CASE STUDY

DIFFERENTIAL DIAGNOSIS OF PAROXYSMAL STATES: LITERATURE REVIEW AND ANALYSIS OF A CLINICAL CASE ON THE EXAMPLE OF CLOCCS-SYNDROME IN A YOUNG MAN

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Anna A. Voitiuk[1,2], Tetyana A. Litovchenko[1], Olena N. Borodai[1,3], Nataliia A. Rudkivska[3]
[1]KHARKIV MEDICAL ACADEMY OF POSTGRADUATE EDUCATION, KHARKIV, UKRAINE
[2]MEDICAL CENTRE "NEURON", KHARKIV, UKRAINE
[3]KHARKIV MILITARY HOSPITAL OF NORTH REGION, KHARKIV, UKRAINE

ABSTRACT

Diagnosis of paroxysmal conditions in neurology is one of the most difficult problems. Particular difficulties are caused by differential diagnosis of epileptic and non-epileptic paroxysmal states. There are no absolutely pathognomonic signs of epileptic and non-epileptic seizures. False positive diagnosis of epilepsy occurs in 2-71% of cases.

Diagnosis of paroxysmal conditions requires an integrated approach to the problem and includes not only a clinical examination, but also a thorough history taking, neurophysiological, neuroimaging, laboratory research methods, involves the involvement of other specialists.

The article presents a clinical case of 27-year-old young man who was initially misdiagnosed. Using the methods of functional and laboratory diagnostics, the patient was diagnosed correctly. Instead of idiopathic epilepsy, he was diagnosed with cytotoxic lesions of the corpus callosum (CLOCCs-syndrome associated with an infectious process) with motor paroxysms of non-epileptic genesis.

Thus, using the example of this clinical case, it has been shown that the differential diagnosis of epileptic and non-epileptic paroxysmal states presents significant difficulties for a practicing neurologist.

KEY WORDS: epilepsy, non-epileptic states, diagnostic, Epstein-Barr virus, CLOCCs-syndrome

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INTRODUCTION

The paroxysmal conditions are one of the most common pathological disorders in the daily practice of a neurologist. The *paroxysm* is usually understood as a sudden deterioration in health, which is manifested or accompanied by episodes of illness, or a sharp, short-term (more often repeated) exacerbation of a chronic painful condition. The paroxysmal conditions, as a rule, are not independent nosological forms, but represent a manifestation of a particular pathology of the central nervous system, but it is the presence of paroxysmal symptoms that often causes seeking medical help. These conditions are not only a medical problem, but also a social problem [1].

The urgency of the problem of paroxysmal pathology is due to the fact that some paroxysms threaten the lives of patients, and most of the paroxysmal conditions are disabling.

According to the classification according to V. A. Karlov, all paroxysms are divided into:

1) epileptic;

2) non-epileptic (syncopal states, fainting, collapse, stress attacks with compression of the vertebral artery, facial paroxysms, hypo- and hyperkaliemic myoplegia, myasthenic crisis, as well as vegetative disorders, muscle dystonia and other paroxysmal motor diseases, restless legs syndrome and periodic movements in sleep, various paroxysmal neuralgia) [2].

Non-epileptic states can be defined as sudden, destructive, changing behavior, sensitivity, thinking, sensations that are usually limited in time and similar to or mistaken for epileptic seizures [3].

These paroxysmal disorders are extremely heterogeneous in nature. A significant part of them is associated with neuroses and psychogenic disorders. However, somatogenic disorders (migraine, panic attacks, vestibular paroxysms, hyperparathyroidism, etc.) occupy an equally significant place in the genesis of these conditions [4].

A seizure is the transient manifestation of abnormal excessive or synchronous electrical brain activity that causes convulsions, loss of consciousness, and or lapses of consciousness. The underlying cause of seizures is a state of neuronal hyperexcitability that may be temporary (e.g., due to electrolyte imbalances) or more permanent in nature (e.g., due to inherited or acquired neural abnormalities). Seizures can be triggered by a variety of circumstances depending on age, environmental factors, and underlying conditions. Acute symptomatic seizures (provoked seizures) have identifiable precipitating factors (e.g., stroke,

Table I. Probability of error in patients with suspected epilepsy according to population and cohort studies

Author	Presumably the diagnosis of epilepsy	Misdiagnosis	CVD syncope
Scheepers B. (Seizure 1998)	261	49	15
King M.A. (Lancet 1998)	496	178	60
Smith D. (QJM 1999)	184	46	13
Grubb B.P. (Ann Intern Med 1991)	15	10	10
Linzer M. (Am J Med 1994)	12	12	5/7
Zaidi A. (JACC 2000)	74	31	29

traumatic brain injury, alcohol withdrawal), whereas unprovoked seizures occur in the absence of identifiable causes. Reflex seizures are states that occur consistently in response to a particular trigger [5].

