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Drug-resistant epilepsy treated with avagus nerve stimulator – case report and literature review

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ABSTRACT

Introduction and purpose

The average prevalence of epilepsy worldwide is estimated at 7.60 cases per 1,000 inhabitants, with an average annual incidence of 67.77 cases per 100,000 inhabitants. Epilepsy is one of the most common neurological conditions. However, it is not a disease entity, but a set of symptoms that can occur against a background of various morphological and metabolic changes in the brain. Symptoms of epilepsy include epileptic seizures, i.e. transient disturbances of bioelectrical activity in the nerve cells of the brain.

Epilepsy is a brain disorder characterized by a persistent predisposition to induce epileptic seizures, and the condition has neurobiological, cognitive, psychological, and social consequences.

Successful treatment of epilepsy may require a variety of methods. In this paper, we would like to present a case report on the treatment of drug-resistant epilepsy with a vagus nerve stimulator (VNS).

Conclusion

The described case can prove the effectiveness of the treatment of focal drug-resistant epilepsy with a vagus nerve stimulation (VNS). It is crucial to select an appropriate, effective treatment method for children with drug-resistant epilepsy; it is especially worth thinking about novel methods such as VNS.

Keywords: epilepsy, drug resistant epilepsy, vagus nerve stimulator.

1. Introduction

Epilepsy is abrain disorder characterized by a persistent predisposition to induce epileptic seizures, and the condition has neurobiological, cognitive, psychological and social consequences. According to the definition of the International League Against Epilepsy (ILAE), epilepsy is a brain disease that meets one of the following conditions:

1. at least two unprovoked (or reflex) seizures have occurred, with an interval of at least 24 hours between them
2. one unprovoked (or reflex) seizure occurred, and the risk of another seizure is at least 60%
3. epileptic syndrome was diagnosed [1].

An epileptic seizure is defined as the occurrence of symptoms (subject or object) caused by abnormal, excessive or synchronous activity of neurons present in the brain. Seizures can begin in a limited area of the brain - these are focal onset seizures - or arise in both hemispheres simultaneously - generalized seizures. An unprovoked seizure is a seizure in which there are no triggers, as well as cases with no identified etiologic factors or risk factors in patients with nonprogressive damage to the central nervous system, patients with brain tumors or degenerative diseases [2]. Epilepsy can have a variety of etiologies - genetic defects, structural changes, metabolic disorders can be the cause, and in some cases the cause remains unknown [3].

There are two basic types of seizures - focal seizures and generalized seizures. We divide focal seizures into seizures without disturbance of consciousness and seizures with disturbance of consciousness. Focal seizures can have both motor (e.g., seizures, myoclonus) and non-motor (e.g., sensory, emotional, autonomic) symptoms. Generalized seizures can take the form of a motor seizure (e.g., tonic-clonic, atonic seizures) or a seizure without motor manifestation (e.g., absence seizures) [4]. Unconscious seizures are of short duration, manifested by loss of consciousness, are not accompanied by motor symptoms, and patients quickly return to their pre-seizure state. In atonic seizures, there is a brief loss of muscle tone, often resulting in a sudden fall. In generalized tonic-clonic seizures, there is a tonic phase - increased muscle tone - and a clonic phase - muscle spasms. During the seizure, respiratory arrest or involuntary urination may occur. The clonic phase is followed by relaxation and deep

unconsciousness continues. A person who has experienced such a seizure does not remember these symptoms, and maybe tired and disoriented [5].

An epileptic seizure is defined as the onset of symptoms (subject or object) caused by abnormal neuronal activity in the brain. Seizures can start in a limited area of the brain - focal seizures - or arise in both hemispheres simultaneously - generalized seizures. The clinical manifestations of epileptic seizures are highly variable. Epilepsy can have a variety of etiologies - the causes can be genetic defects, structural changes, metabolic disorders, and in some cases the cause remains unknown. Determination of the epileptic syndrome, i.e. a specific set of seizure types and electroencephalographic and imaging features, is the final stage of diagnosis [1, 2, 3, 4, 5].

Epilepsy can be considered drug-resistant if seizure control has not been achieved despite the use of at least two appropriately selected and properly used antiepileptic drugs [4, 5].

The purpose of this work is to present the therapeutic process of a clinical case inwhich treatment of drug-resistant epilepsy was undertaken with avagus nerve stimulator.

2. Case description

A male patient, born in 2006, with a history of severe perinatal cerebral palsy, diagnosed with cerebral hemorrhagic stroke twice, drug-resistant epilepsy, mental disability, bronchial asthma, hypothyroidism, hypertension, axonal motor polyneuropathy and an implanted valve between the frontal lobe cyst and the lateral ventricle.

