

Z.I. Suleimenova<sup>1</sup> , S.T. Doskozhaeva<sup>1\*</sup> , E.A. Park<sup>2</sup> , S.D. Tokburaeva<sup>3</sup> 

<sup>1</sup>National Educational Institution «Kazakhstan-Russian Medical University», Kazakhstan, Almaty

<sup>2</sup>Multi-specialty City Hospital of Taraz, Kazakhstan, Taraz

<sup>3</sup>Zhambyl Oblast Center for Prevention and Control of AIDS Kazakhstan, Almaty

\*e-mail: Sdoskojaeva@mail.ru

## TOXOPLASMOSIS OF THE CENTRAL NERVOUS SYSTEM IN HIV PATIENTS

Currently HIV infection in Kazakhstan is mainly spread among population groups with risk taking behavior (injection drug users – IDUs, sex workers – SWs). The lesions and fatalities in patients with HIV infection are mainly caused by complications, i.e. the development of opportunistic infections and secondary diseases. Timely diagnosis of these conditions determines the success of treatment and life expectancy of patients. Among superinfections the following ones take the lead: mycoses (pneumocystosis, candidiasis, cryptococcosis, coccidioidosis), diseases caused by a group of herpes viruses (herpes simplex, herpes zoster, cytomegalovirus infection, Epstein-Barr virus infection, Kaposi's sarcoma), bacterial infection (tuberculosis, atypical mycobacteriosis, salmonellosis), protozoosis (toxoplasmosis, cryptosporidiosis). Multi-infections are common as well. Opportunistic infections are insidious in humans and take the form of endogenous infections; they as well are activated with the development of clinical manifestations along with formation of immunodeficiency and, accordingly, cause severe and even fatal diseases.

**Keywords:** HIV infection, opportunistic infections, secondary diseases, toxoplasmosis.

### Introduction

Infection rate of the population with toxoplasmosis in different countries of the world varies between 6 and 90% of the population. In various countries of the world the infection mostly hits the areas where it is customary to eat undercooked meat. It is hard to determine the morbidity rate since there is no mandatory registration of patients with toxoplasmosis. The rural population is infected more than the urban population due to the large number of cats [1]. According to A. P. Kazantsev, the infection rate of men is less than 1% of those observed, while among women it makes up 3-5% of those surveyed.

Opportunistic infections are insidious in humans and take the form of endogenous infections; they as well are activated with the development of clinical manifestations along with formation of immunodeficiency and, accordingly, cause severe and even fatal diseases [2].

Within secondary diseases in HIV patients, toxoplasmosis ranks third, along with pneumocystis pneumonia, and follows tuberculosis and CMV infection, and accounts for 7.4%. There is an increase in the number of patients in the late stages of HIV infection who develop opportunistic, secondary infections. Toxoplasmosis is the most important opportunistic infection of the central nervous system (CNS) in HIV patients. It accounts for 50-70% of all parasitic diseases in AIDS and it ranks third among fatal outcome in patients at the late stage of HIV infection. Almost all cases of toxoplasmosis in HIV

patients are associated with reactivation of a latent infection [3].

According to A.B.Peregudova central toxoplasmosis is the most common cause of CNS pathology, making up 32%. Other secondary lesions of the CNS were recorded less frequently: tuberculous meningoencephalitis – 22.4%, fungal encephalitis – 6%, secondary purulent meningitis – 7.6%, malignant tumors of the CNS – 3.7%, CMV encephalitis – 1.6% and others.

In the Republic of Belarus, Gomel region within opportunistic diseases, neuroAIDS (29.1%) ranks second after tuberculosis. In the etiological structure of neuro AIDS, toxoplasmosis of the brain prevails (32%) and mortality is 19.5% [4-5].

### Materials. Case Report

M., born in 1986, delivered to the emergency department of the regional hospital in Taraz by an ambulance team (EMS) in an unconscious state, not reacting to painful stimuli.