The problem of differential diagnosis of paroxysmal states is one of the most difficult tasks in neurology. It is due to a number of subjective and objective reasons: an insufficiently complete and accurate description of the clinical features of the seizure by patients and their relatives, often low information content of additional laboratory and instrumental research methods, the transient nature of disorders and often the absence of objective symptoms in the interparoxysmal period, insufficient awareness of doctors and medical staff about the clinical features of a number of paroxysmal conditions, etc. Among neurological paroxysmal conditions, the most difficult, requiring highly qualified clinicians is the differential diagnosis of epileptic and non-epileptic states. Sudden disturbances of consciousness, paroxysmal motor disorders, paroxysmal changes in behavior, crisis vegetative states are often mistaken for epilepsy [6].

Published retrospective and prospective studies suggest that 1 out of 4 patients with "epilepsy" was mistakenly diagnosed based on the analysis of clinical manifestations and the results of tilttest.

According to leading epileptologists, up to 20-30 % of patients diagnosed with epilepsy and receiving antiepileptic treatment suffer from non-epileptic states. Up to 45 % of patients diagnosed with refractory epilepsy have non-epileptic states (Table I).

Y. Xu et al (2016) in their review cite data indicating a significant number of false diagnostics of epilepsy even in specialized highly qualified medical institutions (Fig. 1) [7].

The diagnosis of paroxysmal states in neurology is one of the most difficult problems. The differential diagnosis of epileptic and non-epileptic paroxysmal states causes particular difficulties, due to the lack of absolutely reliable clinical markers of the disease in the interparoxysmal period, not always sufficient information content of instrumental research methods and insufficient awareness of doctors [8].

The problem of differential diagnosis of paroxysmal conditions is difficult, since it belongs to the category of multidisciplinary. The he main problems of differential diagnosis of paroxysmal states lie in the field of neurology, cardiology and psychiatry in patients [8].

The article presents a clinical case of an erroneous interpretation of the diagnosis in a 27-years-old young man, taking into account complaints, anamnesis of the disease and life, neurological status, laboratory results, features of the EEG, MRI.

ETHICAL ASPECTS

The work complies with the ethical standards of the Declaration of Helsinki by the World Medical Association. A written informed consent was obtained authorizing the publication of the medical history and the results of the examination.

CASE REPORT

Patient P., 27 years old (06.08.1993), was admitted to the military hospital on 08.04.2021 with complaints of periodic, with a frequency of 1-2 times a month, attacks of tonic tension of the muscles of the right extremities, which last several seconds, are provoked by active movements.

It is known from the anamnesis of the disease that periodic attacks of tension in the right extremities have been bothering since the age of 12, the patient has not sought medical help until now.

The patient notes the deterioration of the condition in the form of increased frequency of seizures and an increase in their duration for the last 2 years.

He consulted a unit doctor in March 2021. An MRI scan of the brain was performed, it was not found pathology. The patient was referred to the neurological department of military unit for further examination and treatment.

At the time of the examination, the patient's general condition is satisfactory. A man for a regular physique. The skin is clean, normal color. The visible mucous membranes are normal color. The thyroid gland is not enlarged, it is painless. Peripheral lymph nodes are not enlarged. Above the lungs, a pulmonary sound is heard,

