

**OPIS PRZYPADKU / CASE REPORT**

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**Opryszczkowe zapalenie mózgu – opis przypadku i przegląd literatury**  
***Herpes simplex encephalitis – case report and literature review*****Julia Siek<sup>1</sup>, Michał Borys<sup>2</sup>**<sup>1</sup> Studenckie Koło Naukowe przy II Klinice Anestezjologii i Intensywnej Terapii Uniwersytet Medyczny w Lublinie<sup>2</sup> II Klinika Anestezjologii i Intensywnej Terapii Uniwersytet Medyczny w Lublinie**Streszczenie**

Wirus Herpes simplex (HSV) był pierwszym zgłoszonym ludzkim wirusem opryszczki [1]. Oba jego typy (HSV-1 i HSV-2) głównie infekują i replikują się w komórkach nabłonka śluzówki, wywołują objawy w miejscu infekcji, a następnie rozwijają utajoną infekcję w otaczających neuronach. HSV-1 jest zwykle związany z infekcjami powyżej, a HSV-2 poniżej talii. Szacowana ogólnoswiatowa częstość występowania zakażenia HSV-1 wśród osób w wieku 0-49 lat w 2012 r. wyniosła średnio 67% dla wszystkich grup wiekowych [2]. Opryszczkowe zapalenie mózgu jest stosunkowo rzadkie, częstość występowania szacuje się na 1-3 przypadków na milion, ale jest też najczęstszą przyczyną okazjonalnego śmiertelnego zapalenia mózgu [3]. Przy braku leczenia rokowanie jest złe, ze śmiertelnością około 70% [4]. Autorzy chcieli przedstawić przyczyny zapalenia mózgu i ryzyko tak poważnego powikłania u młodej osoby na podstawie opisu przypadku i przeglądu literatury. *Anestezjologia i Ratownictwo 2021; 15: 237-242. doi: 10.53139/AIR.20211525*

*Słowa kluczowe:* wirus Herpes, opryszczkowe zapalenie mózgu

**Abstract**

Herpes simplex virus (HSV) was the first human herpes virus reported [1]. Both types (HSV-1 and HSV-2) mainly infect and replicate in mucosal epithelial cells, cause symptoms at the site of infection, and then develop latent infection in surrounding neurons. HSV-1 is usually associated with infections above and HSV-2 below the waistline. The estimated worldwide incidence of HSV-1 infection among people aged 0-49 years in 2012 was on average 67% for all age groups [2]. Herpes simplex encephalitis is relatively rare with an estimated incidence of 1-3 cases per million, but it is also the most common cause of occasional fatal encephalitis [3]. In the absence of treatment, the prognosis is poor, with a mortality rate of around 70% [4]. The authors wanted to present the causes of encephalitis and the risk of such a serious complication in a young person based on a case report and a literature review. *Anestezjologia i Ratownictwo 2021; 15: 237-242. doi: 10.53139/AIR.20211525*

*Keywords:* Herpes virus, Herpes simplex encephalitis

## Introduction

Herpes simplex encephalitis is most often caused by the HSV-1 virus. It is the only viral encephalitis with an effective antiviral treatment [5]. Pathological changes occur in the temporal lobe [6]. The pathological and immunopathological influence of the virus damages the temporal lobe, which is manifested by the presence of erythrocytes in the cerebrospinal fluid, the presence of paroxysmal, focal neurological abnormalities and other symptoms characteristic of viral encephalitis. HSV is the most common etiological factor responsible for encephalitis with high mortality [7], despite appropriate treatment. The disease affects all age groups equally and does not depend on the season of the year.

## A case report

A 31-year-old female patient was admitted to the Intensive Care Unit (ICU) due to acute respiratory failure, hypotension and consciousness disorders. Immediately before the stay at the ICU, the patient was hospitalized at the Department of Infectious Diseases, where she was transferred from the Department of Neurology of the Provincial Specialist Hospital in Lublin. The following symptoms fever, malaise deteriorated and herpes labialis had occurred one week before admitting the patient to the Intensive Care Unit. At the Department of Neurology, tests of the cerebrospinal fluid were performed, which clearly indicated a viral infection.

