Case Report

Bilateral Stereotactic Anterior Cingulotomy is Effective in the Treatment of Drug-Resistant Psychosis and Impulse Control Disorders Caused by Traumatic Brain Injury: A Case Report

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Background: *Psychotic disorders due to traumatic brain injury (PDDTBI) represent severe form of neuropsychiatric problems that can occur after traumatic brain injury (TBI). Some patients develop treatment-refractory psychiatric symptoms. Psychosurgery is a viable option with good efficacy in such debilitating cases.*
Objective: *To report efficacy of anterior cingulotomy for suppressing intractable psychotic and impulsive symptoms caused by TBI.*
Case Report: *The authors report a case of 37-year-old male with a history of TBI which required craniectomy with hematoma evacuation and subsequent cranioplasty. He developed severe paranoid delusion with auditory hallucination, anxiety and impulsivity. The patient was admitted to the psychiatric hospital for recurrent, severe, treatment-refractory psychotic symptoms and impulsivity. Despite multiple drug regimens, his psychiatric symptoms did not improve. He underwent psychosurgery using bilateral anterior cingulotomy.*
Results: *His symptoms were significantly improved after the surgery. His delusion, hallucination and impulsivity disappeared and his mood became stable. He could resume daily activity. There was no recurrent symptom at 2 years postoperatively.*
Conclusion: *Anterior cingulotomy is an effective treatment option for refractory PDDTBI, especially if the psychotic manifestation coincides with affective symptoms.*

Keywords: *Psychotic disorder due to traumatic brain injury, Delusion, Impulse control disorder, Psychosurgery, Anterior cingulotomy*

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Road injuries are major health problem worldwide. The World Health Organization (WHO) estimates that road injuries are the first leading cause of global disability-adjusted life years (DALYs) loss in the population age 15 to 39 years[1]. Traumatic brain injury (TBI) is the leading cause of mortality from accidents and a large percentage of survivors develop TBI-related disability[2]. Neuropsychiatric problems are common among people living with chronic TBI-related disability, including cognitive impairments, disorders of mood and affect, posttraumatic stress disorder, behavioral disturbances, and in rare cases, psychotic disorders[3].

According to DSM-5 nomenclature, psychotic disorder caused by TBI is classified as PDDTBI (psychotic disorder due to traumatic brain injury). PDDTBI is a severe form of neuropsychiatric sequelae after TBI with significant morbidity. The diagnosis of PDDTBI is challenging due to delayed onset of psychotic symptoms after TBI and no distinctive features of PDDTBI from schizophrenia. However, there are some suggestive features of

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PDDTBI, such as temporal association between insults and onset of psychotic symptoms or atypical features[4,5].

Other neuropsychiatric disorders are more common after TBI and may coexist with PDDTBI[4,6]. Emotional dyscontrol (affective lability, irritability, agitation) and behavioral dyscontrol (disinhibition and aggression) mostly occur in early period after TBI and tend to improve with time. However, these problems may become chronic and debilitating in some patients[6].

Treatments of neuropsychiatric problems after TBI are mostly relied on their non-traumatic counterparts. Psychotherapy and pharmacologic treatments are major options with aiming for symptomatic control. Most of patients tend to improve with time[4-6]. Nonetheless, like in non-traumatic counterparts, some patients develop intractable symptoms and therefore other modalities of treatments may be needed, but the other alternatives are very limited nowadays[7,8].

With infamous history and once almost extinct, psychosurgery now becomes more important therapeutic role for treatment of psychiatric diseases. Improved neurosurgical techniques lead to significant reduction in morbidity and mortality. Better understanding of neuropathophysiology also leads to more precise target for therapy with hopefully more efficacy. The need for effective therapy in treatment-refractory psychiatric cases and advanced in knowledge in this field will lead to rapid expansion of indications for psychosurgery; however, most indications are still investigational[9-11].

