Bilateral anterior capsulotomy and amygdalotomy for mental retardation with psychiatric symptoms and aggression

A case report

Shizhen Zhang, MD, Peizhi Zhou, MD, Shu Jiang, MD*, Peng Li, MD, Wei Wang, MD*

Abstract

Rationale: Mental retardation (MR) is a chronic condition that often has no readily identifiable cause or treatment. Aggression and psychiatric symptoms are prevalent in children with MR. Surgical treatment of aggression and psychiatric symptoms of MR is seldom investigated and studies are limited.

Patient concerns: We encountered a 19-year-old female who had MR with aggression and psychiatric symptoms.

Diagnoses: She was diagnosed with mild MR with aggressiveness and psychiatric symptoms.

Interventions: Because the patient was refractory to conservative treatment, bilateral anterior capsulotomy and amygdaloid neurosurgery were performed for her psychiatric symptoms and aggression. The benefits and side effects of the surgery were analyzed.

Outcomes: After surgery, the patient showed significant alleviation of her psychiatric symptoms and aggression with no observed side effects.

Lessons: Bilateral anterior capsulotomy in combination with amygdaloid neurosurgery may resolve both psychiatric and aggressive symptoms. Future investigations of control studies with large patient cohorts are needed.

Abbreviations: CSTC = cortico-striato-thalamo-cortical, DBS = deep brain stimulation, LM = logical memory, MR = mental retardation, MRI = magnetic resonance imaging, OAS = overt aggression scale, PFC = prefrontal cortex, VR = visual reproduction, WCST-S = Wisconsin card sorting test-simplified, YMRS = young manic rating scale.

Keywords: aggression, amygdalotomy, capsulotomy, mental disorder, mental retardation

1. Introduction

Mental retardation (MR) comprises a series of conditions with a common feature of an intellectual limitation that develops before the age of 18 years, which afflicts 2% to 3% of the global population.[1] MR is characterized by subaverage general intellectual functioning accompanied with significant limitations in adaptive functioning.[2] MR is a chronic condition that often has no readily identifiable cause or treatment. Coexisting symptoms may include aggressiveness, psychiatric symptoms, and self-harming behaviors.[1,2] Although desirable surgical outcome of patients with mental diseases or aggressiveness has been reported, surgical management of MR with aggressiveness and psychiatric symptoms is limited.[1–8]

2. Case report

The parents reported that the patient was dull and slow to respond at the age of 2 years, and began to talk and walk later than her peers. She significantly presented inattentiveness and learning difficulties in school. Moreover, she was often ridiculed by her classmates and finally dropped out of middle school. She scored 68 points on the Wechsler intelligence test for children, indicating a mild intelligence deficit. She was diagnosed with mild MR by a psychiatrist at the age of 13 years. Five years ago, she presented soliloquy, irritable, staying up, hallucinations, and aggressiveness. These symptoms included crying for no reason, shouting, throwing objects, delusion of persecution, self-biting, pulling her hair, slapping her face, and hitting her parents with aggression that mainly presented as self-harming behaviors. [1,2] Although desirable surgical outcome of patients with mental diseases or aggressiveness has been reported, surgical management of MR with aggressiveness and psychiatric symptoms is limited.[1–8]
aggressiveness and psychiatric symptoms at the age of 16 years. Based on our experience of surgery in patients with obsessive–compulsive disorder, depression, Tourette syndrome and other neuropsychiatric diseases,[9] we carefully specified her treatment options, which included further medical treatment, deep brain stimulation (DBS), or capsulotomy and amygdalotomy. Her parents opted for capsulotomy and amygdalotomy for financial reasons. The surgery was approved by the ethics committee of West China Hospital. Informed consent was acquired from her parents.

Preoperative magnetic resonance imaging (MRI) of the patient was normal. To assess the benefits of surgery and detect postoperative neurocognitive impairments, neuropsychological evaluations were conducted using the overt aggression scale (OAS),[10] the young manic rating scale (YMRS),[11] the logical memory (LM) and visual reproduction (VR) subtests of the Wechsler memory scale,[12] the similarities and block subtests of the Wechsler adult intelligence scale,[13] and the Wisconsin card sorting test-simplified (WCST-S).[14] Both the LM and VR were conducted immediately and after a 30-minute delay. Parts of neuropsychological evaluations were usually applied in the patients with mental disorders before surgery; we described carefully in our reported study.[9] Only parts of the preoperative neuropsychological evaluations were conducted before surgery because of her psychiatric symptoms and bursts of aggressiveness during the evaluation process. Neuropsychological assessments were completed before surgery and every year after surgery during a 3-year follow-up by the same psychiatrist, who knew the patient underwent surgery (Table 1).