Normally, the cerebrospinal fluid (CSF) should be water-clear and clear. A yellow discoloration of the

cerebrospinal fluid may indicate a breakdown of blood cells due to bleeding into the CSF or the presence of bilirubin. A significantly elevated protein concentration indicates a viral infection. In normal CSF, only small amounts of protein are present due to the fact that protein molecules are large and can hardly cross the blood-brain barrier. Such a drastic increase in the protein concentration noted in the patient may suggest us meningitis. Viral infection is also indicated by an increase in the number of leukocytes. Due to the suspicion of neuroinfection, broad-spectrum antibiotic therapy was initiated and acyclovir was continued. The patient was also ordered chest X-ray, magnetic resonance imaging (MRI) of the head with contrast, computed tomography (CT) of the head without contrast, moreover, cultures (blood, urine, anus, vagina, nasopharyngeal cavity and cerebrospinal fluid) were taken for microbiological examinations.

Chest X-ray showed a left-sided pneumothorax, a slight displacement of the mediastinum to the right, and a lowering of the left diaphragmatic dome. There was no pneumothorax on the right side. Pulmonary fields without parenchymal densities. Active drainage was established. Due to the progressive respiratory failure, it was decided to intubate the patient and mechanically ventilate the lungs during sedation. Initially, the ventilation parameters in the SIMV-PRVC (Synchronized Intermittent Mandatory Ventilation, Pressure Regulated Volume Control) mode PEEP 6 (Positive End Expiratory Pressure), FIO<sub>2</sub> 0.6 (Fraction of Inspired Oxygen). The oxygen concentration was gradually reduced to FiO<sub>2</sub> 0.35. A central venous

Tabela 1. Porównanie wyników badań dodatkowych wykonanych w dniu przyjęcia na OIT (8.06.2019) i 9 dni później

Table 1. Comparison of the results of additional tests performed on the day of admission to the ICU (June 8, 2019) and 9 days later

CEREBRO-SPINAL FLUID	08.06.2019	17.06.2019
Color after centrifuging	Water clear	yellow
Color before centrifuging	Water clear	yellow
Protein	100.81 mg/dl	1451.00 mg/dl
Chlorides	125 mmol/l	117.8 mmol/l
Glucose	61 mg/dl	42 L mg/dl
Mononuclear	99%	99%
Leukocytosis	183.0 cells/ul	199.0 cells/ul
Transparency before centrifuging	Transparent	Transparent
Transparency after centrifugation	Transparent	Transparent
Multinucleated antibodies	1%	1%

Tabela 2. Wyniki badań mikrobiologicznych

Table 2. Results of microbiological tests

<b>Culture (vaginal swab)</b>	PLENTY GROWTH OF ESCHERICHIA COLI
<b>Culture (cerebrospinal fluid)</b>	LACK
<b>Culture (nasopharynx)</b>	GROWTH OF THE STAPHYLOCOCCUS AUREUS
<b>Culture (MINI BAL alveolar lavage)</b>	THE GROWTH OF THE CANDIDA ALBICANS STORE
<b>Culture (anus)</b>	GROWTH OF CANDIDA ALBICANS
<b>Culture (blood)</b>	PHYSIOLOGICAL FLORA OF THE GASTROINTESTINAL TRACT
<b>Culture (cerebrospinal fluid)</b>	LACK

catheter and a Picco catheter were inserted. Enteral nutritional intervention and intensive fluid therapy under the control of haemodynamic monitoring were also initiated. The circulatory system was insufficient and required the Noradrenalin (Levonor) infusion under the control of hemodynamic monitoring PICCO (Pulse Contoru Cardiac Output). Blood, urine, anus, vagina, nasopharyngeal and cerebrospinal fluid cultures were collected for microbiological testing.

