

PROGNOSIS OF SURGICAL TREATMENT OF PHARMACORESISTANT EPILEPSY: THE ROLE OF MENTAL AND COGNITIVE DISORDERS

Abduvoyitov Bobur Bakhodirovich

Samarkand State Medical University, Neurosurgery Department

The review is devoted to the role of mental and cognitive disorders in the prognosis of surgical treatment of drug-resistant epilepsy. The analysis of historical aspects of surgical treatment of epilepsy is given, modern data on the prognosis of surgical intervention in relation to seizure control, cognitive functioning, mental disorders are presented. The issues of the role of a psychiatrist in the structure of preoperative and postoperative patient management are considered.

Key words: epilepsy, drug resistance, mental disorders, cognitive disorders, surgical treatment of epilepsy.

Epilepsy is not only “one of the most common and severe, but at the same time potentially curable and socially significant diseases of the brain” [1, 2], but also reflects a broad interdisciplinary problem, in which the interests of neurologists, pediatricians, psychiatrists, neurosurgeons, etc. intersect. The prevalence of epilepsy in industrialized countries is 40-70 patients per 100,000 population per year [2, 3], and in developing countries - 35-190 per 100,000 [3]. In the general population of our country, this figure is 3.39 per 1000 population [4, 5]. Despite the obvious successes in the treatment of epilepsy, as well as the emergence of new effective anticonvulsants, the problem of resistance remains key in epileptology. Moreover, more than 30-40% of patients with epilepsy do not achieve complete control over seizures [6, 7]. According to WHO estimates, 15 out of 50 million patients with epilepsy continue to have seizures despite treatment with anticonvulsants [8]. Approximately 30% of patients with focal epilepsy develop drug resistance during their lifetime, in which the chance of achieving complete seizure control with continued drug therapy is no more than 8% [9]. Generally accepted criteria for drug resistance were proposed by A. Berg [10]: 1) persistence of seizures when using 2 anticonvulsants; 2) 1 seizure per month during 18 months of observation; 3) a seizure-free period of no more than 3 months during 1.5 years of observation. Drug resistance as one of the most serious problems in epilepsy therapy leads to many severe complications, including trauma, damage to a number of organs and systems, an increased risk of death and severe psychological and psychiatric consequences. Such patients are significantly more likely to develop concomitant cognitive and mental disorders [11], they are 1.5-2 times more likely to receive traumatic brain injuries, burns, dental damage, etc. [12]. Their mortality rate is higher compared to curable patients [8], especially in cases of nocturnal and generalized seizures, in which the risk of sudden death increases by 40 times [13, 14]. There are many studies devoted to mental disorders in drug-resistant epilepsy [15, 16],



which consider the issues of differential diagnosis of true resistance and pseudo-resistance [17, 18, 19], a close association of drug resistance with an increased risk of psychotic [20, 21, 22], affective [23, 24, 25], anxiety [26, 27], cognitive [28, 29, 30] and other disorders, which, together with uncontrolled seizures, significantly reduce the quality of life of patients [31, 32, 33]. Moreover, not only drug resistance is a risk factor for mental disorders, but mental disorders themselves significantly increase the risk of developing drug resistance [34, 35] by increasing the severity of brain dysfunction [36]. Methods for overcoming resistance can be both medicinal and non-medicinal [37]. There is data in the literature on a decrease in the frequency of attacks when verapamil [38] and statins [39] are added to basic anticonvulsant therapy. More and more information is accumulating on the anticonvulsant properties of phytocannabinoids [40]. Non-medicinal methods include various diets (ketogenic diet, modified Atkins diet), which, according to A. Sharma et al. [41], also help to reduce the frequency of attacks or achieve remission. There is scattered data on the effectiveness of acupuncture, psychotherapy, and, in particular, biological feedback, autogenic training, as well as deep and progressive relaxation [42]. Non-drug methods of overcoming drug resistance also include surgical treatment, the indications for which are: seizures of focal onset, limiting everyday life and reducing the quality of life; establishment of drug resistance criteria or the presence of pronounced side effects from taking anticonvulsants [43]. Currently, the main types of surgical treatment are: resection interventions (removal of the pathological focus - arteriovenous malformations, cavernous malformations, brain tumors, selective amygdalohippocampectomy, cortex resection, partial lobectomy, lobectomy, hemispherectomy), palliative interventions (callosotomy, multiple subpial incisions), alternative methods (vagus nerve stimulation, deep brain stimulation, stereotactic destruction, ablations) [44]. More than half of all surgical procedures for drug-resistant epilepsy are performed using the anterior medial lobectomy method for temporal lobe epilepsy [45, 46], aimed at removing the epileptogenic zone, which includes both the seizure “onset” zone and potentially epileptogenic areas.

