Possible Concomitant Neurological and Laboratory Control in the Prevention of Complications after Viral Neuroinfections (with Clinical Follow-up)

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ABSTRACT

The article reports the clinical case of severe acute meningoencephalitis out of the epidemic. We identified serological titer of 1:128 influenza A (H1N1) 09 in the patient with severe acute meningoencephalitis out of the epidemic, which had been reducing from 1:32 to negative in the period of reconvalescence. Taking into the consideration a pandemic situation of influenza A (H1N1) 09 currently it is recommended organization of dispensary observation of patients with viral neuroinfections of any etiology in the Sakha Republic to identify progressive forms of torpid encephalopathy, due to the unpredictable potential effects of the viral interference, not only in the former, unstable foci of Vilyui encephalomyelitis, but also outside of them.

Keywords: meningoencephalomyelitis, torpid encephalopathy, persistence, viral interference, population immunity, dispensary observation, grading assessment of organic neurological micro symptoms.

Abbreviations: VEM – Vilyui encephalomyelitis; ONMS – organic neurological, micro symptoms.

INTRODUCTION

In the Resolution of the Chief state doctor of the Russian Federation 04.08.2009 № 50 (9) epidemiological modern period is characterized, among other features, typical for the region of Yakutia: -development of an influenza pandemic caused by a strain of the virus A/H1N1/09: the identification of new previously unknown infectious agents of humans and animals, - the emergence of rare infectious diseases (legionellosis, psittacosis), activation of the epidemiological process of returning infections (tuberculosis), natural focal infections (HFRS, rabies CCHF), an uncontrolled release or spread of organisms, especially genetically modified, with unknown mechanisms of impact on ecosystems.

Taking into account the recommended measures of prevention and development of treatment of the planned monitoring for communicable and non-communicable diseases, development and functioning of the system of environmental monitoring should take into account regional features of biological ecosystems. In the Republic of Sakha, in our opinion, it is necessary to pay attention to the state of population immunity of the indigenous population. At the population

level examines the role of immunity as a selective factor determining genetic polymorphism and adaptation of populations to infectious conditions of the danger zone of life (5). In this sense, it is impossible not to take into account the "secular" formation of the immune system of the Sakha people, as well as representatives of indigenous peoples of the North (evens, evenks and others) in extremely harsh climatic conditions, lack of food, suffering from many infectious diseases (4,7). In terms of the formation of the multidimensional and multifunctional computer database, analyzing not separate isolated biological event or biological factors, and their actual quantitative relationships and interactions in medical and environmental systems (1), you should consider multi-year biomedical development, which to date has not been given due attention.

In particular, this applies to the "disappearing" disease of the Vilyui meningoencephalomyelitis (VEM), the epidemic which swept across many regions of Yakutia in recent times (6). To the reasons of failing the isolation of an infectious VEM agent, which according to morphological studies defined as the persistent virus (7), as well as the gradual self-destruction of the VEM epidemic , you can, among other assumptions, to include the mechanisms of viral interference in combination with increased intensity of population immunity.

Interference may occur between strains of the same virus (homologous interference), and between viruses of different in immunological respect (heterologous interference) that is used in the development of new approaches in combating dangerous viral infections (10). Interfering activity, and sensitivity to the interfering action have almost all infectious viruses.It is reasonable to assume that the reduction in the incidence by the VEM deaths cases during spreading of the disease by migrants from the Vilyuy district to a more favorable life conditions of the Central regions of Yakutia (6) occurred against the backdrop not installed yet natural viral interference or the background throughout prevaccination introduced population. This seemingly positive development may be unsustainable against the background of modern influenza pandemics as it is most often severe, reliable acute VEM has developed on the background of flu-like conditions.

