Effects of COVID-19 on the Course of Epilepsy

G. V. Odintsova, O. V. Nezdorovin, and V. G. Nezdorovina

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A comparative analysis of two case histories showing the effects of COVID-19 and immunization with the Sputnik V vaccine on the dynamics of epilepsy is presented. The study was part of the “Epilepsy and COVID-19” research initiative in a cohort of patients with epilepsy divided into two groups: those experiencing COVID-19 and those immunized with vaccine against COVID-19. We present here a comparative analysis of two case histories: recurrence of seizures in COVID-19 in a young (male) patient and good tolerance of vaccine in an older (female) patient with comorbid pathology after surgical treatment of drug-resistant epilepsy. Patient K (age 32 years, male) had generalized genetic (idiopathic) epilepsy with remission of seizures for three years. On the background of mild COVID-19 the patient experienced recurrence of generalized clonic seizures with deterioration of electroencephalographic indicators. Patient F (age 59 years, female) had focal drug-resistant epilepsy with remission of seizures for three years following surgical treatment, with comorbid endocrine pathology. No side effects were seen on immunization with Sputnik V vaccine and clinical-electroencephalographic remission persisted. The results showed good tolerance of Sputnik V vaccine, with persisting remission of seizures after neurosurgical treatment of drug-resistant epilepsy in the older patient with comorbid pathology and the potential for recurrence of seizures in the young patient on the background of mild COVID-19. These results will help practicing physicians determine management tactics in epilepsy patients. Continuation of this research on the effects of COVID-19 disease and vaccination on the dynamics of epilepsy in a larger cohort is needed.

Keywords: epilepsy, COVID-19, vaccination, Sputnik V, seizures, remission.

The COVID-19 pandemic is one of the most acute medical-social problems in contemporary society. Reports on the neuroinvasiveness of SARS-CoV-2 have raised the question of whether infection might be associated with increases in the risk of exacerbation or recurrence of epileptic seizures in COVID-19. COVID-19 has now been shown to affect the nervous system [1]. Neurological manifestations are not leading in the clinical picture of coronavirus diseases, though neurological complications are seen in more than 30% of cases [2].

From the pathogenesis point of view, neurological impairments in COVID-19 may be due to cytokine storm, hypoxemia, deranged homeostasis (encephalopathy of critical states), and the neurotropism and neurovirulence of SARS-CoV-2 (isolated lesions to the cranial nerves, focal and diffuse CNS damage), as well as the combined actions of these factors [3]. There are as yet no data indicating increases in the incidence of the new coronavirus infection or a more severe course of illness in epilepsy patients. However, given the high prevalence of comorbid diseases in epilepsy patients aged over 60 years and the need to maintain constant use of antiepileptic drugs and follow up epilepsy patients, there is a whole series of difficulties in the management of these patients in the conditions of the COVID-19 pandemic [4]. COVID-19 in epilepsy patients can present in a rather different way as compared with the typical course of illness [5]. Convulsive syndrome is among the manifestations of COVID-19 in 0.8% of patients admitted to hospital for severe illness [6].

The problem of vaccination attracts just as much attention. Questions around vaccination in epilepsy are always related to dangers due to the risk of adverse impact.
on seizure frequency [7]. Vaccines were developed recently and experience of their use is still insufficient for accurate prediction of the risk of vaccination in epilepsy [8]. Vaccines against coronavirus infection due to SARS-CoV-2 must meet a number of requirements: safety, efficacy, and quality [9]. The fear of side effects of vaccines and lack of confidence in vaccine reliability are, as this is a new vaccine, major causes of indecisiveness and refusal to accept COVID-19 vaccine [10]. The Russian vaccine Sputnik V, the world’s first registered coronavirus vaccine, is the most studied vaccine at the current time. Sputnik V is among the preferred vaccines after the Pfizer/BioNTech vaccine and Russia is the most trusted vaccine manufacturer, along with the US [11].

The aim of the present work was to present a comparative analysis of two case histories demonstrating the effects of COVID-19 disease and immunization with Sputnik V vaccine on the dynamics of epilepsy.

The study is part of a prospective, uncontrolled observational study commissioned by Russian Ministry of Health (Topic No. 122011900530-8, “Risk stratification, selection of optimal surgical treatment strategy and prediction of outcomes in patients with drug-resistant structural epilepsy”). It was carried out at Polenov Neurosurgical Research Institute, a branch of Almazov National Medical Research Center, Russian Ministry of Health, in a cohort of patients with epilepsy divided into two groups: those experiencing COVID-19 and those immunized with vaccine against COVID-19.