The patient's history was taken from his father: the son came to Taraz to undergo alternative therapy and on May 31, 2019 he got an electric shock session. On therapy epileptic seizures occurred with loss of consciousness and tonic spasms every 5 minutes. In total 3-4 epileptic seizure clusters were recorded. An ambulance team was called, which delivered the patient to the intensive care unit (ICU) due to ongoing seizures.

From the recorded medical history of the patient. Between 08.04 and 16.04.2019 he underwent

medical examination and took treatment at the regional hospital in Almaty. According to the patient the first focal convulsive seizures occurred in April 2019. MRI examination of his brain on 04/09/2019 showed the following: a pattern of unspecified mass in the right hemisphere; taking into account the ring-shaped accumulation of a contrast agent, it is required to differentiate between a parasitic lesion and an oncological disease. He visited a neurosurgeon and an oncologist. Received symptomatic therapy. He then was discharged from the hospital with the following diagnosis: Residual encephalopathy. Space-occupying mass in the right parietal region. Hypertensive syndrome. Convulsive syndrome. Condition after an epileptic seizure. It was recommended to have an MRI with contrast 2 months later. Starting from 20.05.2019 he had been experiencing weakness in the left arm and leg, had had difficulty walking.

From his life history: he grew and developed according to age. According to his father, he had no viral hepatitis, tuberculosis nor venereal diseases. No blood transfusions. He had no closed craniocerebral injuries. No history of allergies. Works as a choreographer.

Objective condition at admission: general condition is severe due to cerebral insufficiency. Satisfactory nutrition. Normostenik. The skin and visible mucous membranes are of normal color, clean. Peripheral lymph nodes are not enlarged. The musculoskeletal system is unremarkable. Body temperature is 36.6°C. The chest is of the usual form, both halves are equally involved in breathing. By percussion: percussion sound in all lung cavities. By auscultation: vesicular respiration, no wheezing sounds. RR is 18 per minute. There is no pathological pulsation of large vessels. Cardiac borders: the right border is along the right edge of the sternum, upper border is in the 3rd intercostal space, left border is 1.0 cm outward from the mid-clavicular line. Heart sounds are muffled, the rhythm is correct. BP is 130/80 mm Hg. Heart rate – 98 beats / min. No swallowing problems. The tongue does not stick out. The abdomen is not swollen, soft on palpation. The liver and spleen are not palpable. No stool for 2 days. Kidney punch is negative on both sides. Urination through a catheter. No peripheral edema. CNS: level of consciousness according to the Glasgow scale is 8b, coma – 1. He does not respond when addressed. Weak response to painful stimuli. Rigidity of the occipital muscles is 1.5 – 2 p / p. Skull brain nerves: palpebral fissures D=S,

pupils are uniform, no anisocoria, photoreaction is preserved, quick. Weakness of convergence from both sides. Trismus of masticatory muscles, pharyngeal reflexes and a reflex from the soft palate are evoked. Tendon reflexes – D > C. Sensitivity and muscle strength are not differentiated. Tonic convulsions are observed in left arm and left leg. Pathological foot signs: Babinski's sign (+) on the left. There are no meningeal signs.

MRI of the brain (06/01/2019): MRI signs of the mass in the parietal lobe on the right and the frontal lobe on the left with multiple foci. Differentiate between a parasitic lesion of the brain (toxoplasmosis) and NEO. An MRI of the brain with contrast is recommended.

Ultrasound of the abdominal cavity organs (06/03/2019): Diffuse changes in the liver and pancreas. Chronic cholecystitis. Bilateral pyelonephritis, Uratic diathesis. ECG (06/01/2019): left atrial hypertrophy. Syndrome of early repolarization of the ventricles. T-wave inversion in the septal region.

X-ray of the chest (06/05/2019): no focal and infiltrative shadows on the lung cavities were detected on the plain chest radiograph in the direct projection. The lung pattern is deformed. The roots are structural, compacted. Sinuses are free. The heart is not enlarged. Indirect signs of chronic bronchitis.