The case presented in this study is an example of severe neuropsychiatric problems after TBI in the form of treatment-refractory psychotic disorder and behavioral dyscontrol. He had a good response to anterior cingulatomy.

Case Report

A 37-year-old Thai male had a history of traumatic brain injury owing to motor vehicle accident when he was 19-year-old in 1997. Computerized tomography (CT) scan of the brain revealed traumatic intracranial hematoma which required decompressive craniectomy and evacuation of the hematoma. He was admitted 45 days after the surgery. His neurological condition gradually improved. The patient could return to work, but had frequent memory deficits. Subsequent cranioplasty was performed in an appropriate time.

Four years later, in 2001, the patient developed severe anxiety and jumped from a building. He had fracture and dislocation of the right hip which required hip arthroplasty. In 2003, the patient had the onset of auditory hallucination, anxiety and paranoid delusion. He had an idea that other people would hurt and kill him (persecutory delusion). His father took him to treat these psychotic symptoms at a psychiatric hospital. The diagnosis of paranoid and impulse control disorders was given. His symptoms had not responded well to medical treatment. Electroconvulsive therapy (ECT) was contraindicated in this patient because of the artificial hip joint. Between 2003 and 2014, the patient was admitted to the psychiatric hospital several times due to paroxysmal aggravation of the psychosis.

In 2015, the patient was readmitted to the psychiatric hospital owing to severe paranoid psychosis. He had the same paranoid ideation, auditory hallucination, irritable mood, delusion of fear, agitation, impulsivity and driveling speech. These symptoms made him disabled and caused many impacts to the patient and his family. Multiple medical therapies could not relieve the psychotic symptoms, therefore treatment with psychosurgery was considered by the psychiatrist and neurosurgeons. Pre-operative head CT revealed evidences of brain injury and prior cranial operation (Fig. 1). After discussing operative risk and benefit of psychosurgery with the patient and his father, they gave informed consent for the procedure. The authors chose bilateral stereotactic anterior cingulotomy to treat intractable psychosis in this case.

The operation was conducted under general anesthesia. The Leksell stereotactic frame was applied, and then the anesthetized patient underwent navigation CT scan of the brain. The neurosurgeons used imaging data of the CT scan for planning of stereotactic ablation of the anterior cingulum by Brainlab Neuronavigation System. In sagittal view of neuroimaging, the target for anterior cingulotomy was localized at the bilateral anterior cingulated gyrus 20 to 25 mm posterior to the anterior border of the lateral ventricle, and 7 mm lateral to the midline in coronal brain imaging (Fig. 2). Lesioning with a temperature of 90°C for 90 seconds was performed using Radionic RF Lesion Generator System. Multiple consecutive lesions were made for creating a large lesion on each side of the brain. Three tracts of trajectory of ablation, including the anterior, middle and posterior tracts, were determined. The target was situated at the bottom of the middle tract (0 cm). After the target was ablated, tip of the radiofrequency (RF) probe was moved more superficially 3, 6 and 9 mm (-3, -6 and -9 mm). RF ablation was done in each site of the tip, respectively. After

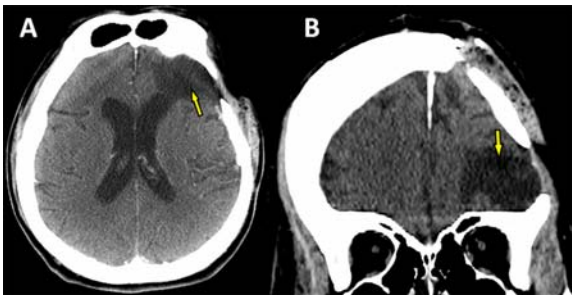

Fig. 1 Preoperative CT brain in axial (A) and coronal views (B) showing encephalomalacic changes caused by traumatic brain injury in the left frontal operculum and orbitofrontal region (arrow), as well as evidences of the left cranial surgery with cranioplasty.

