Case Report

Case Series: The Paradox of Epilepsy Surgery and Psychiatric Disorder

Charcrin Nabangchang MD*, Piradee Sanguankiat MD* ,
Kamornwan Katanyuwong MD**, Siraruj Sakoolnamarka MD***

** Division of Neurology, Department of Pediatrics, Phramongkutklao College of Medicine, Bangkok, Thailand*
*** Division of Neurology, Department of Pediatrics, ChiangMai University Hospital, Chiang Mai, Thailand*
**** Division of Neurosurgery, Department of Surgery, Phramongkutklao College of Medicine, Bangkok, Thailand*

De novo psychiatric disorder following epilepsy surgery is an infrequent but very interesting phenomenon. The authors described 4 distinct cases with medically intractable epilepsy who had epilepsy surgery and developed postsurgical psychiatric disorder. The onset of psychiatric disorder was during dramatic improvement of their epilepsy after surgery. There was no history of psychiatric disorder in their familial members or in the patients prior to the surgery. Since three patients also had mental retardation, presurgical cognitive impairment may be one of the risk factors for developing postsurgical psychiatric disorder. Potential mechanisms include volume reduction of gray matter in frontal, temporal and parietal cortexes secondary to epilepsy surgery as well as forced normalization. Several other mechanisms may also play important role for this phenomenon and further studies will be required which may reveal the connection between these two aspects.

Keywords: *Epilepsy surgery, Temporal lobectomy, Psychiatric disorder*

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Epilepsy surgery becomes a standard treatment for patients with medically intractable epilepsy. It has been increasingly recognized that psychiatric disorders may complicate the postsurgical outcome. Postictal psychosis is the most common form of the epilepsy-related psychosis. The episodes usually follow an increase in seizure frequency or intensity. Epilepsy-related psychiatric disorder following epilepsy surgery is infrequent but potentially serious complication after operation. The onset of psychiatric symptoms is typically in the first year following the surgery. It was previously reported to be commonly seen following right temporal lobectomies[1]. There is no clear relationship between postsurgical seizure frequency and psychiatric symptoms.

The identification of risk factors for the development of postoperative psychiatric disorder has potential benefit as it would aid the early identification of those at high risk for developing the disorder after the surgery.

The authors reported four distinct cases who developed psychiatric symptoms after epilepsy surgery and described the relationship between site of surgery, postsurgical seizure outcome, psychiatric symptoms and possible risk factors.

Correspondence to:
Nabangchang C, Division of Neurology, Department of Pediatrics, Phramongkutklao College of Medicine, Bangkok 10400, Thailand.
Phone: 0-2354-7600 ext. 94163
E-mail: c_nabangchang@yahoo.com

Case Report

Patient A

A 16-year-old female with medically intractable temporal lobe epilepsy presented with psychosis after right temporal lobectomy. The onset of her psychosis began during the tapering off period of carbamazepine as she had been seizure-free for 1 year after the surgery.

History of seizures

Seizure onset was at the age of 3 years. They were characterized by behavioral arrest followed by automatism of both hands and non-versive head turning toward the right side. Electroencephalogram revealed frequent epileptiform abnormalities over the right temporal region. Video-EEG monitoring demonstrated ictal onset exclusively arising from the right temporal area. Mild right hippocampal atrophy without definite signal change was observed on brain MRI.

Perioperative course

Presurgical neuropsychiatric assessment revealed that she had moderate mental retardation without previous psychiatric symptoms. Right temporal lobectomy was performed. Histopathological examination revealed neuronal loss in the hippocampus without definite hippocampal sclerosis. The peri-operative course was uneventful. At the time of surgery, antiepileptic drugs regimen included valproic acid (1,000 mg/day), carbamazepine (300 mg/day) and topiramate (200 mg/day).

Postoperative course

The onset of her de novo psychosis began during the tapering off period of carbamazepine as she had been seizure-free for 1 year after the surgery. Her psychosis was characterized by outburst behavior, aggression, visual/auditory hallucination and delusion. She was subsequently admitted to Phramongkutklao Hospital for several weeks. Serial Electroencephalogram revealed neither epileptiform abnormalities nor subclinical seizures. There was no intercurrent illness and optimal investigations did not reveal any explainable causes of her psychosis. After a few months, her psychosis had gradually but significantly improved with antipsychotic drugs.

Patient B

A 19-year-old male with mental retardation had left frontal corticectomy plus corpus callosotomy for medically intractable epilepsy. The onset of frank psychosis began 6 months after the surgery despite worthwhile improvement of epilepsy.

History of seizures

Seizure onset was at the age of 18 years. They consisted of several tonic seizures per day. Electro-encephalogram revealed generalized spike-waves with intermixed paroxysmal fast activities. Cortical dysplasia along left frontoparietal and left parasagittal areas was found on brain MRI.