Historical aspects of surgical treatment of epilepsy: control of mental disorders

Surgical methods of treating epilepsy have long been the subject of empirical research by individual groups of enthusiastic scientists in different countries of the world. However, their work played a decisive role in the further history of the development of this new direction of therapy. At that time, these studies did not have a strict scientific methodology, methods and techniques. However, even then, scientists were concerned about the most pressing problems that arise when assessing the results of surgical intervention, such as seizure control, the level of social adaptation, cognitive impairment and mental disorders. The history of surgical treatment of epilepsy begins in ancient times, when Greek and Roman doctors performed craniotomy to stop epileptic seizures that developed after traumatic brain injury (TBI) [47]. There are separate references to this method of surgical intervention in the works of authors from the Middle Ages [48] and the Renaissance [49]. It was only in 1828 that the American surgeon B. Dudley [50] first



published a description of a series of clinical cases devoted to the effectiveness of trepanation for the treatment of epilepsy, and in 1886 V. Horsley performed the first operation on the brain of a patient with post-traumatic epilepsy, which resulted in a complete reduction of seizures [51]. In our country, surgical treatment of epilepsy was first described in 1895 by V.M. Bekhterev [52]. During the same period, V.I. Razumovsky (1893), and subsequently G.F. Zeidler (1896) successfully used the Horsley operation (surgical extirpation of the cerebral cortex) in patients with Jacksonian epilepsy [53]. The introduction of electroencephalography (EEG) methods into practice contributed to the further development of surgical treatment of epilepsy. Thus, in the 1930s, research groups headed by W. Penfield and H. Jasper determined the significant role of neurophysiological studies in epilepsy surgery and the need for resection of mesiotemporal structures to achieve seizure control [54]. The results of the first temporal lobectomies were published by W. Penfield and H. Flanigin [55] in 1950. The selection of patients for surgery was based on the clinical picture of seizures, the absence of "gross" mental disorders, as well as EEG data, pneumographic and radiographic studies. The effectiveness of surgical intervention was quite high: complete seizure control was noted in 53% of patients, a decrease in seizure frequency by more than 50% - in 25% of patients. At the same time, the authors did not reveal significant changes in the behavior and cognitive functioning of patients. In the USSR, temporal lobectomies were first performed by A.G. Zemskoy (1960), Yu.N. Savchenko (1962) and Yu. I. Belyaev (1963) [56]. Since the mid-20th century, more and more works have appeared in foreign literature devoted to the effect of surgical treatment of epilepsy on mental disorders. Thus, according to a study conducted in 1951 by P. Bailey [57], out of 25 operated patients, 4 showed an improvement in their mental state ("they became calmer, more serene and compliant"), while 3 showed a worsening of their condition ("they became more talkative and hyperactive"), 2 of whom required hospitalization in a psychiatric hospital. The results of another study [53], conducted during the same period, showed that after temporal lobectomy, patients showed impairments of auditory-verbal memory, a decrease in the level of aggressiveness, "a switch from aggression to depression with and without hypochondriacal experiences," as well as an improvement in interpersonal contacts and changes in the sexual sphere (usually in the form of increased libido). In their study, English neurosurgeons M. Falconer and E. Serafetinides [58], evaluating the effect of surgery on comorbid mental disorders, revealed a decrease in the number of attacks, accompanied by an improvement in the mental state of patients. In 1972, D. Taylor [59] published the results of a prospective (2-12 years) study involving 100 patients who underwent surgical treatment of epilepsy using the anterior temporal lobectomy method. Efficiency in the postoperative period indicated heterogeneous postoperative dynamics of the mental state of patients and, according to the authors, was associated with the results in achieving seizure control: an improvement in the mental state in the group of "neurotics" (mainly in relation to anxiety, depressive and phobic states) and "psychopaths" (mainly due to a decrease in aggressiveness), the absence