Patient questionnaires were conducted from February 2021 using a questionnaire with four sections: demographic data, history of epilepsy, tolerance of disease/vaccination, and dynamics of epilepsy after disease/vaccination. The updated “Epilepsy and COVID-19: clinical-epidemiological and therapeutic aspects” database was registered (Database Registration Certificate No. 2021621297 of June 18, 2021). The data are currently undergoing statistical analysis in an observational, comparative, open cohort study. All patients signed informed consent. The study was approved by the Ethics Committee.

A comparative analysis of two case histories is presented: recurrence of seizures in COVID-19 in a young (male) patient and good tolerance of vaccination in an older (female) patient after surgical treatment of drug-resistant epilepsy with comorbid endocrine pathology.

**Clinical Case 1.** Patient K (male, age 32 years) attended the epileptologist in March 2021 complaining of recurrent epileptic seizures on the background of COVID-19 disease after remission for three years.

The history revealed a diagnosis of “G40.3. Generalized genetic (idiopathic) epilepsy (IGE) with generalized convulsive seizures (GCS) on waking. Onset of disease at age 13 years with morning GCS.” The diagnosis “Single epileptic seizure” was made. Antiepileptic drugs (AED) were not given. A second GCS occurred after six months, in the morning. Benzobarbital was initiated at a daily dose of 200 mg. On this background, GCS with a frequency of one every 4–6 months was noted. In 2017, benzobarbital was changed to valproic acid. Use of valproic acid at a daily dose of 1500 mg produced remission of seizures from 2017 with electroencephalographic remission from 2019.

The patient contracted acute COVID-19 on November 24, 2020, with elevation of temperature to 37.4°C. Increased temperature persisted for two days with a peak of 37.4°C. The clinical picture included weakness for one week and anosmia for three days, but no cough or pneumonia. A positive PCR test for SARS-CoV-2 was obtained. Generalized tonic-clonic seizures (GCS) occurred in the mornings in the hour after waking on day 4 of COVID-19 illness on the background of normal temperature, and were accompanied by headache, weakness, and drowsiness in the postictal period. No signs of postcovid syndrome were seen four months after illness.

**Neurological status** – no focal abnormalities. No motor, sensory, coordination, autonomic, or mental disorders seen.

The patient underwent electroencephalographic (EEG) investigation – 3-h video-EEG monitoring – two months after recurrence (Fig. 1). The major biorhythmics were age-appropriate. Mild diffuse changes in brain bioelectrical activity, more in the anterior areas, were seen. Sleep was modulated in terms of phases and stages. Diffuse, bilaterally synchronous and moderate asynchronous discharges of the “sharp (peak) – slow-wave complexes” type were seen during sleep and at 3 min of hyperventilation, with the accent on the anterior areas, usually right > left.

Considering the recurrence of seizures and deterioration of EEG data, the valproic acid dose was increased to 2000 mg/day. Safety investigations (clinical, blood biochemistry) showed no pathology. The duration of follow-up after recurrence of epileptic seizures was about a year and seizure monitoring continues.

Thus, a patient with IGE in remission of seizures for three years experienced recurrence of GCS with deterioration...
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with lacosamide and levetiracetam did not result in seizure control. Despite the focal nature of the seizures, without loss of consciousness, the patient experienced significant degradation of wellbeing and quality of life.

A brain MRI scan (3 T, epilepsy protocol) with targeted investigation of the temporal lobe (Fig. 2) revealed cortical dysplasia in the projection of the left temporal lobe, with early sclerotic changes to the left hippocampus and left amygdaloid body, and external hydrocephalus ex vacuo. A brain PET/CT scan with 18F-deoxyglucose showed signs of hypometabolism in the lateral parts of the prefrontal cortex of both hemispheres, mainly in the left hemisphere, in the parasagittal parts of the prefrontal cortex, and the inferior areas of the left parietal lobe of the left hemisphere. Video-EEG monitoring showed marked diffuse changes in brain bioelectrical activity, a stable focus of interictal epileptic activity in the left temporal areas with periodic propagation into the left frontal, central, and parietal areas, and recording of an ictal pattern in the left temporal area.

Given detection of the epileptogenic lesion (focal cortical dysplasia in the left temporal lobe) with a location corresponding to the irritation zone and the seizure initiation zone, as well as the fact that drug resistance had developed, a meeting of the functional epileptology group of the institute took the decision to carry out temporal resection. Microsurgical removal of the epileptogenic focus was performed on June 13, 2018, i.e., left-sided microsurgical anterior temporal resection, amygdalotomy, and anterior hippocampotomy, under electrophysiological control. Video-EEG monitoring on postoperative day 12 revealed diffuse changes in brain bioelectrical activity with deformation of the main rhythm. The fronto-temporal area of the left hemisphere periodically showed pathological activity consisting of regional bursts of EEG indicators on the background of mild COVID-19, requiring correction of the AED dose consisting of an increase in the daily valproic acid dosage.

