A 30-Year-Old Female with Moyamoya Disease and Associated Depression

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A 30-year-old white female was admitted voluntarily to our unit with symptoms of depression and had passive thoughts of suicide for the previous few months that progressively worsened in the week before her admission. She did not have previous suicidal attempts. The patient had a certificate from the university hospital psychiatric emergency department stating that she was referred by her therapist to the emergency department with complaints of depressed mood, hypersomnia, fatigue, feelings of worthlessness and indecisiveness, irritability, anxiousness, and suicidal thoughts accompanied with a plan. She also stated that suicidal thoughts had been present for the past 3 months and had markedly increased in the past week.

The patient had previously been diagnosed with Moyamoya disease (MMD) and a history of transient ischemic attacks. She also had a history of craniotomies (performed in 2002 and 2012). At times, she has had symptoms of tingling and weakness in her left upper body and the left side of face, as well as symptoms of aphasia. She has had multiple visits to the emergency department for her symptoms and she has also been followed by a neurosurgeon since age 12 years. The patient denies manic symptoms being present currently or in the past. She denies delusions, paranoid thoughts, or ritualistic behavior of any type. She also denies any history of seizures or problems with memory. She states no history of drug and alcohol abuse.

Unfortunately, this is not the first episode of depression from which the patient has suffered. The patient reports that her depression had an onset at age 12 years (about the same time she was diagnosed with MMD), and that she has had a chronic course with episodic variations since then. She has been treated with citalopram, escitalopram, buproprion, and venlafaxine in the past and reports no adverse side effects from them. Currently she is taking levetiracetam, aspirin, fluoxetine, and buspirone.

Her family history reveals an abusive/violent father as well as several paternal family members with psychiatric disorders. The patient also has two siblings, both of whom are on psychotropic medications for anxiety and depression. She currently is in a romantic relationship. She is employed as a manager in a research laboratory. She worries about losing her job in the near future because she is at the completion of her research project.
The patient also has MMD along with economic, educational, occupational, and other psychosocial and environmental problems. The patient was admitted to the inpatient unit and treatment options and medications were reviewed with her. Along with supportive therapy, the patient did well with introduction of sertraline, which was increased gradually to 100 mg/day. She was discharged home after 5 days, with a plan to be followed up at the outpatient clinic.

**DISCUSSION**

MMD is a rare cerebrovascular disease of unknown etiology. It is a progressive vascular disease that leads to stenosis of the main intracranial arteries.\(^1\) The disease was first described in 1957 as a “bilateral hypoplasia of the internal carotid arteries.”\(^2\) The incidence of disease is higher in Japanese and Asian Populations. The incidence of MMD is 0.35 to 0.94 per 100,000, and the prevalence is 3.2 to 10.5 cases per 100,000 of population.\(^3,5\) In a study published in 2005, hospital discharge data of 298 patients from 1987 to 1988 in the western United States with MMD was analyzed and the overall incidence was found to be 0.086 per 100,000 persons, lower than reported in Japan, but the rate among US Asians was similar. Among ethnic groups in California, MMD incidence rate for Asians was 0.28 per 100,000, similar to the incidence in Japan. The incidence rates were lower for blacks, whites, and Hispanics, and were 0.13, 0.06, and 0.03 per 100,000, respectively.\(^6\)

The etiology of MMD is poorly understood. The high incidence among Japanese and Asian populations and familial occurrence in approximately 10% to 15% of cases strongly suggest genetic etiology.\(^3,5\) A mode of autosomal inheritance with incomplete penetrance is the most probable explanation.\(^7\) Evidence suggests that RNF213 gene on chromosome 17q25.3 is an important predisposing factor for MMD in East Asian populations.\(^8,13\) The disease is most common in children and young adolescents, with two peaks of incidence: the first decade of life and the third decade of life.\(^14\) Women seem to be affected more frequently than men, with a ratio of 1.8:1.\(^3,5\) The most common clinical symptoms of the disease are sudden-onset hemiplegia, headaches, vertigo, seizures, and cognitive and neuropsychological dysfunction.

Depression is a mood disorder that can affect a person’s thoughts, behavior, feelings, and sense of life. When people are depressed they may feel sad, anxious, empty, worthless, helpless, guilty, or hurt. Loss of interest in activities that were once pleasurable may also occur, as well as disturbed eating habits and problems with memory and cognition. Depression can be a solo psychiatric disorder, it can be a symptom of some other medical or psychiatric condition, or it can be a normal reaction to certain life events.

There are indications for the presence of a relationship between occlusive diseases of the cerebral system, such as MMD, and neuropsychiatric disorders.\(^15\) One study conducted in Shanghai in 2013 involving 26 adult patients with hemorrhagic MMD concluded there is a strong connection between the disease and depression, as 19 of the 26 (73%) patients in the study developed depression.\(^16\)

A case report published in 2010 describing a 25-year-old female with a history of MMD and depressive disorder also supports a connection between the two diseases.\(^17\) In this report, magnetic resonance imaging revealed abnormal appearance in the anterior cerebral circulation with extensive periventricular collateral vessel involvement. Neuropsychological assessment of that patient revealed deficits in problem solving and inhibition, consistent with frontal lobe dysfunction.\(^17\) A similar presentation in our patient points out dysfunction in a similar area of the brain system.

An article published in 2012 also discusses cognitive impairment in patients with MMD.\(^18\) In that study of 30 patients with MMD, 11 patients (37%) presented with significant emotional distress (depression and/or anxiety) and seven patients (23%) presented with significant cognitive impairment (test scores more than one standard deviation below the normal mean). This study also concluded that cognitive impairment and emotional disorders exist in patients with MMD.

There is limited information on the associated cognitive and emotional sequelae of MMD, particularly those that present in a psychiatric setting. The syndrome usually manifests itself with motor or cognitive
abnormalities. Ischemia due to the progressive narrowing of the cerebral vessels leads to the development of abnormal collateral vessels that predispose these patients to develop hemorrhages. Our patient has had an unusual presentation of the disease. Her disorder manifested itself only as depression and some behavioral abnormalities. A previous case report stated that lesions to the basal ganglia can lead to a variety of cognitive and behavioral abnormalities. Apathy, disinhibition, and a major affective disturbance characterized the behavioral change in patients in prior studies. Abulia, memory dysfunction, and confusion are also very common in patients with ischemic strokes in the putamen or the globus pallidus area. In 1995, Milandre et al. reported another case report of a patient with MMD who exhibited athymhormic syndrome after sustaining ischemic lesions in the right globus pallidus and left lentiform nucleus with no involvement of the caudate. This syndrome consists of apathy, lack of drive and motivation, and total flatness of affect.

Five cortico-striato-thalamo-cortical circuits cross through the striatum. This is the reason why lesions in this area can present with widespread motor, cognitive, and emotional effects. Through these circuits, the striatum receives input from sensory, motor, and limbic regions of the cortex. Interruption in any of these pathways has been implicated in the production of psychiatric symptoms and behavioral disturbances.

CONCLUSION

In our patient, the abnormalities did not present acutely, but rather had been present chronically since age 12 years, which was also when she was first diagnosed with MMD. There is a high probability based on the history and the presentation of the patient that she possibly had developed a lesion in the area of the basal ganglia, leading to her chronic emotional and behavioral problems.

It is unclear whether MMD itself can actually be an underlying cause of depression, but in such patients an underlying subclinical ischemic disease of the basal ganglia should be considered, and brain imaging may be an appropriate next step in the course of management. Further research is needed to support the relationship of MMD and depression so we can develop protocols to manage these patients appropriately.

REFERENCES