

SURGICAL TREATMENT OF DRUG-RESISTANT EPILEPSY

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Abstract: Epilepsy is one of the most common chronic neurological diseases: according to WHO, about 50 million people worldwide currently suffer from active epilepsy with ongoing epileptic seizures or the need to take antiepileptic drugs (AEDs), and about 5 million new cases of this disease are diagnosed annually. According to the results of a large-scale study conducted in 14 regions of the Russian Federation, the age-standardized prevalence of epilepsy was 3.4 people per 1000 population. This article will describe a specific clinical case of a patient suffering from drug-resistant epilepsy, examination of his brain and the nature of the surgical operation performed by the Department of Neurosurgery at Samara State Medical University.

Keywords: disconnection; pathological process; lobectomy

Relevance: According to the latest data, the average incidence of epilepsy in the world is 50-75 people per 100,000 population per year. At the same time, the incidence in countries with medium and low incomes is 70-280 people, and in developed countries - 40-60 people per 100,000 population per year. In Russia, the prevalence of epilepsy is estimated at 34-50 people per 100,000 population, while the annual increase in drug-resistant patients requiring surgical treatment is approximately 1,500 people, which elevates this nosology to the category of socially and economically significant.

Approximately 60% of all people with epilepsy have focal epilepsy syndromes. About 15% of these patients have seizures that are not adequately controlled with antiepileptic drugs (AEDs), making them potential candidates for surgical treatment.[1] Almost a third of all people with new-onset epilepsy have incompletely controlled epilepsy.[2] Importantly, most people with epilepsy are under 18 years of age, and nearly a quarter of these people have medically incurable epilepsy.[3] Surgical correction of epilepsy has been widely recognized as an effective method of treating drug-resistant forms of the disease in children and adults [1-8] and is a relevant and promising direction in the development of modern neurology and neurosurgery. Surgical treatment methods include: resection operations (temporal and extratemporal resections, hemispherectomy), disconnection methods (callosotomy and multiple subpial transections) and stimulation operations (stimulation of the vagus nerve, thalamus and transcranial stimulation).

To detect structural changes in the brain, a standard examination protocol for patients with drug-resistant epilepsy was used. The exact localization of structural and morphological changes, the relationship of the pathological process to functionally important areas of the brain, signal intensity and density, accumulation of contrast agent, the presence of a perifocal edema zone, the size of the hippocampi and changes in the subarachnoid spaces and ventricular system were determined. If it was impossible to localize epileptic activity based on neurophysiological research data, PET, SPECT and invasive research were used. Clinical data included the age of disease onset, age at the time of surgery. Patients were divided into two groups: children (under 18 years) and adults (over 18 years). Surgical interventions included temporal and extratemporal resections, callosotomy, multiple subpial transections and hemispherectomy. Histological examination was mandatory after resection operations.

The standard anterior temporal lobectomy technique *14+ involves resection of both the convexital and medial temporal lobes at a distance of 4 (on the dominant side) to 6 cm (on the subdominant side) from the apex of the pole. Authors using this technique report the safety of resections within the specified boundaries for preserving verbal functions. The most successful candidates for this

technique are patients with combined lesions of both the neocortical and medial temporal lobes. An alternative technique is "Taylored" lobectomy - a resection whose boundaries are determined by the distribution of epileptic activity and functional mapping (lobectomy tailored to electrocorticography and functional mapping) *15+. Recently, a technique has been proposed that involves the use of limited resections of neocortical sections (2-2.5 cm from the apex of the pole on the dominant side and 3-4 cm on the subdominant side) with their possible expansion depending on the data of intraoperative electrocorticography *10+. The technique proposed by DD Spencer, also called by the author "anteromedial temporal lobectomy", is fundamentally different from the technique of PH Crandall. It involves resection of the lower sections of the pole of the temporal lobe to facilitate access to the inferior horn and, in fact, is a variant of selective amygdalohippocampectomy. There is a risk associated with interventions on the temporal lobe. When using invasive research methods, liquorhea, infectious complications with a favorable outcome and transient neurological disorders are mainly encountered. During implantation of intracerebral electrodes, cases of intracerebral hematomas have been described, which can cause the development of persistent neurological disorders and pose a threat to life.

