cysteinate dimer (Tc99m-ECD) SPECT showed decreased perfusion in the left frontal lobe (white circles). Given the left frontal lobe’s role in cognition and affect, a correlation between the left frontal lobe hypoperfusion and her symptoms was suspected. Given concern that this hypoperfusion could be caused by the small cerebellar lesion, the patient was referred to the neurosurgery department for cerebellar lesion resection.

The patient underwent craniotomy for tumor resection through neuronavigation. The resected tissue was pinkish, firm, and hemorrhagic with a relatively distinct margin. Postoperative MR images demonstrated gross total resection (Figure 2A). Histologic examination showed stromal cells with small nuclei and clear cytoplasm intervening with the vascular component (Figure 2B). Immunohistochemical analysis demonstrated positive inhibin alpha staining in the stromal cells (Figure 2C) and positive CD34 staining in the vascular endothelium (Figure 2D). These findings are consistent with those of hemangioblastomas (HBs). Her depression dramatically improved within 1 week of surgery, concomitant with regression of peritumoral edema seen on follow-up CT scans. Based on the histologic diagnosis, we conducted a systemic evaluation which revealed no lesions associated with von Hippel-Lindau disease. Postoperative HAM-D testing was normal with a score of 5/63. The HADS scores also improved to 7 and 6 for anxiety and depression, respectively. Her cognitive function also recovered to MMSE 30/30, but she still had mild impairments in executive function and processing speed at discharge. The patient demonstrated further recovery by the follow-up visit with complete return to normal activities of daily life. MR imaging conducted 4 months after surgery showed complete regression of perifocal edema (Figure 2E). ECD-SPECT was also repeated 4 months after surgery, which showed an improvement in CBF in the left frontal lobe (Figure 2F). Written agreement for publication was obtained from the patient.

**Discussion**

Historically, the primary function of the cerebellum was thought to be coordination and regulation of movement. It has recently become evident that the cerebellum also plays a substantial role in cognitive and affective processing. Schmahmann et al. evaluated 20 patients with cerebellar lesions using detailed neuropsychological assessment. Based on the analysis of patterns of behavioral abnormality, they termed these conditions as “cerebellar cognitive affective syndrome (CCAS)”.

This syndrome is characterized by the following 4 symptoms: (1) impairments of executive function, (2) visual-spatial disorganization, (3) personality changes, and (4) language production difficulties. Postoperative cerebellar mutism is another well-known form of cognitive dysfunction mostly

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**Figure 1** (A–C) Images at Initial Presentation

(A) T1-weighted axial MR brain with gadolinium contrast shows a nodular enhancing mass (arrow) in the culmen of cerebellar vermis. (B) MR fluid-attenuated inverted recovery images show perifocal edema. (C) Technetium-99m ethyl cysteinate dimer single-photon emission tomography shows decreased perfusion in the left frontal lobe (white circles).
seen after surgery for cerebellar tumors in the pediatric population.\textsuperscript{4} CCAS is currently recognized as a clinical entity that includes postoperative cerebellar mutism.\textsuperscript{5,6,8} The mechanism of CCAS is considered to be disruption of the cerebro-cerebellar circuit.\textsuperscript{1} Although postoperative cerebellar mutism is not rare—especially among pediatric patients—reports of cerebellar tumors associated with preoperative CCAS are extremely scarce. Our literature search identified only 2 reports of cerebellar tumors with possible CCAS: one was a large cystic HB\textsuperscript{9} and the other was a fourth ventricular ependymoma.\textsuperscript{10} The paucity of reports may be due to the masking of dysfunction in cases with focal cerebellar symptoms or elevated intracranial pressure and, therefore, inadequate evaluation. However, the present case indicates that pure cognitive affective dysfunction can be caused by an isolated cerebellar lesion. Importantly, as the condition may be reversible with treatment, patients with cerebellar lesions should be carefully screened for cognitive affective dysfunction.

It is difficult to suspect an association between a small cerebellar lesion and cognitive affective dysfunction and to determine the surgical indication for small cerebellar tumors with no typical cerebellar symptoms. Some previous studies have demonstrated that the disrupted circuit in CCAS may be radiologically detected as hypoperfusion in the contralateral cerebrum, referred to as crossed cerebellar diaschisis, on SPECT or PET.\textsuperscript{1,10,11} Previous reports also described left-sided cerebral hypoperfusion due to midline cerebellar lesions,\textsuperscript{1,11} which may indicate that the cerebro-cerebellar circuit is more frequently developed in the dominant hemisphere. Resolution of the left frontal lobe hypoperfusion after surgery in the present case supports the HB as the cause of hypoperfusion. Thus, assessment of CBF may be useful in the diagnosis of CCAS.

The diagnostic process in this case was complicated by abnormal findings suggesting active inflammation, such as a positive oligoclonal band and elevated CSF protein, as well as a temporary improvement after pulse steroids. However, given that the tight junctions of the blood-brain barrier are reportedly interrupted in hemangioblastoma,\textsuperscript{12} the positive oligoclonal band and the elevated CSF protein in this patient may have been caused by the disrupted blood-brain barrier of that lesion.\textsuperscript{13,14} Temporary responses to the pulse steroids may simply be explained by the improvement of peritumoral edema.

We reported a rare case of a small solitary hemangioblastoma that presented with CCAS. This case suggests that even cerebellar tumors too small to cause motor discoordination or mass effect can result in cognitive dysfunction and depression, which can be reversed with appropriate treatment.

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References

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