Before the surgery, the patient had MRI without head frame. In addition, a repeat MRI was performed with head frame using the same parameters as those used in the first scan. We then used SurgiPlan workstation (Elekta Instrument AB, Stockholm, Sweden) and Leksell stereotactic operation system (Elekta Instruments AB) to calculate the targets (Fig. 1) and inserted the lesion electrodes into the targets. Next, multiple lesions were performed utilizing the Elekta neurostimulator at 75°C for 60 seconds each. The length of the lesions was 12 to 15 mm in the anterior limb of the internal capsule and 4 to 8 mm in the amygdala (Fig. 2). The above-mentioned surgical procedures were described carefully in our reported study.[9]

The patient’s aggression disappeared on postoperative day 2. Slow reaction, lack of concentration, mild somnolence, and indifferent were observed during hospitalization after surgery, but most of these symptoms disappeared within 2 weeks. As a 12-month follow-up, her parents reported that the patient’s hallucinations, delusion of persecution, and aggressiveness had disappeared. Furthermore, significant improvements in staying up, soliloquy, irritability, and loss of concentration were observed. The patient was gentler and could focus attention more easily. She developed a normal sleep time and pattern. In addition, she could handle activities of daily living and play with

| Table 1                      |
|------------------------------|
| Neuropsychological evaluations at 3-year follow-up. |
| Before the first surgery | 1 year after the first surgery | Before the second surgery | 1 year after the second surgery |
| OAS  | 9     | 0     | 4     | 0     |
| YMRS  | 43    | 14    | 23    | 13    |
| LM    | 5     | 16    | 14    | 15    |
| VR    | 3     | 8     | 6     | 8     |
| LMD   | Cannot perform | 9     | 9     | 8     |
| VRD   | Cannot perform | 5     | 6     | 6     |
| Similarities | 12 | 14 | 13 | 14 |
| Block | Cannot perform | 18   | 16   | 22    |
| WCST-S | Correct | Cannot perform | 26   | 24   | 29 |
|       | Error  | Cannot perform | 22   | 24   | 19 |
|       | PE     | Cannot perform | 21   | 22   | 15 |
|       | NPE    | Cannot perform | 1    | 2    | 4    |
|       | Categories | Cannot perform | 5    | 4    | 5    |

LMD = logical memory carried out after a 30-minute delay, LMI = logical memory of the Wechsler memory scale carried out immediately, NPE = nonperseverative errors, OAS = overt aggression scale, PE = perseverative errors, VRD = visual reproduction carried out after a 30-minute delay, VRI = visual reproduction of the Wechsler memory scale carried out immediately, WCST-S = Wisconsin card sorting test-simplified, YMRS = young manic rating scale.
neighboring children. Her parents reported that she was more tractable and could follow their instructions, which greatly improved their normal daily life and social activities. (See video after the first surgery, http://links.lww.com/MD/B496.) The OAS and YMRS showed significant decreases in both aggression and psychiatric symptoms. The neuropsychological evaluations were easier to carry out and the results were better than preoperatively. At 16 months after surgery, her parents reported mild and infrequent recurrence of aggression, which presented as self-biting and shouting for no reason. However, these symptoms were milder than before surgery. Further medical and behavioral treatments for 7 months were of little help. Finally, her parents decided on a second surgery. (See video before the second surgery, http://links.lww.com/MD/B497.) In order to prevent severe neurocognitive impairment, small and mild lesions were produced in the amygdala in the first surgery. We then considered another bilateral amygdalotomy to produce larger lesions in the amygdala than during the first surgery (Fig. 3). At a 15-month follow-up after the second surgery, her parents reported that antipsychotics were discontinued and there were no further episodes of aggression. The patient was as gentle and tractable as after the first surgery. (See video after the second surgery, http://links.lww.com/MD/B498.) After the second surgery, the daily life and social activities of all family members further improved. The results of the neuropsychological evaluations at 1 year after the second surgery showed further decreases in OAS and YMRS and no observed neurocognitive impairment.

3. Discussion

Current knowledge of the mechanisms underlying mental disorders and aggression remain incomplete. Dysfunction and disorder of the cortico-striato-thalamo-cortical (CSTC) pathways is a popular conception of mental diseases, which project from the frontal cortex toward corresponding targets and back to the original frontal territory where the loop started.[15] The prefrontal cortex (PFC) which projects through the internal capsule is relevant to mental disorders. [16] Thus, anterior capsulotomy may affect projections in the internal capsule of CSTC and projectional fibers from the PFC, which would result in significant improvement in psychiatric symptoms. [9] The amygdala is part of the limbic system and relevant to fear, anxiety, impulsivity and aggression. [13,17] Prefrontal cortex—amygdala circuits are responsible for several mental diseases, including aggression. [18] Therefore, amygdalotomy may alleviate aggression and psychiatric symptoms through projections and chemistry of the prefrontal cortex-amygdala circuits and amygdala.

Studies of surgical treatment for aggression are limited.[4–8] Jiménez et al.[5] reported that bilateral capsulotomy and cingulotomy may reduce aggressive behavior and improve clinical evaluations in the long term. Harat et al.[6] described the use of DBS of the nucleus accumbens for a patient with severe aggressiveness refractory to conservative treatment, which resulted in cessation of aggressive behavior and no side effects. Franzini et al.[7] reported a series of patients affected by MR with aggressiveness who consistently benefited from high-frequency
amygdalotomy, which produced sufficient alleviation of her aggressiveness. We consider that repeated amygdalotomy for the mild return of aggression, which further alleviated her aggressiveness, could achieve more satisfactory outcomes and fewer side effects, as compared to other encephalic regions.