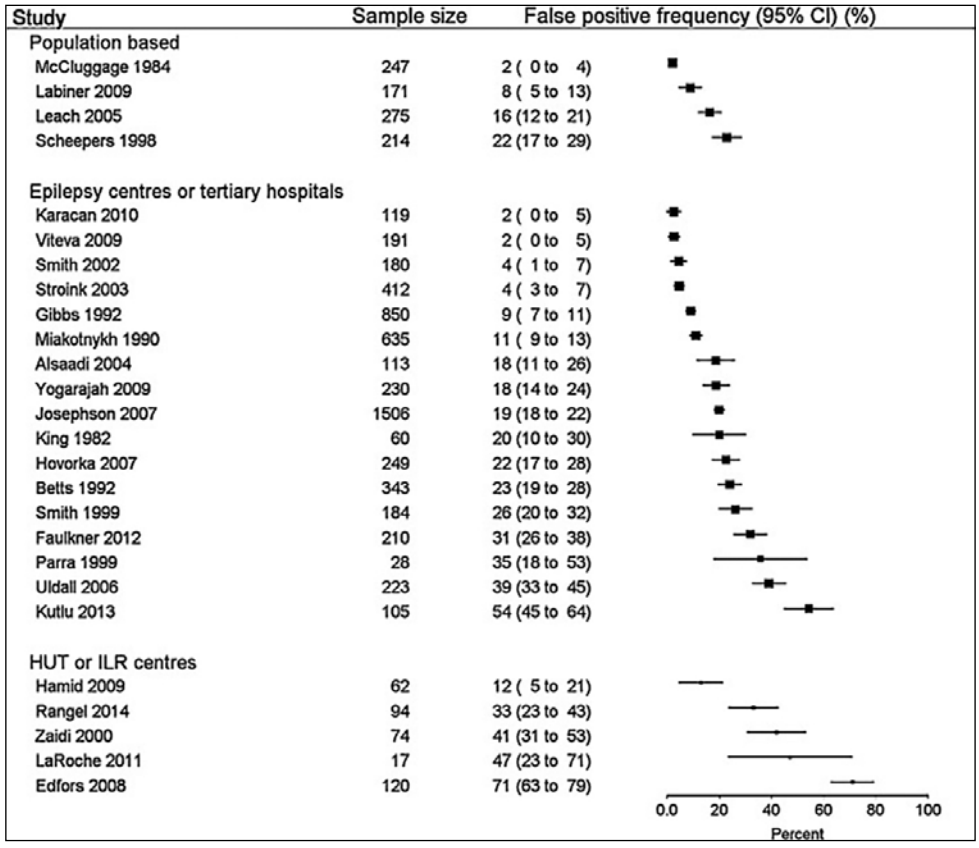

Fig. 1. Observational studies of the frequency of false positive diagnosis of epilepsy

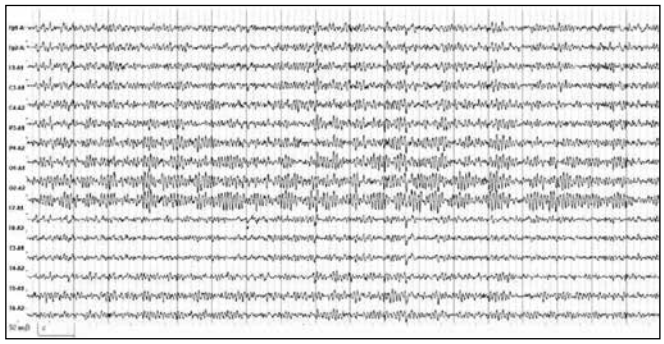

Fig. 2. The EEG fragment of patient P., 1993

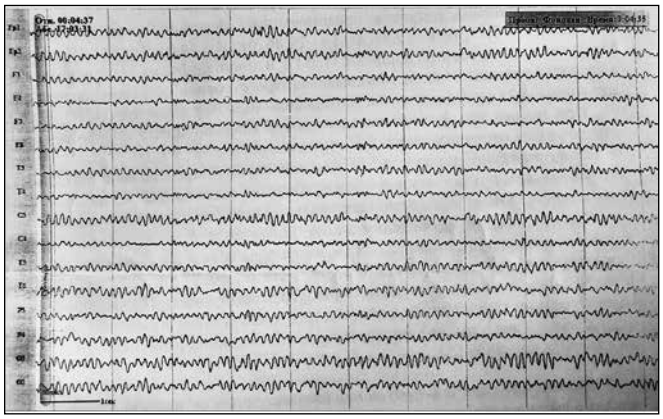

Fig. 3. The EEG-video monitoring fragment of patient P., 1993. Rec=23-05-2021 16-58 {All record}

vesicular breathing. The pulse is rhythmic, heart rate is 66 beats/min, blood pressure is 120/80 mm Hg. The boundaries of the heart are within the normal range. The heart tones are clear, the rhythm is correct. The abdomen is soft, painless on palpation. The liver and spleen are not enlarged. Pasternatsky symptom is negative on both sides. There are not edemas. Physiological functions are controlled.

In the neurological status: the level of consciousness is clear, it is oriented correctly in time and place, intelligence corresponds to age. He is available to the productive contact in full. Meningeal signs are negative. Palpebral fissures, pupils are D=S. The light reflex is of average vivacity. The movements of the eyeballs are possible in full. Convergence is weakened. Nystagmus, diplopia are absent. The nasolabial folds are symmetrical. The pharyngeal reflex is triggered, swallowing is not disturbed. The tongue is moist, is not overlaid, along the middle line. Speech is not broken. Phonation is normal. There are not bulbar violations. Muscle tone is preserved. Muscle strength is sufficient. Tendon and periosteal reflexes from the hands D=S, knee D=S, Achilles D=S, of average vivacity. There are not pathological feet signs. Sensitive disorders are not detected. The finger and knee-heel tests are performed satisfactorily. He is persistent in the Romberg pose. The coordination tests are performed satisfactorily. The vegetative reactions are revived.