Perioperative course

Presurgical neuropsychiatric assessment revealed that he had moderate mental retardation with no psychiatric symptoms prior to surgery. Left frontal corticectomy plus corpus callosotomy was performed after invasive intracranial monitoring with functional mapping. Histopathological examination revealed neuronal heterotopia. No intraoperative or immediate postoperative complications were noted. At the time of surgery, antiepileptic drugs included levetiracetam (3,500 mg/day) and topiramate (450 mg/day).

Postoperative course

Six months after the surgery; he developed aggression, behavioral change and insomnia despite worthwhile improvement of epilepsy (Engel's category IIA). Optimal investigations did not reveal any explainable causes. His symptoms had gradually improved over the course of several weeks after administration of antipsychotic drugs.

Patient C

A 15-year-old female with mild mental retardation had left parieto-occipital corticectomy for intractable epilepsy. Her psychiatric manifestations had progressed over one year period, during which the patient was seizure-free after epilepsy surgery.

History of seizures

Seizure onset was at the age of 4 years. They consisted of tonic limbs stiffening with eyes rolling upward several times per day. Electroencephalogram revealed frequent epileptiform abnormalities over the left cerebral hemisphere. Cortical dysplasia over the left parieto-occipital area and right hippocampal sclerosis were found on MRI.

Perioperative course

Presurgical neuropsychiatric assessment revealed that she had mild mental retardation with no psychiatric symptoms prior to surgery. Left parieto-occipital corticectomy was performed under two stages operation with invasive intracranial monitoring and functional mapping. Histopathological examination revealed neuronal heterotopia. No intraoperative or immediate postoperative complications were noted. At the time of surgery, antiepileptic drugs included phenytoin (200 mg/day), clonazepam 4 mg/day and valproic acid (1,000 mg/day).

Postoperative course

Over the course of one year after surgery, she had been academically unsuccessful and had become severely depressed with behavioral change and poor appetite despite being seizure-free (Engel's category IA). She was hospitalized and was diagnosed to have major depression with psychosis. She made a slow recovery over several months from combined treatment with sertraline hydrochloride 50 mg/day, risperidol 2 mg/day and the same regimen of anticonvulsant.

Table 1. Comparative features of patients

Patient	A	B	C	D
Sex	female	male	female	male
Family history of psychiatric disorders	No	No	No	No
Age of epilepsy onset (year)	3	18	4	4
EEG: epileptiform abnormalities	unilateral	bilateral	unilateral	unilateral
Mental retardation	Yes	Yes	Yes	No
Age at operation	15	19	14	17
Site of operation	Rt. temporal	Lt.Frontal	Lt.Parieto-occipital	Rt. Frontal
Timing of postoperative psychosis after surgery (month)	12	6	12	5
Neuropathologic findings	Neuronal loss in hippocampus	Neuronal heterotopia	Neuronal heterotopia	Reactive gliosis
Engel's category	IA	IIA	IA	IA

Patient D

A 17-year-old male had right parietal corticectomy for medically intractable epilepsy. The onset of frank psychosis was at 5 months post-operatively despite complete seizure control.

History of seizures

Seizure onset was at the age of 4 years. They were characterized by unresponsiveness followed by automatism of both hands. Electroencephalogram revealed epileptiform abnormalities over the right fronto-parieto-temporal areas. Tumor mass at the right parietal lobe was observed on neuroimaging. Tumor removal was performed and histopathology revealed pilocytic astrocytoma. Follow-up brain MRI after the operation revealed no residual tumor. Over the next four years, there had been no seizure and the child was free of anticonvulsants. Cluster of complex partial seizures began four years after the initial surgery and was medically intractable, when he was referred for epilepsy surgery at Phramongkutklao Hospital.

Perioperative course

During presurgical neuropsychiatric assessment, he had normal cognition with no psychiatric symptoms. Right parietal corticectomy was performed after invasive intracranial monitoring with functional mapping. Histopathological examination revealed reactive gliosis. Immediate postoperative complication with right epidural and subdural hematoma were noted and surgery for clot removal was performed. At the time of surgery, antiepileptic drugs included topiramate (400 mg/day) and phenytoin (300 mg/day).

Postoperative course

Five months after surgery, he became depressed and had auditory hallucination despite the fact that he became seizure-free. Electroencephalogram revealed neither epileptiform abnormalities nor subclinical seizures. His depression had improved significantly over the next few weeks on Quetiaprine, Clonazepam and Haldol,

Discussion

To our knowledge, de novo psychiatric disorder following epilepsy surgery is infrequent. The onset of psychiatric symptoms is frequently reported in the first year following the operation[1]. Similarly, the onset of psychiatric symptoms in the presented series ranged from 5 months to one year following the surgery (Table 1). In addition, all of the patients had dramatic improvement of postoperative seizure control (Engel's category IA-IIA) when their psychiatric symptoms emerged. However, most of the presented patients had extratemporal resection, in contrast to patients in most of the literature with temporal lobe resection[2] as all the presented patients were in the adolescent age group with a higher incidence of extratemporal epilepsy.