The study of the state system of interferons as well as intrathecal synthesis of immunoglobulin IgG in VEM (6,8) focused on the diagnosis of a current of inflammatory process in the CNS of the patient of chronic VEM and to identify predisposition to the disease in patients at risk. The latter include practically healthy persons from social environment authentic VEM patients, and persons with detectable so-called torpid encephalopathy (TE) (2,3,6). Recommendations scoring of severity of TE organic neurological micro symptoms (ONMS) is used as following subchronic and latent clinical manifestations of the VEM, and in the dynamics of observation of patients after acute neuroinfections of unknown etiology. This methodology, although focused mainly on establishing the functional component of the neurological clinical

diagnosis, however, allows to identify relevant, gradually progressing TE ONMS with 3-4 degrees of severity, to prevent the development of progressive forms of subacute, chronic and fatal stages of slow infection VEM (2,3).

Clinical and epidemiological observations Vladimirtsev A. I. (1986) showed the possibility of development of authentic VEM TE up to 27 years for 4.3% of registered patients with ONMS risk. Observations of the last 3 decades have identified 20 such patients with increasing ONMS to pathologic state similar to reliable, chronic VEM.

With this in mind, we recommend you to apply the methods of grading assessment of ONMS in patients undergoing acute serous meningoencephalitis of unknown etiology in stable and unstable foci of VEM.

ONMS algorithm, described in detail in our previous work (3), may consist of the manifestations of the Cerebro-asthenic syndrome and psychovegetative disorders with their symptoms, drillable standard battery of neuropsychological tests. The existence of vestibulopathies, pyramidal, cerebellar syndromes, movement disorders it is convenient to clarify the generally accepted scale of Lindmark (11).

ONMS-1, can be characterized by the presence of two or more easily expressed symptoms (impairment of one of the XII pairs of cerebral nerves, even the brisk reflexes, rare singular pyramidal signs) alltogether do not fit within an explicit syndrome; but ONMS-2 – several symptoms (often pyramidal), lively up to 2 -3 degrees of symptoms that characterize the mild syndrome with the presence of non-permanent complaints asthenic content; the increase in the intensity of complex syndromes from ONMS-3 to ONMS-4 marked disorders from mild to noticeable. When ONMS-4 possible the appearance of dysarthria, dysphagia, asymmetric increase of the deep reflexes, increase of the latent paresis of the extremities (syndromes Barre-Mingazzini, automatic pronation of the hand), variance of muscle tone in the extremities, change from slightly disorders of walking to ataxia, spasticity, frontal dysbasia. The appearance of pathological extensor and flexor reflexes (symptoms Babinski, Rossolimo, etc.), reflexes of oral automatism, pyramidal spinal homo - and/or heterolateral phenomena like Balducci's, central disorders of urination, constipation should be alerted.

The severity of encephalopathy from OHMC3 to ONMS-4 is determined not only by severity of individual symptoms, but a combination of complex syndromes.

For torpid encephalopathy VEM more typical is the gradual increase of bilateral pyramidal syndrome, with the shimmer observations in the dynamics of other syndromes. However, the accuracy of the diagnosis of VEM, especially at the stage of TE is determined by the process of

elimination of post-traumatic, vascular, somatogenic encephalopathies, tumors, brain aneurysm, TIA, antiphospholipid syndromes and other diseases.

The functional component of the neurological diagnosis at such a detailed dynamic monitoring allows you to monitor the effectiveness of assigned courses of treatment with antioxidants (mexidol, cytoflavin, noben), neuro - and vascular protectors (cerebrolysin, ceraxon, tanakan, ginkgo biloba), tranquilizers, nootropics (tenoten), vitamin B1, B6, E, C; immunomodulators.

In order to demonstrate the effectiveness of this event here is an extract from a medical card of the patient who suffered acute viral meningoencephalitis severe, revealed a high serological titre of influenza A(H1N1)09.

An extract from a medical card of the stationary patient No. 673.

Name: SAA. **Date of birth:** 08.03.1997/ 18 yrs old;

Residence: Suntarsky district, v. Suntary

Clinical diagnosis (primary): Acute meningoencephalitis of unknown origin, severe severity, stupor.