In 2010, the patient was admitted to a hospital due to the onset of an epileptic seizure in the form of convulsions with head and eyeballs turning to the right side and subsequent headache in the right temporal region. On physical examination, the patient was found to have skull asymmetry with a defect in the right frontoparietal region, scoliosis, asymmetry of the chest, waist, and spinal axis, abnormal gait, limb asymmetry, muscle weakness (mainly of the left upper limb), contractures of the ischiofemoral muscles and hip flexors, valgus knees with high patellar alignment, and skin striae. During hospitalization, an EEG was performed, which showed the presence of focal lesions. Symptomatic (focal) epilepsy and epileptic syndromes with complex partial seizures were diagnosed. Pharmacological treatment of epilepsy was introduced. The MR examination of the central nervous system showed an irregular fluid space with a septum in the right frontotemporal region, atrophic changes of the

right parietal lobe with widening of the brain surface dirt and associated malar areas, features of gliosis in the right parietal and occipital lobe and the frontal horn area of the left lateral ventricle, asymmetry of the midbrain and cerebral condyles - thinning of the right cerebral condyle and completely thinning of the corpus callosum, asymmetric cerebral ventricular system in terms of the lateral ventricles - the right lateral ventricle deformed, wider than the left lateral ventricle, modeled by the described fluid space, retention cysts of the maxillary sinuses.

After years of ineffective pharmacotherapy, the patient qualified for vagus nerve pacemaker implantation. During the next hospitalization, which took place in late 2015, the vagus nerve stimulator was evaluated and modified. A history of reduced epileptic seizures was noted.

In April 2019, the patient presented to a hospital, seeking medical attention for the emerging left upper limb paresis and volvulus of the left upper limb and left lower limb. An RM study of the brain and brainstem was performed. No new pathological changes were found. No increased number of epileptic seizures was observed.

In May 2020, the patient was admitted to the neurological department because of visual disturbances in the form of double vision when looking into the distance and the occurrence of episodes of dizziness with rapid, irregular eye movements with subsequent drowsiness. A head MR examination was performed, which did not reveal any new pathologies.

In mid-2023, the patient presented to the pediatric neurology department due to atrophy of the shoulder girdle muscles, left thumb club, unintentional weight loss (BMI = 20.78), and decreased exercise tolerance. He reported no history of epileptic seizures. Neurological examination revealed quadriparesis with left-sided predominance. An EMG study was performed and showed damage to axonal motor fibers in the form of a prolongation of latency, a slight decrease in amplitude, and a slight slowing of conduction velocity. A diagnosis of axonal motor polyneuropathy was made and it was decided to start immunoglobulin therapy. During the hospital stay, an EEG was also performed - with no significant abnormalities. A cardiology consultation was performed. FOP/ASD II was diagnosed, and an exercise test was performed, which confirmed decreased exercise tolerance.

In late 2023, during hospitalization, a genetic consultation was held, during which molecular testing of the genes HINT 1, CACNA1, and their variants, which maybe

a factor in neuropathy, was performed. However, the genetic diagnosis needs to be expanded.

At the beginning of 2024, another hospitalization took place. On neurological examination, improvement in left upper limb function was noted. From the history, information was obtained about the patient's lack of epileptic seizures.

3. Discussion

As defined by the International League Against Epilepsy, epilepsy can be diagnosed if at least two unprovoked epileptic seizures more than 24 hours apart are noted, one unprovoked epileptic seizure with a high probability of another seizure within the next 10 years, or if a specific epileptic syndrome is diagnosed. The average prevalence of epilepsy worldwide is estimated at 7.60 cases per 1,000 inhabitants, with an average annual incidence of 67.77 cases per 100,000 inhabitants. Epilepsy is one of the most common neurological conditions. However, it is not a disease entity, but a set of symptoms that can occur against a background of various morphological and metabolic changes in the brain. Symptoms of epilepsy include epileptic seizures, i.e. transient disturbances of bioelectrical activity in the nerve cells of the brain [6].

Of great importance in the diagnosis of epilepsy is an early subjective examination, physical examination, and a meticulous, thorough history from the patient and witnesses to the epileptic seizure. Video recordings depicting an epileptic seizure are also often useful. During the diagnostic process, it is reasonable to perform an EEG as soon as possible after the seizure. An ECG and tests identifying metabolic abnormalities are also important. MR imaging of the brain should be performed in any child with unprovoked, newly developed seizures [7, 8, 9, 10, 11]. According to the ILAE, conditions that can cause a seizure also include, but are not limited to: pre - and perinatal trauma and stroke [12]. The described patient likely developed epilepsy on the background of a history of hemorrhagic stroke.

During the occurrence of focal seizures, the EEG performed during the interval between seizures usually shows focal epileptic discharges, which emphasizes the importance of performing this test in the diagnostic process. However, it is worth noting that a normal EEG result does not exclude the diagnosis of epilepsy. Careful analysis of the aforementioned examination and clinical symptoms during seizures can be extremely useful in distinguishing focal from generalized epilepsy [13, 14, 15].