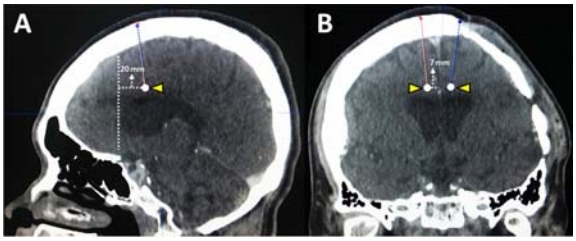

Fig. 2 Stereotactic planning of bilateral anterior cingulotomy (A) in sagittal neuroimaging, the target (arrowhead) located 20 mm posterior to the anterior border of the lateral ventricle (vertical dotted line); (B) in coronal neuroimaging, the target (arrowhead) located 7 mm lateral to the midline.

that, the probe was moved to the anterior and posterior tracts 5 mm paralleled to the first tract. In each tract, four lesions at the point of 0, -3, -6 and -9 mm were made, respectively. So that twelve small ablative lesions were generated at the unilateral anterior cingulate gyrus. The other 12 stereotactic lesions were engendered on the contralateral anterior cingulate gyrus with the same method.

Postoperatively, paranoid psychosis, unreasonable fear, persecutory delusion and auditory hallucination disappeared. Bilateral large stereotactic lesions were demonstrated on postoperative CT brain (Fig. 3). The patient had trivial adverse effects of the procedure, including drooling and urinary incontinence which resolved with time. His mood became stable; he had no driveling speech anymore and resumed doing daily activities. Several months after the cingulotomy, dosage of mood stabilizing agents could be diminished. At postoperative two years there was no recurrence of paranoia and impulsivity. The patient and his family

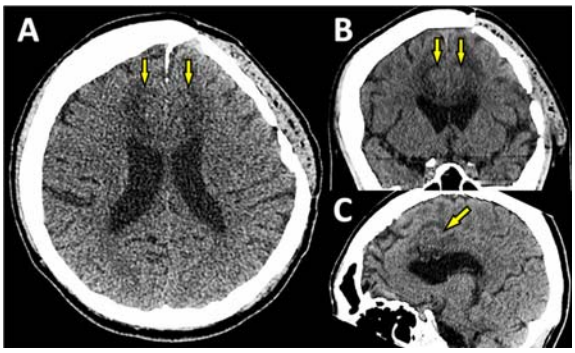

Fig. 3 Cranial CT scan after bilateral anterior cingulotomy showing large bilateral stereotactic lesions of the anterior cingulate gyrus (arrow) in axial (A), coronal (B) and sagittal views (C).

satisfied with outcome of the surgery.

Discussion

TBI is a common and important clinical problem worldwide, especially in developing countries. The patients who survive after TBI may have various health consequences, including neuropsychiatric problems. The neuropsychiatric disorders associated with TBI are in the forms of cognitive impairments, disorders of mood and affect, posttraumatic stress disorder, behavioral disturbances, sleep disorders, psychotic disorders, and many others.

PDDTBI is an uncommon but serious neuro-behavioral disorder. Incidence of PDDTBI in closed head injuries ranges from 0.9 to 8.5%[4]. The diagnosis of PDDTBI requires presence of hallucinations or delusions that are consequences of TBI, and no better explained by other mental disorders or delirium, and cause clinically significant functional impairment[12]. PDDTBI can be classified into 2 categories; delusional disorder (DD) and schizophrenia-like psychosis (SLP). In DD, patients have only delusions, whereas both hallucinations and delusions are found in SLP. The most common symptom of SLP is hallucination (97%) with 88% of patients presenting with auditory hallucination and others with visual hallucination. For delusions, persecutory delusion is the most common type (65%) followed by bizarre delusions. Unlike schizophrenia, negative symptoms are presented in about 40% of PDDTBI with blunt affect being the most common negative symptom[4,5].