Related: Acute respiratory disease with an acute nasopharyngitis.Vegetovascular Dystonia with paroxysmal disorders due to psycho-emotional load at the time of the Unified State Exam.

From the anamnesis of disease: Acute disease onset from the 04.06.2015.

04.06.15. in the morning it was good health and spirits; during the day, while the exam in the school she turned to the nurse with complaints of weakness and dizziness, observed temperature rise to 38.2°C, BP=110/80 mm.Hg. Then she lost consciousness, was observed convulsions; foam from the mouth, bite the tongue was not. By ambulance she was taken to the medical ward with a diagnosis of situational conditions, anemia. In the Therapeutic Department cerebral symptoms were revealed –stiff neck is up to 3-4 cross fingers;repeatedtonic-clonic seizures (20 times), she did not recognize relatives, was hallucinating. With suspicion on a serous meningitis she was transferred to the Department of resuscitation and intensive therapy.In General analysis of blood leukocytosis 14 $x10^{9/l}$ In CSF analyses without pathology.

Her disturbed consciousness up to sopor in the morningon 05.06.2015, she did not recognize relatives, was disoriented in place, time.Muscle tone of extremities increased periodically, rigidity of muscles of neck continued. The leukocytosis increased to 32 $x10^{9/l}$. The bacterial inoculationfrom the CSF wasnegative on 05.06.2015. Treatment (including zovirax) conducted on the recommendation of the correspondence consultations of main specialists of Yakutsk. Against the background of treatment without improvement, therefor her sent by an air ambulance to the Emergency Department of the Republican Hospital No. 2. She was transferred to the Department

of infectious diseases in Yakutsk City Hospital where they spent further examination and treatment with 6.06.2015 on 22.06.2015 with a diagnosis of viral meningo-encephalitis unspecified etiology.

Table 1

Dynamics of indicators of the General analysis of cerebrospinal fluid of the patient SAA

Date	Protein (mg/l)	Cell count (per 1 mm3)	Glucose (mmol/l)
05.06.2015	33,0	1	-
06.06.2015	0,099	5	3,6
10.06.2015	50,0	2	3,88
26.07.2015	-	10	3,1

Conclusion EEG from 11.06.2015: Moderate diffuse changes in the activity of cortical neurons with signs of involvement diencephalon-stem structures of the brain. Epileptiform activity was not detected.

Brain MRI from 08.06.2015: In both frontal lobes are defined by small foci of leuckopathy sizes up to 0.3 cm. Conclusion: MRI signs of residual encephalopathy.

During treatment, despite a positive dynamics has been a violation of the sleep phases . The double vision passed. Stool after enema. Meningeal symptoms were registered before 15.06.15. Hypertonicity of the muscles of the right leg decreased 16.06.15, movement in the leg appeared (lifts one leg in bed).Stiff neck,Kernig symptoms from 16.06.15 became negative. Remained bradylalia, appeared tactile and painful sensitivity in the right leg. 17.06.15. consulted by a neurologist, recommended to prepare for transfer to reabilitation treatment in the neurological Department. However, at the insistence of the mother of the patient and the patient was discharged with improvement 22.06.15., recommendations treatment with nootropics, vitamins of group B.

T he patient was actively called for a consultation three weeks later. When viewed from 15.07.15. complained of fatigue, decreased background mood, loss of memory (forget all the formulas in physics, mathematics), weakness, insufficient sleep, constipation, no period.

In neurological status from 15.07.2015 – Only the mild failure of convergence of the eyeball to the right and a small deviation tongue to the right. Called proboscis reflex, Marinescu-Radovici from both sides, mandibular reflex.Determined ONMS 3 degrees in the form of pyramidal syndrome with extremity paresis. Neuropsychological examination revealed moderately expressed depression, lightly mnestic-cognitive disorders. The patient was again hospitalized for examination and treatment in the infectious diseases Department from 22.07.15 to

27.07.15. In General and biochemical blood tests, urine tests without deviation from the norm. A positive result of serological titer A(H1N1) 09 was received by the time of re-admission of the patient to the infectious Department.

