Rapid-Cycling Bipolar Disorder and Cerebellar Cognitive Affective Syndrome Associated With Cerebellum and Frontal Neurosurgical Lesions

Hugo Bottemanne, MD[a,b,c,*]; Julie Tang, MD[b]; and Anne Claret, MD[b]

Mood disorders are a major public health concern, associated with an increased human and financial cost.[1] Many studies have shown an association between cerebellar lesions and mood changes.[2,3] Paraneoplastic cerebellar degeneration or spinocerebellar ataxia may induce bipolar disorder. These mood disorders associated with neurologic lesions are often unresponsive to conventional thymoregulators.[4] Although their neurologic basis remains unexplained, the higher frequency of association between bipolar spectrum symptoms and cerebellar lesions may suggest a specific involvement of cortico-cerebellar circuits in controlling mood, cognition, and behavior.[3,5]

Case Report

We report the case of a 45-year-old patient diagnosed with an ultra–rapid-cycling bipolar disorder that appeared after cerebellum and frontal neurosurgical lesions. The patient was initially monitored during childhood for a vermian medulloblastoma with a neuroblastic differentiation. The tumor invaded the cerebellar tonsils medial part and extended into the lateral recess and upper triangle of the fourth ventricle. A neurosurgical exeresis and a right ventriculoperitoneal valve surgery were conducted, leading to a cerebellar atrophy. Subsequently, the care was completed with 2 chemotherapy sessions combining vincristine, procarbazine, and methotrexate and an external bypass in the right ventricular horn. Cerebellar cognitive affective syndrome began shortly after the intervention, initially characterized by an emotional lability, cognitive disabilities, and a static cerebellar syndrome.

The succession of depressive and hypomanic episodes in the following years led to the diagnosis of bipolar disorder at the age of 29 years old, and a bitherapy combining valpromide and lithium was introduced with a partial efficiency. At age 37 years, a radiation-induced right frontal convexity meningiomatosis associated with a perilesional edema was diagnosed. The surgical exeresis led to sequelae with a severe hypometabolism of the right frontal region objectified on 18F fluorodeoxyglucose positron emission tomography scan images. We noticed an acceleration of the bipolar cycles as the patient experienced 3 depressive and 2 hypomanic episodes in 2019, with short euthymic states of a few weeks only between 2 episodes (Table 1).

At age 44 years, the depressive episodes were aggravated by melancholic patterns. Thus, ketamine therapy was introduced, consisting of 6 sessions of 0.5 mg/kg with 48 hours between each session, combined with lamotrigine. One week after the final ketamine session, the patient switched to hypomanic symptoms and was stabilized with thymoregulatory therapy comprised of lamotrigine 150 mg/day and oxcarbazepine 300 mg/day. Finally, a left parietal meningioma was resected by γ knife neurosurgery, and the patient received reinforced neuropsychiatric monitoring and treatment with quetiapine 400 mg/day.

Discussion

Bipolar disorders have been associated with cerebellar lesions, dispelling the theory that the cerebellum is limited to controlling motor coordination and equilibrium.[6,7] In 1998, Schmahmann and Sherman[8] introduced the theory of cerebellar cognitive affective syndrome, a disorder characterized by the combination of emotion dysregulation, cognitive disturbance, and cerebellar syndrome and associated with bipolar disorder.[5] These secondary mood disorders should be suspected in patients with neurologic deficits, atypical neurologic history, early onset of disorder after surgery, or late onset of disorders after the age of 40 years old.[5]

Current studies tend to suggest that the anterior and posterior lobe of the cerebellum are involved in motor ability control and management of cognitive and affective functions, respectively.[7] Particular interest was also given to the cerebellar vermis, a region potentially involved in emotion-modulating processes through cerebellar-limbic connections.[9] Following the major role of emotional regulation in mood disorders,[10] the cerebellum could then

[a]Paris Brain Institute—Institut du Cerveau (ICM), INSERM, CNRS, Sorbonne University, Paris, France
[b]Department of Psychiatry, Pitié-Salpêtrière Hospital, DMU Neuroscience, Sorbonne University, AP-HP, Paris, France
[c]Department of Philosophy, Sorbonne University, SND Research Unit, Paris, France
*Corresponding author: Hugo Bottemanne, MD, Paris Brain Institute-Institut du Cerveau (ICM), UMR 7225/UMRS 1127, Sorbonne University/CNRS/INSERM, Paris, France (hugo.bottemanne@gmail.com).

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Table 1. Time Course of the Patient's Bipolar Episodes, Treatments, and Surgical Procedures

Age, y	Neuro-Oncology	Neurosurgical Procedure	Neuropsychiatric Symptomatology	Neuropsychiatric Treatment
14	Vermian medulloblastoma extending to vermis, lateral recess, and fourth ventricle	Tumor exeresis with cerebellar sequelae, right ventriculoperitoneal valve, and chemotherapy	Postsurgery cerebellar cognitive affective syndrome	None
19	Cerebellar sequelae	Follow-up	First MDD episode, followed by hypomanic episodes	Fluoxetine 20 mg/d, diagnostic wandering with treatment failures
29	Cerebellar sequelae	Follow-up	Hypomanic and depressive episodes leading to the diagnosis of bipolar disorder	Lithium 1,000 mg/d + valpromide 900 mg/d
37	Radiation-induced frontal meningiomatosis and perilesional edema	Exeresis and sequelae	Acceleration of bipolar cycles, mainly depressive episodes	Lithium 1,200 mg/d + valpromide 1,200 mg/d then divalproate 2,000 mg/d
44	Cerebellar and right frontal sequelae	Follow-up	Severe MDD with melancholic patterns and hypomania after ketamine infusions	Ketamine 0.5 mg/kg IV, lamotrigine 150 mg/d + oxcarbazepine 300 mg/d
45	Radiation-induced left parietal meningioma and perilesional edema	γ knife neurosurgery without clinical sequelae	Decreased intensity and frequency of mood fluctuation	Quetiapine 400 mg/d

Abbreviations: IV = intravenous, MDD = major depressive disorder.

constitute an emotional pacemaker for mood regulation.[6]

In our patient, the acceleration of bipolar cycles appeared after neurosurgical lesions of the right frontal region. Although the mechanism remains unknown, this case illustrates the potential implications of cerebellar-limbic and fronto-cortical regions in mood regulation. Nevertheless, these lesion-induced affective disorders remain a significant clinical challenge.

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