During the entire period of stay in the military hospital, the following studies were conducted:

There were not significant deviations from the reference values in general clinical blood and urine tests.

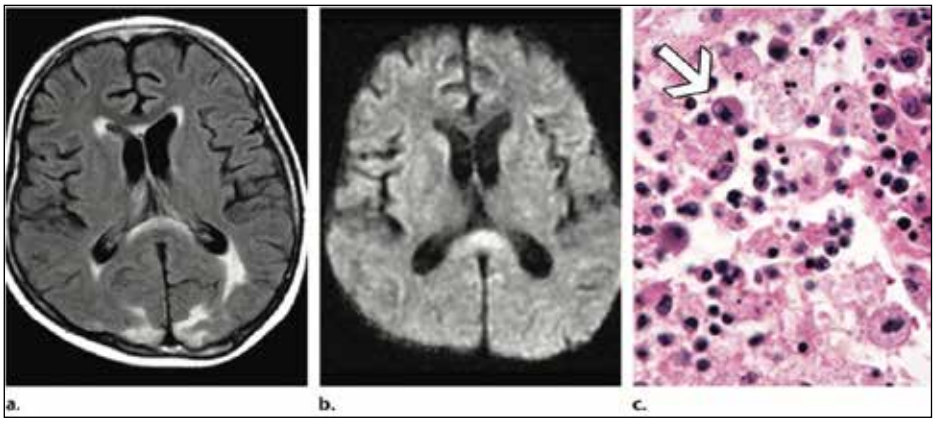

Fig. 4. Infection-associated CLOCCs-syndrome in a 27-year-old man, in whom EBV infection was diagnosed. (a) Axial FLAIR MR image shows a hyperintense oblong splenial lesion and mild involvement of the anterior corpus callosum. (b) Axial diffusion-weighted MR image shows reduced diffusion in the callosal lesions. (c) High-power photomicrograph shows infiltration with hemophagocytic histiocytes (arrow) and atypical lymphocytes, findings consistent with EBV-associated hemophagocytic lymphohistiocytosis. (H-E stain; original magnification, ×400).

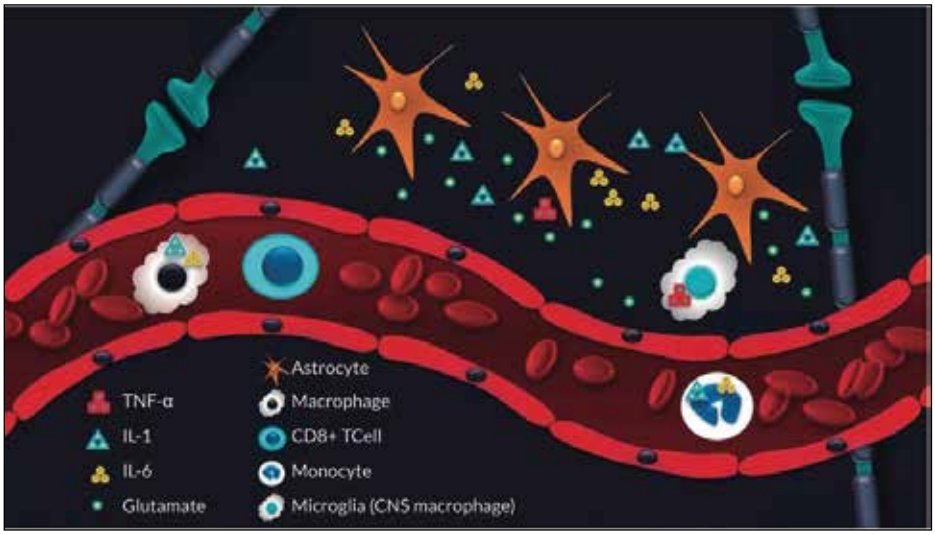

Fig. 5. Drawing shows the cells and cytokines that are important in the development of CLOCCs. Cell-cytokine interactions leads to massively elevated extracellular glutamate levels