PDDTBI is a diagnostic challenging condition due to lack of specific features. Potential characteristics helpful for discriminating between PDDTBI and primary psychotic disorders (mainly schizophrenia) include

absence of psychotic symptoms before the onset of TBI, abrupt onset of psychotic symptoms after TBI (within months), absence of family history of psychotic disorders, focal lesions located in the frontal or temporal region on brain imaging, positive findings in EEG studies (slowing and spike) and lack of negative symptoms[4,5]. Absence of psychotic symptoms before TBI combined with abrupt onset of symptoms after TBI is the strongest evidence to establish TBI as a cause of psychosis. However, there may be a delayed onset of psychosis after sustaining TBI with a mean latency between the injury and onset of psychotic symptoms up to 5 years (range 0 to 48 years)[4,5].

Relationship between severity of TBI and occurrence of psychosis is inconclusive[4,5]. PDDTBI can develop after mild TBI or moderate to severe injuries. Substance-induced psychotic disorders and psychosis caused by seizure disorders are also needed to be distinguished from PDDTBI. These two conditions can occur after TBI and require different treatments[5].

Principle of treatment for PDDTBI is identical to that for schizophrenia which pharmacotherapy being the mainstay of treatment. Most patients require monotherapy of antipsychotic drug. Also non-pharmacologic treatments, such as psychosocial treatments are essential component for psychotic patients[4,5].

Emotional and behavioral dyscontrol is a common consequence after TBI and often coexists with other post-traumatic neuropsychiatric disorders. These conditions are more common in moderate to severe TBI in which patients need hospitalization. Emotional dyscontrol comprises of several disorders which show rapidly and uncontrollable changes of emotion. These disorders include pathological laughing and crying, affective lability, and irritability. Behavioral dyscontrol indicates tendency to act impulsively to internal or external stimuli and includes disinhibition (if the predominant feature is poor impulse control) and aggression (if the predominant feature is aggressive behavior). Treatments of emotional and behavioral dyscontrols rely on a combination of pharmacologic and non-pharmacologic modalities which aim to reduce frequency and severity of the dyscontrol symptoms[6].

In PDDTBI, prognosis is generally good. Most symptoms are controllable with pharmacotherapy combined with non-pharmacologic methods. In some patients who do not respond to treatment, their disorders will become chronic and debilitating. Data from its functional counterpart, schizophrenia, show that approximately 10 to 20% of patients will develop the disease refractory to all modalities of treatments, including ECT[7,8]. For these patients, psychosurgery may be a viable option for treatment of their debilitating disease.

Psychosurgery has a long and interesting history. Gottlieb Burckhardt was the first one who performed psychosurgery in 1888. It was then popularized by Egas Moniz in 1930s after he developed frontal lobe disconnection techniques. In 1930 to 1950s, psychosurgery gained bad reputations because the surgery was overused in an indiscriminate way by a crude technique: transorbital lobotomy developed by Walter Freeman, which led to significant morbidities and mortalities. After introduction of the first antipsychotic drug, chlorpromazine, in 1954, psychosurgery was abandoned[7-10].

The resurgence of psychosurgery emerges from better understanding of pathophysiology of psychiatric diseases, improvement of brain imaging studies and development of stereotactic surgical techniques make psychosurgery being a minimally invasive surgical method with a very low morbidity and almost no mortality. Nowadays, the accepted indications for psychosurgery include treatment-refractory obsessive-compulsive disorder (OCD) and major depressive disorder (MDD). Other indications are Tourette syndrome, drug addiction, severe aggression and self-mutilation disorder. The worldwide accepted psychosurgical procedures are anterior cingulotomy, subcaudate tractotomy, limbic leucotomy, anterior capsulotomy, amygdalotomy, vagus nerve stimulation and deep brain stimulation (DBS). DBS is getting more and more interest due to its reversible and non-destructive nature. However, it is more expensive, needs more maintenance and is more complicated than standard ablative procedures[7-11]. These procedures aim to restore function of brain circuits by manipulating "node" or "pathway" within the circuits, particularly in the limbic system, which are found to be dysfunctioned in psychiatric disorders.