In the first serum blood from 08.06.15 – A(H1N1) 09 – negative; II serum (17.06.15) titer of 1:128; serum;III titer - 1:32; in the serum .IV – negative.

The results of PCR for identification of influenza strains (A, b, A (HINI), A(HINI)v, A(H3N2), A(H5N1) negative.

Health has improved on the background of the treatment. In neurological status from 24.07.15 were not registered syndromes Barre, muscle tone normal, power is 5 points in all the joints of the limbs. In the future, the patient could prepare for the entrance exams and entered the financial-economic faculty; however, after 2 months, dropped out, there were problems with memorization of the material, the phenomenon of lumbar radiculopathy with pain syndrome was recorded, an anxiety attack was registered too. Continues to be monitored by a neurologist on a residence with ONMS -3.

In connection with the identification of the titre of antibodies to influenza A(H1N1) 09, a survey was conducted in the nidus according to the place of residence of the patient at contact classmates, the result was negative.

DISCUSSION

In this case during dispensary surveillance of the patient lasting more than 6 months, who previously treated for severe viral meningoencephalitis 16 patient-days, encephalopathy with ONMS 3 severity degrees was identified after 6 weeks of the onset in the form of pyramidal insufficiency with extremity paresis. Identifying the strain of influenza A(H1N1) 09 have assumed that the patient SAA was the virus carrying of this strain which became more virulent under the influence of hypothermia and stress syndrome (surge). The history of the problem registers sporadic cases of influenza this form during seasonal epidemics. This case should alert in the current situation, the emerging pandemic of this strain of influenza, complications of which with lethal outcomes more often is pneumonia.

Judging by the anamnesis and the results of the brain MRI, the patient had weakness of the Central nervous system in the form of residual (somatogenic) encephalopathy with foci of leukohpathy. The reason o the encephalopathy could be of the patients glomerulonephritis which manifested from age of three years, then the girl was treated for more than 6 years. The development of acute severe meningoencephalitis with coma, stupor, and epileptic seizures characterizes the strain A(H1N1) as possible with the skills of long-term persistence after a latent infection, worsening with the defeat of the Central nervous system of the patient, especially on the

background of premorbid encephalopathy. If in this case there is a recovery with residual effects in the form of ONMS-3, it is unknown what impact possible on the background of torpid encephalopathy the nature of the VEM.

In the Resolution of the Chief state doctor of the Russian Federation 04.08.2009 № 50 "On measures to implement powers of a single Federal Centralized system of state sanitary and epidemiological supervision in the sphere of ensuring biological and chemical security"

CONCLUSIONS, PROPOSALS

This case adjusts to necessary medical examination of patients suffering from acute post-influenza and other viral meningoencephalitis according to the method of graded assessment OHMS in the torpid encephalopathy of different etiology:

1. In identifying patients with ONMS, progressing from 2 to 3-4 the severity of the observation is not to stop for at least 3 years, at intervals of 3, 6, 12, 24, 36 months.
2. When identifying such a patient from the sustained VEM focus , we recommend more long-term (possibly lifelong) follow-up even in case of stabilization of progradience.
3. It also reveals the increasing epidemiological factors: laboratory decoding for 2015 - from 430 cases of influenza strain A(H1N1) was detected in 24 (5,58%) and in 2016 according to PCR data from 171 in 34 (19,8%), similar evidence of growth of epidemic risk does not preclude the creation of conditions of possible formation of complications on the Central nervous system of the patient, as shown in the example under discussion the occasion. In these conditions, as an additional criterion necessary to continue use of the clinical examination of the titre of antibodies in serological tests, PCR data, oligobands IgG, interferons, bearing in mind the impact of viral interference and some mechanisms of persistence of the pathogen.

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