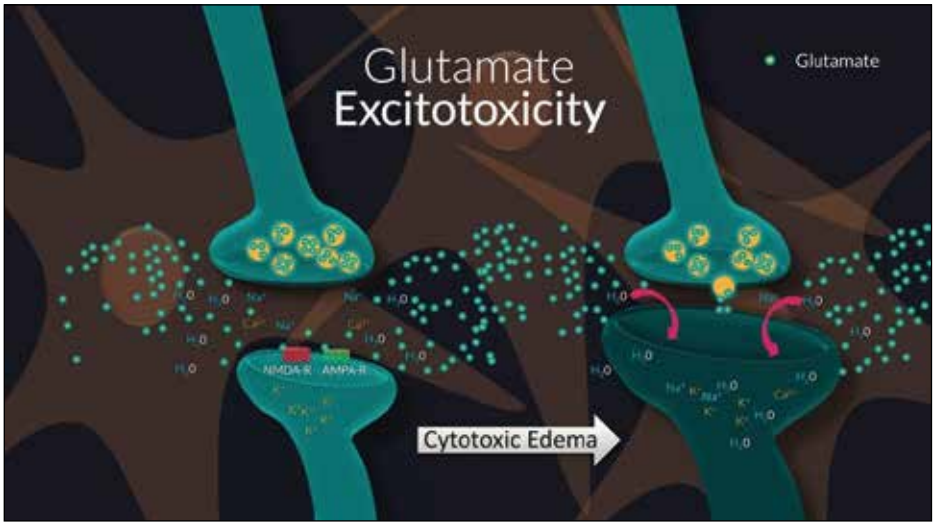

Fig. 6. Drawing shows glutamate excitotoxicity. The extracellular glutamate binds with N-methyl-D-as- partate receptors (NMDA-R) and α-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid receptors (AMPA- R), allowing sodium ions (Na+) and calcium ions (Ca+) to enter cells, potassium ions (K+) to leave cells, and water (H2O) to enter (pink arrows) and become trapped within neurons. This process leads to cytotoxic edema. Because the intracellular water cannot freely move, cytotoxic edema is manifest as reduced diffusion at MR imaging

Biochemical blood assay (09.04.2021): ACT 18,7 Od/L; ALT 16,1 Od/L; blood urea 2,9 mmol/L; creatinine 91,3 mcmol/L; blood glucose teste 5,3 mcmol/L; LPH 55,7 Od/L.

SARS-CoV-2 antibody assay to the nucleocapsid antigen (09.04.2021): IgM and IgG were not detected.

Thyroid hormones (13.04.2021): T4 – 18,8 mmol/L; TSH – 1,09 мсМО/mL; TPO – 11,8 Od/mL.

Rapid Plasma Reagin test (09.04.2021): negatively.

ECG (08.04.2021): sinus rhythm. Early Ventricular Repolarization Syndrome.

Fluorography of chest organs (09.04.2021): without pathological findings.

EEG (15.04.2021): pathological EEG complexes have not been registered.

ECHO (13.04.2021): without pathological findings.

Diagnostic ultrasound of thyroid (13.04.2021): without pathological findings.

Head MRI (27.03.2021): on the hands.

Against the background of a complete collection of complaints, anamnesis of the disease and life, as well as the

results of laboratory and instrumental research methods, this patient was diagnosed with «Idiopathic epilepsy with simple partial tonic seizures. S-shaped scoliosis of the thoracic spine of the first degree» [8], [17].

The patient was prescribed treatment: compliance with the regime, diet, taking carbamazepine 0.2 2 tablets 2 times a day.

During the treatment in the military hospital, the patient did not notice a significant improvement. Isolated seizures of tonic tension of the muscles of the right extremities were recorded. The patient's condition is satisfactory.

The patient is recommended to avoid physical and emotional overloads, observe the work and rest regime, follow up with a neurologist, take levicitam 250 mg 2 times a day for 2 weeks, then 500 mg 2 times a day for a long time. The patient was discharged from the military hospital on 23.04.2021.

Subsequently, patient P. was consulted by a neurologist on 06.05.2021. The patient complained of periodic seizures in the right extremities in the form of muscle contractions, which are provoked by emotional and physical exertion. The patient has paroxysmal states of unclear genesis, which need to be clarified. It has not the features in the neurological status of a patient. It is recommended to do a diagnostic head MRI with 3 T – the presence of cortical dysplasia, the presence of focal pathology; and also to do EEG and EEG video monitoring (24 hours) with the cancellation of levicetam 4 days before the start of the examination. The next inspection after the additional examination.

The patient underwent an EEG (06.05.2021): a medium-voltage EEG torrent with dominant δ-activity. The main violations of bioelectric activity in the alpha-rhythm range, the correctness of its zonal distribution, amplitude values and fusiformity are preserved, the alpha-rhythm is expressed by flashes of up to several seconds, separated from each other by sections of low-amplitude polymorphic slow activity, the intervals between alpha-rhythm flashes are filled with a flat EEG, generalized flashes of slow-wave activity, mainly in the central leads, against the background of normal electrical activity. It were not detected the specific EEG phenomena (Fig. 2) [14], [15].