Generally, outcomes of psychosurgery for treatment of psychotic disorders, mainly schizophrenia, are not as good as other mental diseases, such as OCD or MDD. An extensive review by Leiphart found that anterior cingulotomy might be the most effective ablative procedure for treatment of schizophrenia[10], especially affective component of the disease, such as aggression which was found to be obviously improved[8,10,13]. Jimenez et al reported a couple of patients with schizophrenia and aggressiveness treated by a combination of bilateral cingulotomy and

anterior capsulotomy. They showed good outcome regarding aggressiveness and also psychotic components[13]. Ballantine et al reported a large series of anterior cingulotomy in 198 patients which included 11 schizophrenic patients. Four patients showed considerable improvement and 4 had partial improvement. The complication rate of anterior cingulotomy was very low with no mortality[14]. Recently, a large case series from China by Liu et al reported impressive effectiveness of bilateral anterior capsulotomy for treatment of schizophrenia. Improvement rate was 74%, the most improved symptom was aggression which was found in the majority of patients (94%), followed by delusion[15]. Nevertheless, this report was contradictory to previous report by Talairach, the pioneer of anterior capsulotomy, showing that the outcomes of anterior capsulotomy in psychotic patients were disappointing[7,8,10].

In the present study, our case had a delayed onset of delusion (paranoid and persecutory) and auditory hallucination following severe TBI. He had no psychiatric symptom before the injury, no family member with psychosis and lacked negative symptoms. His CT brain revealed the evidences of focal brain injury (encephalomalacia) at the left frontal operculum and orbitofrontal region. These clinical findings suggested the diagnosis of PDDTBI. Also, he had concurrent affective components as emotional and behavioral dyscontrols (anxiety and poor impulse control). His psychiatric symptoms did not respond to multiple medical therapies and made him disabled with significant impacts to the patient and his family. Because ECT was not proper therapeutic option in this patient due to the implanted prostheses (cranioplasty and arthroplasty), treatment of the intractable symptoms with psychosurgery was considered by the attending psychiatrist and neurosurgeons. After discussing surgical risk and benefit of the surgery with the patient and his family, we chose one of the most effective and safest operations, bilateral stereotactic anterior cingulotomy, for this patient.

After the operation, his symptoms were dramatically improved in both psychotic and affective components. His functional status was also improved after the surgery. The benefit of anterior cingulotomy was still stable at 2 year postoperatively without recurrent symptoms. This report demonstrates benefit and essence of psychosurgery in the treatment of refractory mental illnesses, and shows that anterior cingulotomy is an effective option for drug-resistant neuropsychiatric disorders caused by TBI. With advancement in basic neurosciences, understanding of neuropathophysiology of mental disorders and neurosurgical techniques, psychosurgery is most likely to expand its utilization and indications in the near future.

Conclusion

Neuropsychiatric problems are common after TBI. Psychotic disorders caused by TBI represent severe form and frequently occurs with other psychiatric troubles, such as emotional or behavioral dyscontrol. Despite good prognosis in general, some patients still develop chronic and treatment-resistant psychotic symptoms. Psychosurgery is a viable option which can render favorable outcome in refractory cases. Anterior cingulotomy can effectively eliminate intractable psychotic and affective symptoms following TBI.

What is already known on this topic?

PDDTBI is a severe form of neuropsychiatric disorders found after TBI and may coincide with other psychiatric symptoms. Antipsychotic medications effectively control the psychotic features and usually render favorable results; however, refractory cases can be encountered in clinical practice.

What this study adds?

Psychosurgery still has a role in the treatment of refractory psychiatric disorders, including PDDTBI. Bilateral stereotactic anterior cingulotomy is a relatively safe neurosurgical procedure, which can effectively treat both psychotic features and affective symptoms caused by TBI.

Potential conflicts of interest

None.