Ophthalmologist's comments (06/01/2019): background retinopathy of OU.

Neurosurgeon's comments (06/01/2019): Status epilepticus. Condition after serial convulsive seizures. Todd's post-seizure paralysis on the left. Competing disease: metastasis of the brain? To clarify the diagnosis upon MRI of the brain with contrast.

MRI of the brain with contrast (06/02/2019): MRI signs of a parasitic brain lesion, most likely acute necrotizing toxoplasmic encephalitis. Cerebral edema.

Consultation of an infectious disease specialist (06/03/2019): CNS toxoplasmosis? HIV infection? EIA blood test for HIV, toxoplasmosis, echinococcosis. Spinal puncture after stabilization.

Repeated consultation of an infectious disease specialist (06/06/2019): chronic toxoplasmosis of the central nervous system. Meningoencephalitis, severe. Cerebral edema. Coma 2. B-20. Consultation of an infectious disease specialist of the regional AIDS center: HIV – infection, 4th clinical stage. Toxoplasmosis of the brain. Blood samples were taken for CD4 lymphocytes, viral load, and AIDS-defining diseases. ART was prescribed according to the scheme.

**Table 1** – The results of a general blood test in dynamics

Erythrocytes, $10^{12}/l$	Hemoglobin, g/l	platelets, $10^9/l$	Leukocytes $10^9/l$	Eosinophyla %	Bazophyla %	Banded neutrophils <sup>1</sup> , %	Segmentonuclear neutrophils <sup>2</sup> , %	Lymphocytes, %	Monocytes, %	ESR, mm/h
4.75	146	299	5.420	1	0	10	50	27	12	18
5.16	158	248	9.980	0	0	15	58	18	9	22
5.06	156	236	12.200	0	0	22	68	5	5	22
4.0	122	171	3.290	3	0	10	51	21	15	22
4.28	131	219	6.820	2	0	19	57	15	7	20
4.09	125	249	7.320	2	0	20	51	18	9	22
4.13	127	290	10.970	2	0	26	59	6	7	22

In the general blood test the indicators of red blood (table 1) and the number of platelets stayed within the reference values. The number of blood leukocytes varied from leukopenia ( $3.290 \times 10^9/l$ ) to leukocytosis ( $12.220 \times 10^9/l$ ), but more often normocytosis prevailed. The number of neutrophils: in 2 cases there was neutrophilia, but a stab shift of the formula to the left was a constant sign of a bacterial infection. The absolute number of lymphocytes

ranged from 1796 cells/ml of blood to 611 cells/ml of blood. The number of blood monocytes and accelerated ESR were reduced to permanent numbers. The results obtained indicated the bacterial etiology of the infectious process, without damage to the bone marrow (erythrocyte and platelet sprouts).

In the general analysis of urine, there were observed a large number of leukocytes, erythrocytes 1-2 per HPF, bacteria and mucus. Biochemical liver tests in dynamics show no irregularities (table 2).

**Table 2** – The results of biochemical tests of the liver in dynamics

ALT MU/ml	AST MU/ml	Total bilirubin mmol/l	Sugar mmol/l	Total protein g/l	Na mmol/l	Creatinine $\mu\text{mol/l}$
21	36.6	9.1	7.1	75.2	145.6	92
-	-	-	5.6	55.6	139.9	-
-	-	-	-	56.6	137.5	-

EIA for antibodies of class IgM, IgG for echinococcosis, toxoplasmosis showed negative results. EIA for viral hepatitis B (HBsAg) and viral hepatitis C (anti HCVAT) is negative.

From the first day in hospital, taking into account the primary results of the examination, the following drugs were prescribed: rovamycin (9 million/day), CEF-3 (2.0 g/s), metrogil (300 mg/day) and pathogenetic and symptomatic therapy.