To assess the results of surgical treatment, most clinics still use the J. Engel scale (1993), usually in an abbreviated version. Class I. No seizures that negatively affect the quality of life. I A. No seizures at all. I B. Presence of only auras or simple partial seizures that manifest only as subjective sensations. Class II. Rare seizures (1-2 per year). Class III. Significant improvement — reduction in seizure frequency by 90% or more, but more often than 2 per year. Class IV. No effect. According to randomized trials, class I outcomes were observed in 58% of patients after surgical treatment of drug-resistant temporal lobe epilepsy, and in 8% of patients after refusal of surgical treatment and continuation of anticonvulsant therapy *18+. Factors that negatively affect the prognosis of surgical treatment are: the presence of multifocal lesions on MRI, diffuse changes in bioelectrical activity, discrepancy between MRI and EEG data, the presence of secondary generalized seizures, epileptic status, a history of infectious CNS lesions, and intellectual disability.

Classification of the Outcomes of Surgical Treatment of Epilepsy according to J. Engel

Class I.	Complete absence of seizures
A.	Complete absence of seizures after surgery
B.	Non-disabling simple partial seizures
C.	Some disabling seizures after surgery, but absence of them for at least 2 years
D.	Presence of generalized seizures that occur only when anticonvulsants are discontinued
Class II.	Rare disabling seizures (almost complete absence)
A.	Initially completely seizure-free, then occurrence of seizures in rare cases
B.	Rare seizures after surgery
C.	More often than rare seizures at the beginning, then rare seizures for at least 2 years
D.	Only nocturnal seizures
Class III.	Significant improvement
A.	Significant decrease in seizure frequency
B.	Long intervals of complete cessation of seizures - more than 50% of the total observation time, but not less than 2 years
Class IV.	No significant improvement
A.	Some decrease in seizure frequency
B.	Unchanged
C.	Increase in seizure frequency

- The incidence of epilepsy surgery has remained stable at about 1500 cases per year for over 20 years. The nature of operated cases may be changing with the decline of mesial temporal sclerosis , possibly due to improved outcomes in childhood febrile seizures. At the same time, outcomes in extra temporal epilepsies are improving due to new diagnostic techniques. The mortality rate from surgery is about 0.1–0.5% , which is comparable to the annual SUDEP rate in refractory epilepsy , i.e., the mortality from ongoing refractory epilepsy exceeds the postoperative risk after one year. Complication rates have decreased and are about 3% for major and 7% for minor complications; one of the most common complications is visual field defect after temporal lobectomy . Treatment is cost-effective in the long term, with sustained remission, and almost half of adult patients and 86% of children are able to discontinue AEDs.151. Jobst BC, Cascino GD, RK, et al. Epilepsy resection surgery for drug-resistant focal epilepsy.

- **Clinical case:** The patient, Ashurova Dildora, born in 1971, complained of headaches, frequent seizures and general weakness. The patient considers herself ill since the age of 6. Associates her illness with a head injury received at the age of 6, when a metal object hit her head. The disease began with seizures and mental retardation. She constantly takes carbamazepine 200 mg 1-2 tablets 3 times a day. Due to the intensification of the above complaints, she contacted the Multidisciplinary Clinic of Samara State Medical University.
- **Conclusion :**To clarify the diagnosis and choose treatment tactics, the patient was hospitalized. The patient underwent a series of examinations, including anamnesis, MRI of the brain, EEG and laboratory tests. Based on the results, a surgical operation was performed: frontoparietal craniotomy with right-sided lobectomy and anterior colloidotomy.