Clinical Case 2. Patient F (female, age 59 years), attended after immunization, with Sputnik V for monitoring of EEG remission of epilepsy.

The patient received a second dose of vaccine against the new coronavirus infection with the Sputnik V vaccine on February 29, 2021. The case history revealed a family contact with a COVID-19 patient in October 2020: the patient’s spouse died from the infection though the patient herself did not fall ill; a PCR test for coronavirus SARS-CoV-2 was negative.

The first dose of vaccine was followed by flu-like symptoms: temperature 37.5°C, chills, and weakness on the day of immunization with complete recovery of wellbeing on day 2. No flu-like symptoms were seen after the second dose: there was no rise in temperature and the patient felt normal.

The history showed that the patient had had epilepsy from age 53 years. The diagnosis was “G40.3: Focal structural epilepsy, temporal, remission for three years. Concomitant diagnosis: type 2 diabetes mellitus, insulin-dependent.” The history included seizures without loss of consciousness in the form of unpleasant sensations behind the sternum, spreading in waves to the head, lasting 1 min, and accompanied by palpitations, pallor, weakness, and drowsiness in the postictal period. Seizure frequency during the first year of illness was up to 10 per day. AED therapy was started, with prescription of lamotrigine at a daily dose of 200 mg, which decreased seizure frequency by 25%. Due to insufficient efficacy, lamotrigine was replaced by lacosamide 600 mg/day with improvement, though control of seizures was not obtained. Transfer to multidrug therapy with lacosamide and levetiracetam did not result in seizure control. Despite the focal nature of the seizures, without loss of consciousness, the patient experienced significant degradation of wellbeing and quality of life.

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interactions of AED and drugs used to treat COVID-19, and because of the risk of interruptions to AED therapy, stress in patients, and poor compliance. In the first case, even mild COVID-19 provoked recurrence of epileptic seizures. In these case histories, patient K received valproic acid and patient F multitherapy with lacosamide and levetiracetam. Published data indicate that among wide-spectrum AED, only levetiracetam treatment has maximal safety for epilepsy patients needing treatment for severe viral infections such as COVID-19 [13]. Drugs of other groups, effective in both diseases – epilepsy and COVID-19 – are now being investigated. Research has demonstrated that melatonin can have antiviral, antidepressant, antineoplastic, neuroprotective, antioxidant, and gonadotropic actions and can produce some therapeutic efficacy in COVID-19 due to the valuable effect of being able to decrease proinflammatory cytokines, which corresponds to reductions in the intensity of inflammation and cytokine storm in patients with COVID-19 [14]. Virtually all patients contracting COVID-19 complain of severe asthenization and emotional lability, and sometimes have the features of asthenoneurotic and anxious-phobic disorders and apathetic-abulic syndrome, which requires rehabilitation measures and courses of restorative neurotrophic and nootropic therapy [15]. In terms of long-term prognoses, neurologists have to deal with cognitive and psychoemotional disorders and other pathologies [16]. Microangiopathy, immunothrombosis, and disseminated intravascular coagulation syndrome develop in the severe form of COVID-19, while 40% of patients with the severe form of COVID-19 show impairments to CNS functions [16]. Predictors of a positive course of epilepsy on the background of COVID-19 include young age, absence of comorbid somatic pathology, remission of epileptic seizures, and use of modern drugs without interdrug interactions with the antibiotics and antivirals used in the treatment of COVID-19 [17]. However, the absence of any increase in the incidence of
COVID-19 among epilepsy patients does not exclude provocation of recurrence of epileptic seizures during remission on the background of infection.

An alternative in this situation is vaccination. Vaccines are known to be effective in creating long-lasting immune protection against infectious diseases [9]. The first step towards improving vaccine use by patients may be open discussion of hesitancy on the part of patients and their carers in relation to COVID-19 vaccination, while clinicians should be aware that the vaccine has been approved and is safe and effective [18]. During phase III clinical trials, the Sputnik V vaccine demonstrated high efficacy, immunogenicity, and safety. Study data show that the efficacy of the Sputnik V vaccine against COVID-19 is 91.6%. The level of virus-neutralizing antibodies in volunteers vaccinated with Sputnik V was 1.3–1.5 times greater than in patients recovering from COVID-19 [19].

Thus, research into the dynamics of epilepsy on the background of COVID-19 and tolerance of vaccination continues throughout the world and experience in managing patients in the conditions obtaining in the pandemic is accumulating.

Conclusions. Good tolerance of the Sputnik V vaccine in an older patient with remission of drug-resistant epilepsy following surgical treatment and with comorbid disease and possible recurrence of seizures after three years of remission in a young patient with IGE and mild COVID-19 were demonstrated. Reliable results require research to be continued on the effects of disease and vaccination against COVID-19 on the dynamics of epilepsy with comparisons in a larger cohort.

The authors declare no conflict of interest.

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