LFIA for antibodies to HIV proved positive. Immunoblot for HIV – (+), titer 15.4. Additionally, tests for CD4-lymphocytes and viral load were taken.

The results of the immunogram: CD4 – 18 cells; CD3 are -480 cells/ $\mu\text{l}$ ; CD8 are -445 cells/ $\mu\text{l}$ . The CD4/CD8 ratio is 0.04. VL is 469449 copies / ml / log 10 – 5.67.

Based on the results of an additional examination, the following diagnosis was established: HIV infection, 4th clinical stage. Toxoplasmosis of the brain. ART prescribed: AZT/ZTS+DTG. And cotrimoxazole was prescribed as well.

At the insistence of the parents, the patient was discharged for home treatment after 12 days of treatment in the hospital and died 5 days later.

In the described case during the initial visit of the patient in April 2019 in a hospital setting he was not tested for HIV, although the young man was subject to examination for this disease since he had had focal epileptic seizures since April 2019 at normal body temperature and showed no symptoms of meningoencephalitis upon detection of ring-shaped accumulations of a substance in the right hemisphere on the brain MRI. This indicates that doctor do not raise flags as related to HIV infection and late diagnosis and treatment of the disease. The lack of specific treatment leads to the steady progression of the disease, the addition of opportunistic diseases and increased mortality.

The patient's MRI examination revealed multiple lesions in the frontal and parietal regions of the right hemisphere. According to Ermak T.N. and Peregudova A. B. most often the foci were localized

in the frontal (70.8%) and parietal (61.1%) areas of the brain. Tumash O.L. with co-authors noted multiple foci ranging in size from 2 to 40 mm, which had rounded shape with blurry edges. In addition, the foci often intensified contrast along the periphery, according to the type of «targets», which was noted by the radiologist during the primary MRI.

The anamnesis shows that the patient's disease began with the appearance of focal seizures, which corresponded to the acute onset of the disease, which was noted in 21.3% of patients, but the clinical picture had to be differentiated from acute cerebrovascular accident, less often the disease began with tonic-clinical seizures and they were the only manifestation of the disease. During the first week of illness, 65.9% were hospitalized with an acute onset, and some were admitted after 2–6 months (2). In our case, the patient was admitted for treatment at the end of the 2nd month from the onset of the disease.

The content of CD4-lymphocytes was at a critically low level (18 cells/ml) and at the same time a high viral load was detected – 469,449 copies/ml. The same data are provided by Peregudova A.B. and Tumash O.L. with co-authors. They note the results obtained in 66.2% and 52.2% of cases, respectively. The negative result of the examination for antibodies to toxoplasma must be due to a critical decrease in the number of T-helpers, the main function of which is to stimulate antibody genesis.

### Conclusion

The rapid progression of HIV infection is associated with the development of secondary diseases. Practitioners should be wary of AIDS-associated diseases, which will contribute to early verification of HIV infection.

### References

1. Kazantsev A.P. Toxoplasmosis. – Leningrad: «Medicine», Leningrad branch, 1985
2. Mikhailov N.R., Kalimina T.N., Tuchkov D.Yu., Losin E.I., Abakumov G.G. Toxoplasmosis of the brain in HIV patients in the city of Orenburg // J: Bulletin of the Orenburg State University. – No. 1 (176) / January 2015.
3. Peregudova A.B. Toxoplasmosis in HIV patients. Features of the clinic and diagnosis. Abstract of the dissertation for the degree of candidate of medical sciences. – M., 2013.
4. Ermak T.N., Peregudov A.B. Localization of foci in cerebral toxoplasmosis in HIV patients // Magazine: Therapeutic archive. – 11, 2014. – Pp. 24 – 28.
5. Tumash O.L., Zhavoronok S.V., Kozorez E.I. Toxoplasmosis in HIV-infected people // Magazine: Clinical infectology and parasitology. – 2017. – Pp. 239 – 241.