The patient had both aggression and psychiatric symptoms while the Wechsler intelligence test indicated a mild intellectual deficit. Because conservative treatments had limited effects, we considered capsulotomy and amygdalotomy, which significantly alleviated her psychiatric symptoms and aggression with no observed side effects. The amygdala is part of the limbic system and relevant to emotion. Therefore, in order to prevent severe cognitive impairment and side effects, the lesions produced in the amygdala during the first surgery were small. A second surgery was performed for the mild return of aggression, which further alleviated her aggressiveness. We consider that repeated amygdalotomy for this patient would be safer and could avoid severe side effects and neurocognitive impairment, as compared to the initial amygdalotomy, which produced sufficient lesions. After the second surgery, the neuropsychological evaluations of the patient showed obvious improvements in psychiatric symptoms and aggression with no observed neurocognitive impairment. As confirmed by both surgeries, capsulotomy and amygdalotomy can alleviate aggression and psychiatric symptoms.

We performed surgery to correct psychiatric symptoms and aggression for a MR patient, which has been rarely reported in the literature. Future investigations of control studies with large patient cohorts are needed.

References

[1] Maris AF, Barbato IT, Trott A, et al. Familial mental retardation: a review and practical classification. Cien Saude Colet 2013;18:1717–29.
[2] Walker WO Jr, Johnson CP. Mental retardation: overview and diagnosis. Pediatr Rev 2006;27:204–12.
[3] Ruck C, Karlsson A, Steele JD, et al. Capsulotomy for obsessive-compulsive disorder: long-term follow-up of 25 patients. Arch Gen Psychiatry 2008;65:914–21.
[4] White R, Williams S. Amygdaloid neurosurgery for aggressive behaviour. Sydney, 1967–1977: societal, scientific, ethical and other factors. Australas Psychiatry 2009;17:410–6.
[5] Jiménez F, Soto JE, Velasco F, et al. Bilateral cingulotomy and anterior capsulotomy applied to patients with aggressiveness. Stereotact Funct Neurosurg 2012;90:151–60.
[6] Harat M, Rudas M, Zaelánski P, et al. Deep brain stimulation in pathological aggression. Stereotact Funct Neurosurg 2015;93:310–5.
[7] Franzini A, Broggi G, Cordella R, et al. Deep-brain stimulation for aggressive and disruptive behavior. World Neurosurg 2013;80:S29–e11–4.
[8] Torres CV, Sola RG, Pastor J, et al. Long-term results of posteromedial hypothalamic deep brain stimulation for patients with resistant aggressiveness: clinical article. J Neurosurg 2013;119:277–87.
[9] Zhang S, Li P, Zhang Z, et al. Anterior capsulotomy improves persistent developmental stuttering with a psychiatric disorder: a case report and literature review. Neuropsychiatr Dis Treat 2014;10:553–8.
[10] Yudofsky SC, Silver JM, Jackson W, et al. The Overt Aggression Scale for the objective rating of verbal and physical aggression. Am J Psychiatry 1986;143:35–9.
[11] Young RC, Biggs JT, Ziegler VE, et al. A rating scale for mania: reliability, validity and sensitivity. Br J Psychiatry 1978;133:429–35.
[12] Wechsler D. Wechsler Memory Scale. Psychological Corporation, New York, NY:1945.
[13] Wechsler D. Manual for the Wechsler Adult Intelligence Scale. Psychological Corporation, New York, NY:1955.
[14] Li B, Sun JH, Li T, et al. Neuropsychological study of patients with obsessive-compulsive disorder and their parents in China: searching for potential endophenotypes. Neurosci Bull 2012;28:475–82.
[15] Milad MR, Rauch SL. Obsessive-compulsive disorder: beyond segregat-ed cortico-striatal pathways. Trends Cogn Sci 2012;16:43–51.
[16] Lehman JF, Greenberg BD, McIntyre CC, et al. Rules ventral prefrontal cortical axons use to reach their targets: implications for diffusion tensor imaging tractography and deep brain stimulation for psychiatric illness. J Neurosci 2011;31:10392–402.
[17] Gopal A, Clark E, Allgair A, et al. Dorsal/ventral parcellation of the amygdala: relevance to impulsivity and aggression. Psychiatry Res 2013;211:24–30.
[18] Passamonti L, Crockett MJ, Apergis-Schoute AM, et al. Effects of acute tryptophan depletion on prefrontal-amygdala connectivity while viewing facial signals of aggression. Biol Psychiatry 2012;71:36–43.
[19] Lopes AC, de Mathis ME, Canetans MM, et al. Update on neurosurgical treatment for obsessive compulsive disorder. Rev Bras Psiquiatr 2004;26:62–6.