The patient performed EEG video monitoring (24 hours) on 23.05.2021. The following conclusion was obtained: diffuse disturbances in the bioelectrical activity of the brain and local changes were not registered. Single epileptiform discharges were recorded in the inferior forehead-temporal region. Revealed dysfunction of the median structures of the brain. The seizures recorded during the survey are most likely non-epileptic in nature (Fig. 3) [14], [15].

Head MRI 3 T (epileptic protocol) (09.05.2021): MR-sings of cytotoxic lesions of the corpus callosum (CLOCCs-syndrome). MR-signs of mesial temporal sclerosis and cortical dysplasia of the brain were not detected (Fig. 4).

The neurologist consultation (31.05.2021): The complaints are the same. It has not the features in the neurological status of a patient. Taking into account the data of instrumental research methods, the patient was diagnosed with "Cytotoxic lesion of the corpus callosum (CLOCCs-syndrome) with motor paroxysms of non-epileptic genesis". It were recommended: consultation and examination by an infectious diseases specialist-virologist. Levetiracetam should be gradually discontinued.

After consultation with a neurologist, the patient turned to the laboratory and donated blood to the infection panel, in particular for the presence of antibodies to the Epstein-Barr virus.

Assay for the presence of IgG antibodies to the Epstein-Barr virus capsid antigen VCA (EBV VCA IgG) (04.06.2021): 15,39 Od.

Assay for the presence of IgM antibodies to the Epstein-Barr virus capsid antigen VCA (EBV VCA IgM) (04.06.2021): 0,31 Od.

Assay for the presence of IgG antibodies to the Epstein-Barr virus nucleonic antigen (EBV EBNA-1 IgG) (04.06.2021): 12,82 Od.

Thus, the constant presence of VCA IgG in high titers indicates a chronic phase of infection caused by the Epstein-Barr virus. The reason for the positive result may be the presence of active immunity due to a previously transmitted infection, along with the detection of antibodies to the nuclear antigen (EBNA) and the absence of IgM to the capsid antigen (VCA) of the Epstein-Barr virus.

After another visit to the neurologist, the patient was diagnosed with the following: "The consequences of neuroinfection in the form of cytotoxic lesions of the corpus callosum (CLOCCs-syndrome) with motor paroxysms of non-epileptic genesis. Viral infection caused by the Epstein-Barr virus is in remission".

An example of differential diagnosis of paroxysmal states using instrumental methods was presented to Your attention. This clinical case demonstrated how, thanks to the methods of functional diagnostics, the patient's diagnosis was changed from idiopathic epilepsy to CLOCCs syndrome of non-epileptic genesis associated with infection.

Cytotoxic lesions of the corpus callosum (CLOCCs) is a concept that combines a heterogeneous group of pathological conditions that cause changes in the signaling characteristics of the corpus callosum, in particular, the roller [9].

Cytotoxic lesions of the corpus callosum (CLOCCs) represent a group of conditions that cause MRI signal intensity changes in the corpus callosum. Etiology of this phenomenon is very heterogenous. CLOCCs are associated with a spectrum of metabolic disorders, drug therapy, infections, epileptic seizures and many other causes.

Complex interdependent mechanisms regulate cytokine levels and, ultimately, glutamate levels in the brain. With trauma, infection, and inflammation, macrophages become active and release the inflammatory cytokines interleukin 1 (IL-1) and IL-6, beginning the cascade that leads to cytokinopathy. Monocytes then activate and also release IL-1 and IL-6. T-cells are subsequently recruited and affect the endothelial cells, making the endothelial cells leaky (breaking down the blood-brain barrier) and stimulating them to produce tumor necrosis factor-α (TNF-α). Astrocytes, in turn, are stimulated by IL-1 to release glutamate and block reuptake of glutamate, thus increasing extracellular gluta-

mate. Microglia, which are the macrophages of the central nervous system (CNS), subsequently become activated and produce more cytokines and may initiate demyelination. Many of these cell-cytokine relationships include feedback loops that are exponentially amplified. The result of this cytokinopathy is massively increased amounts of glutamate in the extracellular space at levels 100 times the normal level or more (Fig. 5) [10].

The CLOCCs demonstrate increased signal intensity on fluid-attenuated inversion-recovery (FLAIR) magnetic resonance (MR) images and show decreased signal intensity on T1-weighted MR images [11]. Diffusion is reduced (mean ADC value, 0.31×10^{-3} mm^2/sec; range, 0.13×10^{-3} mm^2/sec to 0.48×10^{-3} mm^2/sec). CLOCCs lack enhancement on contrast material–enhanced images, tend to be midline, and are relatively symmetric. The involvement of the corpus callosum typically shows one of three patterns: (a) a small round or oval lesion located in the center of the splenium, (b) a lesion centered in the splenium but extending through the callosal fibers laterally into the adjacent white matter, or (c) a lesion centered posteriorly but extending into the anterior portion of the corpus callosum (Fig. 6).