Introduction:

- The patient, Ashurova Dildora, born in 1971, complained of headaches, frequent seizures and general weakness. The patient considers herself ill since the age of 6. Associates her illness with a head injury received at the age of 6, when a metal object hit her head. The disease began with seizures and mental retardation. She constantly takes carbamazepine 200 mg 1-2 tablets 3 times a day. Due to the intensification of the above complaints, she contacted the Neurosurgery Department of the Multidisciplinary Clinic of the Samara State Medical University.
- Epidemiological history: Has not traveled abroad in the last 6 months. No blood transfusions or blood substitutes.
- Living conditions: Lives in satisfactory conditions. No allergic reactions to medications or food products were noted.
- Objective condition: The patient's condition is moderate. The skin is pale. The subcutaneous fat layer is developed in accordance with age. The peripheral lymph nodes are not enlarged. Breathing is free, the respiratory rate is 17 per minute. Vesicular breathing in the lungs. Heart sounds are muffled, the rhythm is regular, the heart rate is 77 beats per minute. The abdomen is soft, painless. The liver and spleen are not palpable. Stool is regular.
- Neurological status: Consciousness is clear, 15 points on the Glasgow scale. Elements of motor aphasia are noted. There are general cerebral symptoms and seizures. There are no meningeal symptoms. Delay in psychomotor development. Disorders of the functions of the cranial nerves: V, VII, VIII, XII pairs.
- Epileptic status: Epileptic seizures have been observed since birth. Currently, their frequency reaches 10 per day. The duration of seizures is from 1 to 5 minutes. The patient is prescribed carbamazepine.

Laboratory test results and experts' conclusions:

Coagulogram (12/11/24)

Venous blood clotting time according to Fonio - 3.18-4.20 minutes – [5-6]; Prothrombin time -15 sec [14-20]; Prothrombin index - 107 (%) [70-120]; INR - 0.89 [0.89- 1.3]; Plasma tolerance to gerarin - 8-15 min [8-10]; Thrombin time - 14 sec [14-16]; APTT - 42 sec [40-45]; Plasma fibrinogen - 3.15 g / l [2-3.55]; Blood clot retraction - 0.4% [0.3-0.5];

Biochemistry (11.12.24) Total bilirubin 12.8 [8.55-20.5 μ mol/l]; Blood for AST 0.2 [0.1-0.45 mmol/l] Blood for ALT 0.59-[0.1-0.68 mmol/l] Blood for total protein 63 [65-85 g/l] Creatinine 97.4 [53-97 mmol/l] Blood for RW express reaction – negative

Blood group analysis (11.12.24) +positive A (2) group

Hematological complete blood count (12/11/2024)

Hemoglobin 70.0 g/l [M110-160;120-140]:

Erythrocytes 3.00 10121 (3.79-5.78]; Color index 0.70%-[0.85 -1.05]; Leukocytes – 4.00 109 1 – [4.00-10.00]; Coagulation time – 2.10-3.50 – [N. 20 sec – Min. K. 3 min – 5 min]; Band neutrophils – 2% - [1-6]; Segmented neutrophils 60% - [47-72]; Eosinophils – 3% - [0.5-5]; Monocytes – 4% - [3-11];

Lymphocytes – 31% - [19-37];

Erythrocyte sedimentation rate 15 mm/hour – [M 2-10 F 2-15];

MRI of the brain and intracranial vessels in high resolution mode with tractography:

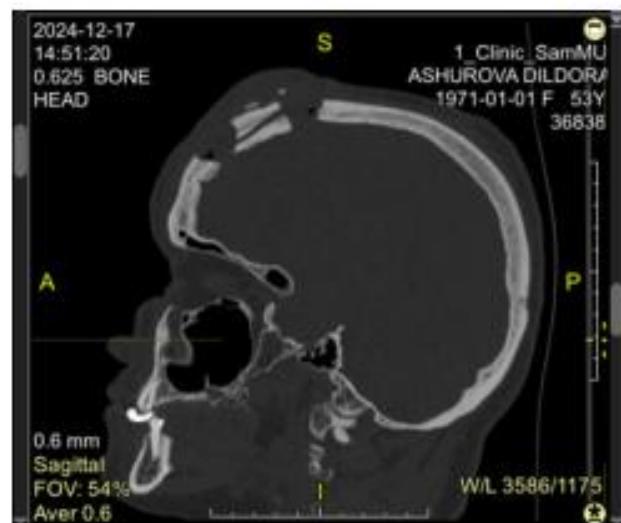
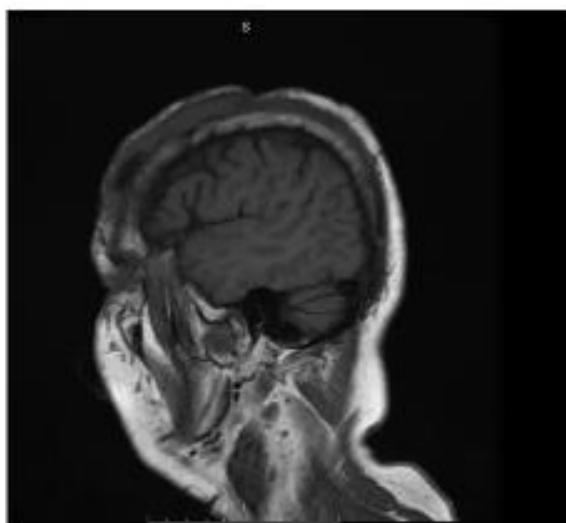
Scanning in T1, T2, FS, STIR, FIESTA modes. Projections: axial, sagittal, coronal.

SPO (extracts not provided). Extensive pathological foci and zones in the cortex and white matter of the frontal-temporal-parietal region of the right hemisphere of the brain, of a heterogeneous structure, with unclear, uneven contours, uneven thickening, deformation of the cortex of the right frontal lobe.

On MR tractography: on the FA map, the level of fractional anisotropy in the area under study is not reduced. On the 3D tractography map, thinning and deformation of the tracts of the right frontal lobe. Extensive chronic hematomas in the subcutaneous tissue of the frontal-temporal-parietal region of the head, more on the left. Multiple foci in the subcortical and periventricular white matter of both hemispheres of the brain, 1-6 mm in diameter, round in shape, homogeneous structure, with fuzzy, smooth contours, weakly hyperintense on T2 VI, Flair signal. No areas of ectopia of gray matter were detected. The hippocampal areas are symmetrical, the temporal horns are not dilated. No focal changes in the brainstem and cerebellum were detected. The corpus callosum is of normal shape and size. Perivasal spaces are not dilated. The midline structures of the brain are not displaced. The lateral ventricles are up to 7 mm wide at the level of the foramina of Monro on the right and up to 7 mm wide on the left. The third ventricle is up to 6 mm wide. The midbrain aqueduct and the fourth ventricle are of normal width. Moderate expansion of the subarachnoid space in the frontal-temporal-parietal regions on both sides. No pathological formations were found in the projection of the cerebellopontine angles. The cerebellar tonsils are located at the entrance to the foramen magnum. The pituitary gland is 6 mm high, with clear contours. The structure of the adenohypophysis is homogeneous. The neurohypophysis is in a normal position. The pituitary infundibulum is in a central position. The suprasellar cistern is unchanged. The cavernous sinuses and visible sections of the internal carotid arteries are normal.

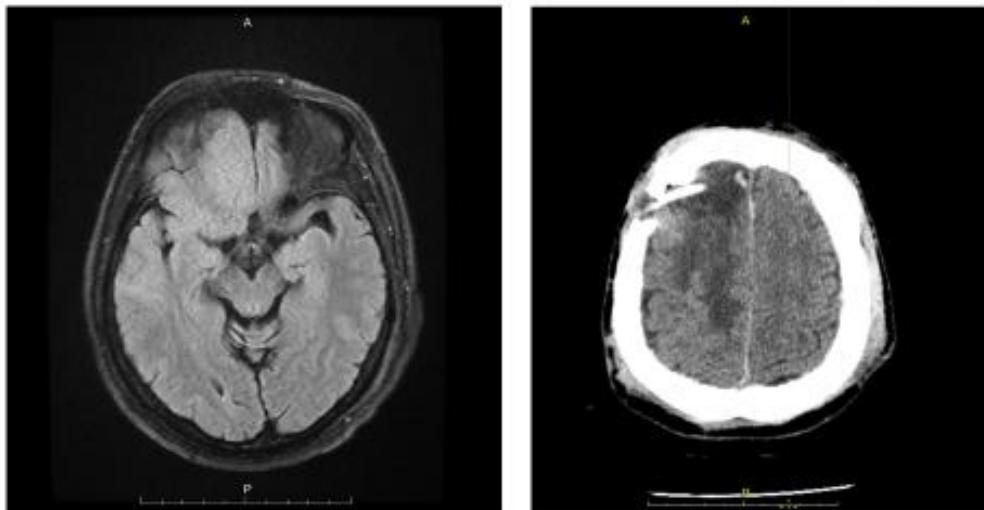
On a series of MR angiograms of intracranial arteries: the circle of Willis is not closed.