The next day, due to worsening respiratory failure, mechanical lung ventilation in analosedation (Fentanyl + Propofol) was applied. Ventilation parameters in SIMV-PVRC (Synchronized Intermittent Mandatory Ventilation, Pressure Regulated Volume Control) PEEP 6 (Positive End Expiratory Pressure), FiO<sub>2</sub> 0.3 (Fraction of Inspired Oxygen) mode. The circulatory system was stabilized by the infusion of noradrenaline. The heart rate was about 86 beats per minute. Spontaneous diuresis. Abdomen soft during

physical examination, no pathological resistance, peristalsis present, nutrition is still enteral with 54 g of protein per day. Despite the numerous measures taken, the patient remained invariably in a very serious condition for the following days, unconscious, without contact, with a tendency to hypothermia. It was possible to observe reflexes from the upper limbs and Babinski's symptom on the left side. On the fifth day of stay, a CT of the head was performed. Visible narrowing of the cerebral furrows in both cerebral hemispheres was found, which indicated cerebral edema. The ventricular system of the brain was symmetrical, constricted, partially constricted. Due to water and electrolyte disturbances in the form of maintaining high sodium levels and increased diuresis, Desmopressin (Minirin) was included in the treatment. In the following days, the patient's condition remained unchanged. The monitored circulatory system required support with a continuous infusion of norepinephrine. Active drain-

Tabela 3. Wyniki badań wykonanych dzień przed przyjęciem na OIT

Table 3. Results of tests performed the day before admission to the ICU

MARKERS OF CONTAGIOUS DISEASES	
<b>Ab against CMV IgG</b>	69.6 AU / ml
<b>Ab against CMV IgM</b>	Unreactive
<b>Ab against Hbc</b>	Unreactive
<b>Ab against HCV</b>	Reactive
<b>Ab against Toxoplasma gondii IgG</b>	38 UI / ml
<b>Ab against Toxoplasma gondii IgM</b>	Unreactive
<b>Hbs antigen</b>	Unreactive
<b>HIV COMBI</b>	Unreactive

P-ciało przeciwko CMV IgG – przeciwciała IgG przeciwko cytomegalowirusowi, P-ciało przeciwko CMV IgM- przeciwciała IgM przeciwko cytomegalowirusowi, P-ciało przeciwko Hbc – przeciwciała przeciwko wirusowemu zapaleniu wątroby typu B, P-ciało przeciwko HCV- przeciwciała przeciwko wirusowi zapalenia wątroby typu C, P-ciało przeciwko Toxoplasma gondii IgG- przeciwciała IgG przeciwko Toxoplasma gondii, P-ciało przeciwko Toxoplasma gondii IgM- przeciwciała IgM przeciwko Toxoplasma gondii, Antygen Hbs, HIV COMBI - test HIV na antygen p24 i przeciwciała typu 1 i 2 ludzkiego wirusa nabytego niedoboru odporności

Ab against CMV IgG- anti Cytomegalovirus IgG antibodies, Ab against CMV IgM-anti Cytomegalovirus IgM antibodies, Ab against Hbc-hepatitis B core antibodies, Ab against HCV- Hepatitis C virus antibodies, Ab against Toxoplasma gondii IgG- anti Toxoplasma gondii IgG antibodies, Ab against Toxoplasma gondii IgM- anti Toxoplasma gondii IgM antibodies, Hbs antigen, HIV COMBI- HIV test for both antigen p24 and antibody of types 1 and 2 of human immunodeficiency virus

Tabela 4. Morfologia krwi pobrana przy przyjęciu  
Table 4. Blood counts taken on admission

<b>HCT</b>	31.1%
<b>HGB</b>	9.7 g/dl
<b>MCH</b>	24.3 pg
<b>MCHC</b>	31.2 g/dl
<b>MCV</b>	77.9 fl
<b>MPV</b>	12.9 fl
<b>The number of erythroblasts</b>	0.00 U/l
<b>NRBC%</b>	0.0 %
<b>PCT</b>	0.24 %
<b>PDW</b>	18.0 fl
<b>P-LCR (megathrombocyte index)</b>	48.8 %
<b>PLT</b>	185 K/uL
<b>RBC</b>	3.99 M/uL
<b>RDW-CV</b>	17.9 %
<b>RDW-CD</b>	49.2 fl
<b>WBC</b>	6.20 K/uL