Previous studies postulated possible risk factors such as the laterality of surgery, of which right sided temporal resection is associated with higher incidence of new-onset psychosis than the left[3,4], which is similar to one of our cases with right sided temporal resection. The second risk factor is

preoperative bilateral electroencephalogram (EEG) abnormalities[3,5]. In this series the authors found only one case with bilateral epileptiform abnormalities and the rest had unilateral EEG abnormalities. Many studies emphasize the possible role of amygdala in the development of psychoses[6-9] when the remaining unoperated amygdala is structurally and functionally abnormal in patients who underwent temporal lobectomy. In the present study, only one patient had temporal resection with normal unoperated amygdale from MRI. Since three patients had underlying mental retardation in addition to their intractable epilepsy, it might be the crucial risk factors for developing postsurgical psychosis. Duration of seizure prior to surgery does not seem to have an impact on the development of psychiatric symptoms after surgery as the duration of seizure in the presented patients ranged from 1 year to 13 years. Among 42 patients who had epilepsy surgery at Pediatric and adolescent comprehensive epilepsy center, Phramongkutklao College of Medicine with age at surgery ranged from 3 years to 19 years, patients with postsurgical psychiatric symptoms were in the relatively older age group with their age at surgery ranged from 14 years to 19 years. Thus, age at surgery may also be an important risk factor as well.

One of the possible mechanisms for post-surgical psychiatric disorder is reduction in gray matter brain volume. In a previous study, the onset of psychosis was associated with reduction in gray matter volume in frontal, temporal and parietal cortex[10]. When comparing to the present series, there was reduction in gray matter of the same distribution as a result of epilepsy surgery. Subclinical ictal activities may be one of the possible causes. The authors found no such findings on electroencephalogram (EEG) monitoring in the presented patients at the time of psychiatric symptoms. Forced normalization is another proposed mechanism first raised by Landolt (1958), of which seizure cessation and normalization of EEG may exacerbate psychosis and seizures improve psychiatric symptoms in the same manner as electroconvulsive therapy does.

Regarding to previous literatures, most studies reported new-onset psychiatric disorder following temporal lobe surgery[1,4,11]. However, there are still limited data focused on patients with new-onset psychiatric disorder following extratemporal resection. The present series reports three cases of postoperative psychiatric symptoms following resection of frontal, parietal and occipital region (Table 1).

The authors hypothesize that several mechanisms may play the important role of new-onset psychiatric disorder following epilepsy surgery. Larger studies with long term follow up will be required which may reveal the connection between these two aspects.

Potential conflicts interest

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รายงานผู้ป่วย: ความผิดปกติทางจิตเวชที่เกิดขึ้นใหม่ภายหลังการผ่าตัดโรคลมชัก

ชาคริินทร์ ณ บางช้าง, ภิรดี สงวนเกียรติ, กมรวรรณ กตัญญูวงศ์, สิรรุจน์ สกุลณมรรคา

อุบัติการณ์ของความผิดปกติทางจิตเวชที่เกิดขึ้นใหม่ (De novo psychiatric disorder) ภายหลังการผ่าตัดโรคลมชักนั้นพบได้น้อย คณะผู้นิพนธ์นำเสนอผู้ป่วย 4 ราย ที่มีความผิดปกติทางจิตเวชที่เกิดขึ้นใหม่ภายหลังการผ่าตัด ผู้ป่วยทั้งหมดเป็นผู้ป่วยโรคลมชักที่ไม่ตอบสนองต่อการรักษาด้วยยา และได้รับการรักษาด้วยการผ่าตัดที่โรงพยาบาลพระมงกุฎเกล้า โดยอาการแสดงทางจิตเวชเริ่มปรากฏในขณะที่อาการชักควบคุมได้ดีหลังการผ่าตัด จากการศึกษาพบว่า ผู้ป่วยทั้ง 4 ราย ไม่มีประวัติความผิดปกติทางจิตเวชก่อนผ่าตัด และไม่มีประวัติทางจิตเวชในครอบครัว ปัจจัยที่สันนิษฐานว่าเป็นปัจจัยส่งเสริมการเกิดความผิดปกติทางจิตเวชที่เกิดขึ้นใหม่ภายหลังการผ่าตัด ได้แก่ การพร่องของสติปัญญา โดยพบว่าผู้ป่วย 3 ใน 4 ราย มีภาวะปัญญาอ่อนก่อนผ่าตัด การฝ่อลงของเนื้อสมองในบริเวณส่วน frontal, temporal, parietal จากการผ่าตัด และ ภาวะ forced normalization น่าจะเป็นกลไกการเกิดปัญหาที่สำคัญ เนื่องจากข้อมูลในปัจจุบันยังค่อนข้างจำกัด การศึกษาความสัมพันธ์ระหว่างอาการชักหลังการผ่าตัดโรคลมชักและความผิดปกติทางจิตเวชที่เกิดขึ้นใหม่ภายหลังการผ่าตัดจำเป็นต้องศึกษาต่อไปในอนาคต