The siphons of the internal carotid arteries have a normal caliber, course, walls without filling defects. The anterior cerebral arteries have a normal course, caliber. The middle cerebral arteries have normal branching and diameter. The basilar artery has a normal course and caliber. The course

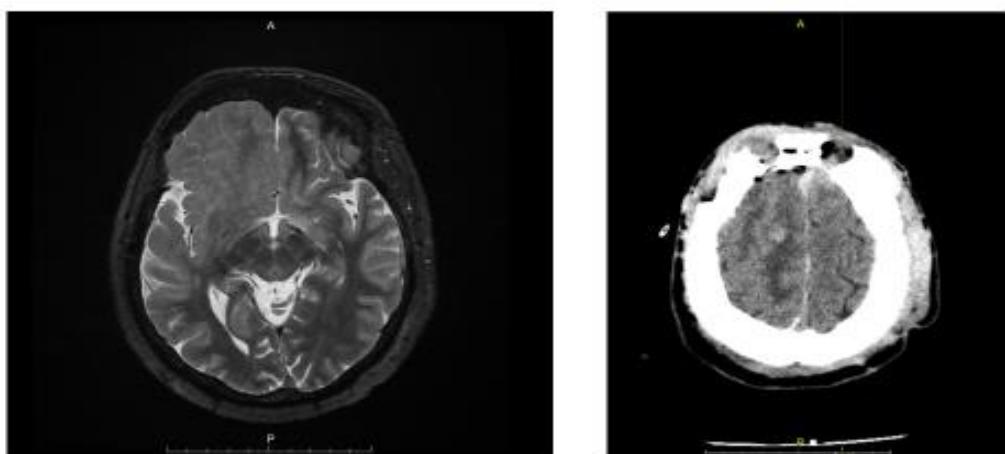


underdevelopment. Unilateral giant convolution of the brain, local micropolygyria are observed. The lesions are localized in the frontal and parietal lobes. Cognitive and pyramidal neurological disorders. Psychomotor development is delayed. Drug-resistant epilepsy is observed.

A mean-voltage EEG with dominant b activity in the right temporal region is recorded. The dominant activity is represented by moderately expressed unmodulated oscillations with an average frequency of $0.75 \text{ k/sec} \pm 0.75 \text{ k/sec}$ and an average amplitude of $50 \mu\text{V}$. The dominant rhythm is observed mainly in the right temporal region, interhemispheric asymmetry is moderately expressed. The background curve shows a weakly expressed unmodulated stable in amplitude Alpha rhythm with a dominant frequency of $8.5 \text{ k/sec} \pm 0.5 \text{ k/sec}$, an average amplitude of $15 \mu\text{V}$ and an index of 93%. Alpha rhythm is observed mainly in the right temporal region, interhemispheric asymmetry is clearly expressed. Beta rhythm with an amplitude of up to $6.7 \mu\text{V}$ and an average frequency of $13 \text{ k/sec} \pm 0.5 \text{ k/sec}$ is presented mainly in the occipital region. Interhemispheric asymmetry is absent.