HCT-hematokryt, HGB-hemoglobina, MCH-średnia zawartość hemoglobiny, MCHC-średnie stężenie hemoglobiny, MCV-średnia objętość krwinki, MPV-średnia objętość płytek krwi, NRBC-jądrzaste krwinki czerwone, PCT-prokalcytonina, PDW-wskaźnik anizocytozy płytek, P-LCR- wskaźnik megatrombocytów, PLT- trombocyty, RBC- krwinki czerwone, RDW- CV-wskaźnik dystrybucji objętości krwinek czerwonych, RDW-CD- wskaźnik dystrybucji objętości krwinek czerwonych, WBC- krwinki białe

HCT-hematocrit, HGB-hemoglobin, MCH-mean hemoglobin content, MCHC-mean hemoglobin concentration, MCV-mean corpuscular volume, MPV-mean volume of platelets, NRBC-nucleated red blood cells, PCT-procalcitonin, PDW-index of platelet anisocytosis, P-LCR-megathrombocyte index, PLT-thrombocytes, RBC-red cells, RDW-CV-red blood cell volume distribution indicator, RDW-CD-red blood cell volume distribution indicator, WBC- white blood cells

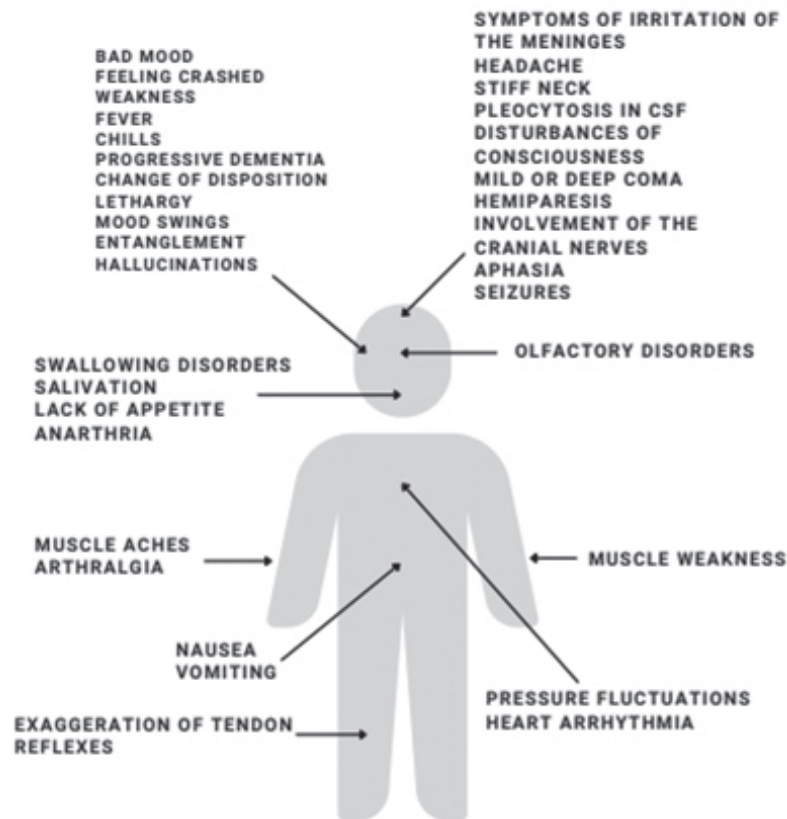
age of the left pleural cavity was maintained. On the seventh day, due to the tachycardia of about 170 / minute and the increase in pressure, Metoprolol (Betaloc) was administered, and the infusion of Fentanyl was also added. The applied action allowed to slow down the heart rate to approx. 110 / minute. On the 20th day of hospitalization, an MRI of the head was performed. The study showed generalized shallowing of the cortical grooves, blurred cortical / white matter differentiation, generalized decrease in the signal of the brain tissue. Displacement of the cerebellar tonsils approx. 4 mm below the plane of the great occipital foramen. The MR image spoke in favour of cerebral death. On the 24th day of hospitalization, the procedure of the commission confirmation of brainstem death was started according to the Resolution of 2007. A commission was established and the procedure for suspicion and confirmation of brain-stem death was initiated according to the protocol in force. The next day, the commission met again, but due to the doubts as to the credibility of the result of the brainstem death certificate, the decision was withdrawn. On the 34th day of hospitalization, a cardiac arrest occurred in the asystole of the patient and the patient was pronounced dead.