CLOCCs are secondary lesions associated with drug therapy, malignancies, infections, subarachnoid hemorrhage (SAH), metabolic disorders, trauma, and other entities. CLOCCs demonstrate reduced diffusion from cytotoxic edema. They are usually ovoid and located in the splenium but may be more extensive, with involvement of the body of the corpus callosum and the genu. CLOCCs are frequently but not invariably reversible. When they are present, their underlying cause should be sought and addressed [12], [16].

VARIANTS OF CLOCCS BY ETIOLOGY

I. CLOCCs associated with drugs/toxins;
– antidepressants (amitriptyline);
– antipsychotics (clozapine);
– chemotherapeutic drugs (cyclosporine, fluorouracil);
– corticosteroids;
– pesticides (methyl bromide);

II. CLOCCs associated with the neoplastic process;
CLOCCs can be a consequence of a malignant process within the central nervous system. There is evidence of the association of CLOCCs with malignant tumors of other organs, which is most likely associated with chemotherapy. The probable mechanism of CLOCCs occurrence in this scenario is the infiltration of tumor cells with the subsequent release of cytokines into the CSF.

III. CLOCCs associated with the infectious process;
There are reports of cases of CLOCCs in brain abscesses, encephalitis and meningitis. The main mechanism is an increase in the level of pro-inflammatory cytokines, an increase in the permeability of the BBB and further events that contribute to the development of excitotoxicity.
– viruses (influenza, measles, herpes, mumps, adenovirus, chickenpox, rotavirus);
– bacteria (salmonella, legionnaires ' disease);
– mycobacteria (tuberculous meningitis);

IV. CLOCCs associated with metabolic disorders;
– electrolyte disorders (hyperammonemia, hyper- and hyponatremia);

Ammonia is one of the main participants in the pathogenesis of hepatic encephalopathy. The acute toxic effect of ammonia is a massive release of cytokines and the further development of excitotoxicity, mainly mediated by NMDA receptors.
– hemolytic-uremic syndrome;
– hepatic encephalopathy;
– hypoglycemia;
– Markiafava-Bignami disease;
– osmotic demyelinating syndrome;
– Wernicke's encephalopathy;
– Wilson's disease;

V. CLOCCs associated with subarachnoid hemorrhages;
In patients with subarachnoid hemorrhages (SAH), increased levels of interleukins 1-beta, 6 and TNF-alpha are found in the CSF, which may be the cause of the appearance of CLOCCs.

VI. CLOCCs associated with traumatic injury;
The most common cause of CLOCCs in the corpus callosum is diffuse axonal damage. The restriction of diffusion in the focus in the corpus callosum is observed in the acute phase. This may be due to several reasons: (a) increased extracellular glutamate due to axon damage and (b) secondary release of cytokines and glutamate [16].

CONCLUSIONS

Cytotoxic lesions of the corpus callosum are secondary lesions to a variety of causes, most notably metabolic diseases, seizures, infectious diseases, and drug action.

The pathophysiological processes leading to signaling changes in corpus callosum (CC) have not yet been fully understood and described. This is probably the result of a cascade of complex mechanisms, especially inflammatory changes and an increase in extracellular glutamate levels in the brain, manifesting as cytotoxic edema.

Clinical manifestations are very variable. Neurological impairment varies from mild to severe, but may also be absent. The most common non-specific symptoms are headaches or fever.

The main examination method is MR with a typical finding of diffusion restriction with correlate on apparent diffusion coefficient (ADC) maps.

The key to successful therapy is to identify and treat the cause. The lesions are reversible in most cases, and the prognosis is very good, but also depending on the underlying pathology.

As the availability of MRI has improved and the number of examinations has increased in recent years, the number of findings that can be termed cytotoxic CC lesions is also increasing. This trend will certainly continue in the future, which will allow a further understanding of the causes, origin, manifestations and other mechanisms of CLOCCs, which have not been described, with a larger number of patients.