Slow-wave activity is represented mainly by oscillations of the 8th range, not exceeding the level of background activity with a frequency of 1.8 fps. Localization of slow-wave activity is mainly in the

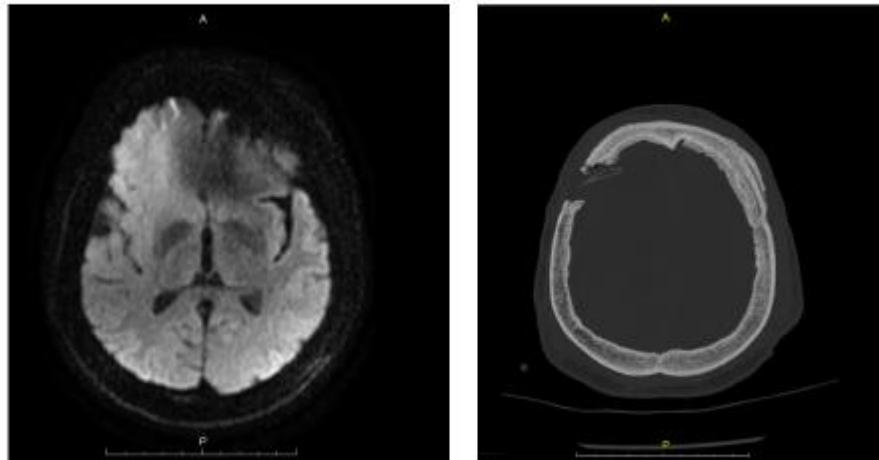


Pathologies: Paroxysmal activity is registered. A decrease in the bioelectrical activity of the brain is noted.

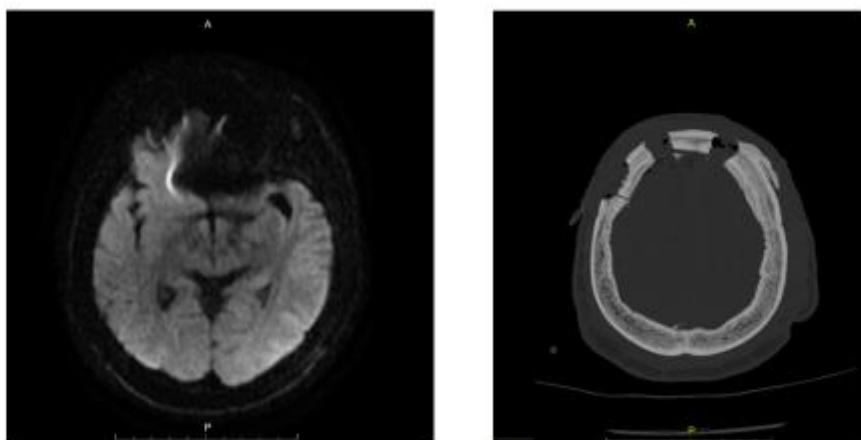
Operation #1105. Date: December 12, 2024. Patient: Ashurova Dildora, born in 1971. Inpatient, case history #17402/1603

Purpose of the operation: Frontoparietal craniotomy with right lobectomy and anterior collotomy. The patient underwent a bifrontal skin and soft tissue incision in the frontal part of the head under general endotracheal anesthesia. After hemostasis, the skin flaps were retracted. Burr holes were made. A craniotomy was performed. During separation of the dura mater (DM) from the bone of the superior sagittal sinus, bleeding was observed from several areas of the sinus. The bleeding was stopped by tamponade with hemostatic materials. The DM was removed. Examination of the brain revealed hypotrophy of the left hemisphere, expansion of the subarachnoid space, the right hemisphere was larger than the left. The cortex of the right frontal lobe was flattened, the tissues were changed, denser on palpation.