## Discussion

The presented case report shows the terminal form of herpetic encephalitis. It is associated not only with high mortality, but also with numerous complications. The incidence is relatively rare, but it is considered the most common cause of sporadic fatal encephalitis [8]. Research indicates that in the United States, 200-500 people die each year for this reason [8]. It is undeniable that initially the clinical picture is not characteristic. During the course of the disease, we can distinguish the period of heralds and the period of neurological symptoms. Indeed, the teasing period may indicate a flu infection, and it usually lasts from 2 to 5 days.

Herpetic encephalitis should be differentiated from tuberculous meningitis, encephalitis, fungal inflammation, brain abscess, vascular incident, brain tumor, hematoma, epilepsy or multiple sclerosis. Examination of cerebrospinal fluid is a considerable diagnostic value in Herpes simplex encephalitis (HSE) and should always be performed after computed tomography or MRI [9].

The cerebrospinal fluid usually looks water-bright, but it can also be yellowish or bloody. A common phenomenon is pleocytosis, amounting to several hundred



Rycina 1. Zespół objawów zależy od anatomicznej lokalizacji zapalenia

Figure 1. The symptom complex depends on the anatomical location of the inflammation

to thousand cells, with a predominance of mononuclear cells [8]. HSV encephalitis manifests due to lymphocytic pleocytosis, a normal or mildly elevated protein level, and normal glucose levels [10]. The virus is rarely present in CSF [8]. Its isolation is quite problematic. In a few, the virus can be uniquely isolated from the oral epithelium, and its presence does not always mean encephalitis. It is not detected in the stool, secretions from the bronchial tree, trachea, as well as urine or blood. The most reliable finding turns out to be the presence of the virus in the brain's tissues by histological methods. It can be isolated in many tissue cultures, showing a pathognomonic cytopathic effect.

The rate of recovery without neurological complications is extremely rare and estimated at around 10% [8]. In 60-90% of cases, an untreated disease leads to coma and death after a period of disturbed consciousness [8]. Prevention of herpetic encephalitis is not the easiest one. This is due to the fact that the cause of the disease is usually the reactivation of

the virus already present in the body in the event of a significant reduction in immunity. Unfortunately the mechanism of reactivation has not been clarified yet [11]. This applies not only to people infected with human immunodeficiency virus (HIV), immunosuppressed, cancer patients or malnourished patients. In general, the causes of herpetic encephalitis include neuroinfection or autoimmune disease. According to the observations of scientists, young people, around 30 years old, who are overloaded with stress and excessive work duties, suffer more and more often [8]. Vaccine development is difficult as it is associated with potential oncogenicity and neurovirulence of the herpes virus. In adults, most infections are caused by the presence of circulating antibodies [8]. Actions that can be taken include limiting the transmission of the virus by trying to limit primary infections and mucocutaneous superinfections, which is extremely important in people with immunosuppression and exposed to contact with infected skin or saliva due to their profession [8].

## Summary

The prognosis depends primarily on early diagnosis, introduction of antiviral therapy and intensive care, usually in an intensive care unit. In antiviral treatment, doctors usually choose acyclovir and vidarabine. Unfortunately, no drug works against the virus in latent form. After discharge, it is important to provide the patient with rehabilitation in order to improve functioning in everyday life. Better and better treatments are being researched all the time. Evidence from in-vitro and animal models suggests that adding corticosteroids to aciclovir may improve prognosis. Careful elaboration will allow the number of deaths to be reduced to a minimum in the future.

Konflikt interesów / Conflict of interest  
Brak/None

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