Abnormal neuroimaging findings have been recognized as a risk factor for recurrent epileptic seizures. Focal seizures have a higher risk of recurrence than generalized seizures. The specific etiology of epilepsy onset, including brain injury, perinatal trauma, or stroke, is also associated with a high risk of subsequent seizure. Imaging of the central nervous system helps identify the cause of epilepsy and determine the risk of recurrent seizures [8].

When drug-resistant epilepsy is diagnosed, neurostimulation is an alternative to pharmacotherapy. The development of vagus nerve stimulation (VNS) began in the 19th century. The implantable device was first approved for the treatment of epilepsy in Europe in 1994 and in the United States in 1997. [16,17].

Vagus nerve stimulation has shown effective action in both focal and generalized epilepsy. It is currently used and safely applied to both pediatric and adult patients. The efficacy of VNS becomes optimal around the sixth month of treatment, with approximately 45-65% of patients achieving a 50- 100% reduction in seizure frequency. After a thorough evaluation of the patient and a positive qualification for the procedure, surgery is performed to implant the pacemaker on the left side of the chest with the electrode wrapped around the left cervical vagus nerve. The choice of the left vagus nerve is not random, as it is associated with a lower risk of the device affecting the atrioventricular node of the heart. This is important in minimizing the risk of developing cardiac arrhythmias. The stimulator at regular intervals, via the vagus nerve pathway, sends electrical impulses to the brain, which reduce bioelectrical discharges in the epileptic focus. The pacemaker's discharges are determined individually for each patient. This reduces the risk of an epileptic seizure. In addition, the patient can turn on the pacemaker pulse immediately, when seizure herald symptoms are observed. VNS can also lead to improvements of 25-35% in depression scores, 35% in anxiety, and 25% in mood scores. Side effects of neurostimulation can include coughing, hiccups, dysphagia, and hoarseness associated with stimulation of the retrobulbar laryngeal nerve. After implantation of a vagus nerve stimulator, periodic monitoring and programming of the ruler is necessary [17, 18, 19, 20, 21, 22].

Currently, no single universally effective method of treatment for epilepsy can be indicated. The choice of a therapeutic option is determined by the patient's condition and an assessment of the benefits and risks of possible side effects during the use of a particular treatment method. In the described case, pharmacological treatment was introduced, which proved ineffective.

Therefore, the decision was made to qualify the patient for implantation of a vagus nerve stimulator. The history and repeated analysis of the patient's neurological condition confirmed the effectiveness of neurostimulation. The presented case shows howimportant it is to choose the right treatment method.

VNS	
Electrodelocation	The cervical trunk of the left vagus nerve.
Implantationmethod	SurgicalImplantation.
Dischargeorganization	Periodic and automatic stimulation
Advantages	Convenient for seizures with loss of consciousness without aura. Better compliance - does not require the patient to remember to take medication.
Sideeffects	Associated with surgical intervention and stimulation.
Disadvantages	Requires surgery with risk of complications. Highercosts.
Year of introduction of the method for treatment	European Union in 1994, and the US in 1997.

Table 1. Summary of the VNS electrostimulation method.

4. Conclusions

The diagnostic and therapeutic process is currently a major challenge for physicians. Effective, personalized treatment is a priority in preventing the development of epileptic seizures. The introduction of new, effective therapeutic methods makes it possible to improve the quality of life of patients. The described case can prove the effectiveness of the treatment of focal drug-resistant epilepsy with a vagus nerve stimulator (VNS). The authors of this article would like to emphasize the importance of selecting an appropriate, effective treatment method.

Author's contribution

Conceptualization, Michał Leśniewski; methodology, Dominika Brzuchacz, Klaudia Szukała; software, Michał Leśniewski; check, Dominika Brzuchacz, Klaudia Szukała; formal analysis, Patrycja Błaszczeć, Agata Miecznikowska; investigation, Michał Leśniewski, Natalia Siwak, Iwona Welian-Polus; resources, Patrycja Błaszczeć, Natalia Siwak; data curation, Dominika Brzuchacz, Iwona Welian-Polus; writing – rough preparation, Michał Leśniewski, Patrycja Błaszczeć; writing – review and editing, Iwona Welian-Polus, Agata Miecznikowska, Natalia Siwak; visualization, Michał Leśniewski, Agata Miecznikowska; supervision, Klaudia Szukała, Magdalena Chrościńska-Krawczyk; project administration, Klaudia Szukała, Magdalena Chrościńska-Krawczyk; receiving funding, Michał Leśniewski.

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Supplementary materials

Table 1: Summary of the VNS electrostimulation method.

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