of dynamics, and in some cases the occurrence of psychotic disorders de novo. During the entire observation period, 37 patients were hospitalized in a psychiatric hospital, 19 of whom had psychotic disorders, and 5 had suicidal attempts. The study of the effect of surgical treatment of epilepsy on mental disorders has also been discussed in the domestic literature [60]. Thus, Yu. V. Konovalov indicated that after surgery, patients experienced “improved memory, elimination of aggressiveness, decreased irritability, stubbornness, cowardice and rapid mood swings” [61]. The results of the study by P. M. Panchenko et al. [62] showed that unilateral surgical intervention on cortical, archi- and paleocortical epileptogenic foci did not lead to an increase in the “personality defect”, and the cessation or reduction in the frequency of attacks had a beneficial effect on the mental state of patients. The results published by V. M. Ugryumov [63] also point out that after surgical treatment of epilepsy, there is no “destruction of the patient’s personality,” and full or partial control over seizures contributes to an improvement in the mental state. I. T. Viktorov [64], when describing clinical variants of “mental defect” (psychoorganic, epileptic, with psychophysical infantilism, schizoepileptic, and a combination of epileptoid and hysterical character traits) in patients with temporal lobe epilepsy after its surgical treatment, emphasized “the possibility of their functional reversibility, especially in the acute phases of the epileptic process.” Researchers were more unanimous in assessing the impact of surgical treatment of epilepsy on cognitive functioning: most authors noted a deterioration in cognitive processes in such patients [65]. Thus, in the work of B. Milner [66], tients after temporal lobectomy on the left (dominant hemisphere) showed a deterioration in verbal memory, and those who underwent it on the right - visual memory. In 1967, C. Blakemore [67] published the results of a prospective 10-year study, which involved 86 patients who underwent anterior temporal lobectomy. In the case of resection of the temporal lobe in the dominant hemisphere, patients developed auditory-verbal memory disorders that persisted for about 3 years and subsequently quickly resolved. The current stage of development of surgical treatment of temporal epilepsy was a consequence of the introduction of neuroimaging and standardization methods into surgical practice. The study of data obtained as a result of magnetic resonance imaging (MRI) made it possible to diagnose epileptogenic brain lesions, previously detected either after surgery or at autopsy in patients who had long-term epilepsy [68]. Signs of hippocampal sclerosis, various heterotopias, focal cortical dysplasias [69], etc. were described. An important milestone in the standardization of the evaluation of the effectiveness of surgical treatment of epilepsy was the inclusion of a neuropsychological examination in preoperative preparation aimed at assessing the persistence and severity of cognitive impairment, as well as the possibility of their compensation after surgery [70]. In addition, standardization of the diagnostic qualification of the mental state of patients with epilepsy began to be carried out using modern psychiatric classifications (ICD-10 and DSM-IV), structured and semi-structured clinical interviews, generally accepted psychometric scales, and the results of surgical treatment of epilepsy - using the surgical



treatment outcome scale [71]. The latter included 4 blocks of parameters (absence of attacks negatively affecting quality of life; rare attacks affecting quality of life; significant improvement; insignificant improvement or deterioration), which made it possible to compare the results of various studies.

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