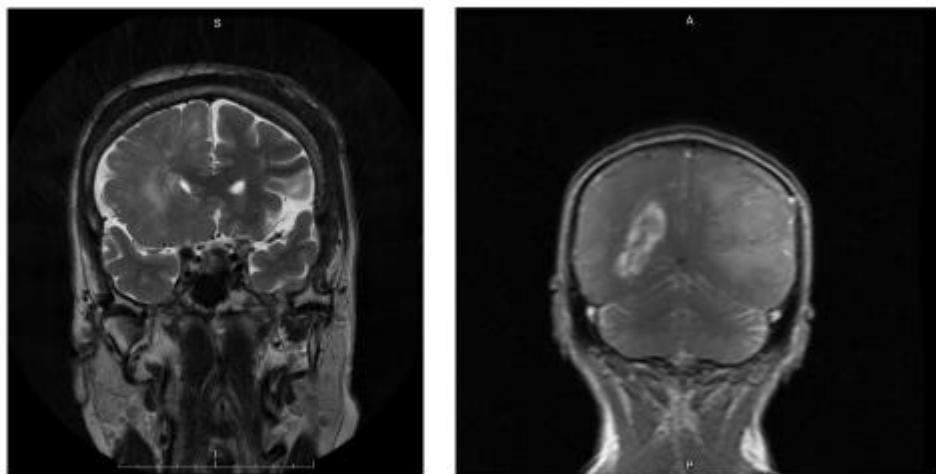
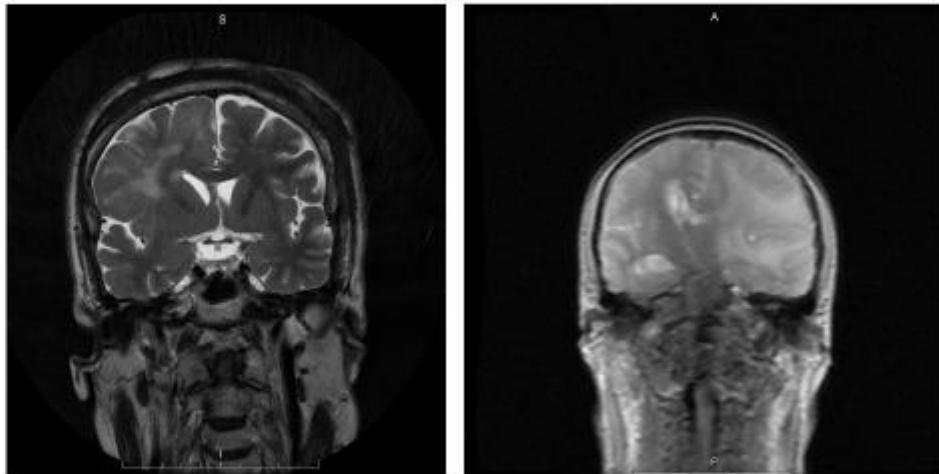
Further manipulations were performed under a microscope using microsurgical instruments. A



lobectomy of the right hemisphere was performed. An incision was made along the corpus callosum to its peduncle. Part of the branches of the right anterior cerebral artery was coagulated.



Callosotomy was performed. The resulting diffuse bleeding was stopped with hemostatic materials. The dura mater was closed with a synthetic material - dura patch. Drains were installed. The bone flap was returned to its place. The wound was sutured and treated with alcohol, iodine, and an alcohol compress with a bandage was applied. Anterior callosotomy. TBI.



Conclusion: Epilepsy may be caused by a wide range of factors, including structural changes in the brain, genetic pathology, infectious agents, and toxic factors, which may lead to the onset of the disease in individuals of both sexes and at different age groups. This course of the disease is called drug-resistant epilepsy (DRE), and patients with DRE are considered candidates for surgical treatment [5]. Patients with the structural form of DRE are most often subjected to surgical treatment [6]. It has been established that resection surgeries aimed at achieving “seizure freedom” (complete absence of epileptic seizures after surgical treatment) are the most effective. Dissociative surgeries are less clinically effective, aimed at reducing the frequency and severity of epileptic seizures, and are performed in cases where the epileptogenic focus cannot be removed, for example, when the focus is localized within functional zones, the focus is extensive, the foci are bilateral, and generalized forms of epilepsy are present. With this type of surgery, the epileptogenic zone

continues to remain in the brain and produce pathological activity, which, however, is transmitted to a lesser extent to the “healthy” areas of the brain, involving them in the pathological process, which is why even with optimal drug therapy, about 20-40% of patients cannot get rid of epileptic seizures or significantly reduce their number.

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