REFERENCES

1. Guzeva V. I. Epilepsiya i neepilepticheskie paroksizmal'nye sostoyaniya u detej: monografiya [Epilepsy and non-epileptic paroxysmal states in children: monography]. M. 2007, 568p. (in Russian)
2. Karlov V. A. Epilepsiya u detej i vzroslyh zhenshchin i muzhchin [Epilepsy in children and women and men]. M.. 2010, 717p. (in Russian)
3. Dubenko A. E., Korostij V. I. Diagnostika i terapiya nepsihoticheskih psihicheskih rasstrojstv u bol'nyh epilepsiej [Diagnosis and therapy of non-psychotic mental disorders in patients with epilepsy]. Zdorov'e Ukrainy. Tematicheskij nomer «Nevrologiya. Psihiatriya». 2011; 1 (16): 54-57. (in Russian)
4. Ajvazyan S. O. Neepilepticheskie paroksizmal'nye sostoyaniya, imitiruyushchie epilepsiyu [Non-epileptic paroxysmal states that mimic epilepsy]. Epilepsiya i paroksizmal'nye sostoyaniya, 2016; 4:23–33. (in Russian)
5. Panayiotopoulos C.P. A Clinical Guide to Epileptic Syndromes and their Treatment. 2nd ed. London: Springer. 2007, 401p.
6. Litovchenko T. A. Differencial'naya diagnostika epilepticheskih pripadkov i sinkopal'nyh pristupov [Differential diagnosis of epileptic seizures and syncopal seizures]. Mezhdunarodnyj nevrologicheskij zhurnal, 2010;4:34. (in Russian)
7. Xu Y., Nguyen D., Mohamed A. et al. Frequency of a false positive diagnosis of epilepsy: A systematic review of observational studies. Seizure. 2016; 41: 167–174. doi: 10.1016/j.seizure.2016.08.005.
8. Vlasov P. N. Differencial'naya diagnostika osnovnyh paroksizmal'nyh sostoyanij v praktike nevrologa i terapevta [Differential diagnosis of the main paroxysmal conditions in the practice of a neurologist and therapist]. Farmateka, 2008;15:72-78. (in Russian)
9. Kim S.S., Chang K.H., Kim S.T. et al. Focal lesion in the splenium of the corpus callosum in epileptic patients: antiepileptic drug toxicity? AJNR Am J Neuroradiol. 2019;20(1): 125–129.
10. Verrotti A., Basciani F., Trotta D. et al. Effect of anticonvulsant drugs on interleukins-1, -2 and -6 and monocyte chemoattractant protein-1. Clinш Exp Med. 2001;1(3):133–136.
11. Kallenberg K., Bailey D.M., Christ S. et al. Magnetic resonance imaging evidence of cytotoxic cerebral edema in acute mountain sickness. J Cereb Blood Flow Metab. 2007;27(5):1064–1071.
12. Perov R.I., Khakimova A.R., Popova N.A. Mild encephalopathy with reversible splenial corpus callosum lesion: literature review and case report in urgent neurologic clinical practice. The Bulletin of Contemporary Clinical Medicine. 2018; 11 (5): 109–114. doi: 10.20969/VSKM.2018.11(5).109-114.
13. Muhin K. Yu., Petruhin A. S., Mironov M. B. Epilepticheskie sindromy. Diagnostika i terapiya. M. 2008, 223p. (in Russian)
14. Zenkov L. R. Klinicheskaya epileptologiya [Clinical epileptology]. M. 2003, 368p. (in Russian)
15. Faulkner H.J., Arima H., Mohamed A. The utility of prolonged outpatient ambulatory EEG. Seizure. 2012;21:491.
16. Mračková J., Tupý R., Rohan V. et al. Cytotoxické léze corpus callosum (CLOCCs). Cesk Slov Neurol N. 2020; 83/116(4): 347–352. doi: 10.14735/amcsnn2020347.
17. Morozov D. V., Morozova E. A. Idiopaticheskie fokal'nye epilepsii s dobrokachestvennymi epileptiformnymi patternami detstva. Komorbidnost'i iskhody [Idiopathic focal epilepsy with benign childhood epileptiform patterns. Comorbidity and outcomes]. Prakticheskaya medicina. 2017; 1 (1): 123–126.

ORCID and contributionship:

Anna A. Voitiuk: 0000-0002-4120-3280 [A,B,D,F]
Tetyana A. Litovchenko: 0000-0002-4647-8507 [A,E,F]
Olena N. Borodai: 0000-0001-8116-6157 [B,D]
Nataliia A. Rudkivska: 0000-0003-4895-6346 [A,E,F]

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CORRESPONDING AUTHOR

Anna A. Voitiuk
Kharkiv Medical Academy of Postgraduate Education
5 Balakirev lane, 61000 Kharkiv, Ukraine
tel:+380509081085
e-mail: a_vojtyuk@yahoo.com

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A – Work concept and design, **B** – Data collection and analysis, **C** – Responsibility for statistical analysis, **D** – Writing the article, **E** – Critical review, **F** – Final approval of the article