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การผ่าตัดเพื่อทำให้เกิดรอยโรคในสมองบริเวณ cingulate gyrus ส่วนหน้ามีประสิทธิภาพในการรักษาอาการโรคจิตและกลุ่มโรคขาดความยับยั้งชั่งใจที่มีสาเหตุจากการบาดเจ็บของสมองซึ่งดื้อต่อยา: รายงานผู้ป่วย 1 ราย

โชติวัฒน์ ตันศิริสิทธิกุล, บรรพต สิทธินามสุวรรณ, อำไพชนิษฐ สมานวงศ์ไทย, ศรุตพันธุ์ จักรพันธุ์ ณ อยุธยา, ศรัณย์ นันทอารี

ภูมิหลัง: โรคจิตที่มีสาเหตุจากการบาดเจ็บของสมองเป็นรูปแบบความผิดปกติทางจิตประสาทที่รุนแรง ซึ่งสามารถเกิดภายหลังการบาดเจ็บของสมอง ผู้ป่วยบางรายมีอาการทางจิตเวชที่รุนแรงและไม่ตอบสนองต่อการรักษา การผ่าตัดรักษาโรคจิตเวชเป็นทางเลือกหนึ่งซึ่งมีประสิทธิภาพในการรักษาผู้ป่วยกลุ่มนี้

วัตถุประสงค์: เพื่อรายงานประสิทธิภาพของการผ่าตัดเพื่อทำให้เกิดรอยโรคในสมองบริเวณ cingulate gyrus ส่วนหน้าในการรักษาอาการโรคจิตและอาการขาดความยับยั้งชั่งใจที่มีสาเหตุจากการบาดเจ็บของสมองซึ่งดื้อต่อยา

วัสดุและวิธีการ: ผู้นิพนธ์ได้รายงานผู้ป่วย 1 ราย เป็นชายอายุ 39 ปี ซึ่งเคยมีประวัติการบาดเจ็บของสมอง ซึ่งได้รับการผ่าตัดนำเลือดคั่งในสมองออกและได้รับการผ่าตัดใส่กระโหลกเทียมในเวลาต่อมา หลังจากการบาดเจ็บของสมองผู้ป่วยเริ่มมีอาการทางจิตคือมีอาการหวาดระแวงร่วมกับได้ยินเสียงแว่วมีอาการกังวล และขาดความยับยั้งชั่งใจ ผู้ป่วยต้องเข้ารับการรักษาในโรงพยาบาลจิตเวชหลายครั้งด้วยอาการโรคจิตและอาการขาดความยับยั้งชั่งใจซึ่งดื้อต่อยาและกลับเป็นซ้ำ อาการทางจิตเวชของผู้ป่วยไม่ตอบสนองต่อการรักษาแม้ว่าจะได้รับยาหลายชนิด ผู้ป่วยได้รับการผ่าตัดรักษาโรคจิตเวชโดยการผ่าตัดเพื่อทำให้เกิดรอยโรคในสมองบริเวณ cingulate gyrus ส่วนหน้า

ผลการศึกษา: หลังผ่าตัดอาการของผู้ป่วยดีขึ้นอย่างมาก อาการหลงผิด อาการได้ยินเสียงแว่วและอาการขาดความยับยั้งชั่งใจหายไป อารมณ์ของผู้ป่วยคงที่ขึ้น ผู้ป่วยสามารถกลับไปทำกิจวัตรประจำวันได้ ไม่มีอาการกลับเป็นซ้ำที่ระยะเวลา 2 ปีหลังผ่าตัด

สรุป: การผ่าตัดเพื่อทำให้เกิดรอยโรคในสมองบริเวณ cingulate gyrus ส่วนหน้ามีประสิทธิภาพในการรักษาอาการโรคจิตที่มีสาเหตุจากการบาดเจ็บของสมองซึ่งดื้อต่อยาโดยเฉพาะถ้าอาการโรคจิตพบร่วมกับความผิดปกติทางอารมณ์