



CLINIC AND TREATMENT OF ACUTE AND RECURRENT HERPETIC STOMATITIS IN YOUNG PATIENTS

Burkhonova Zarafruz Qobilovna,
Samarkhand State Medical University

Kaky Huda Abdul Salam Hekmat
Samarkhand State Medical University

Annotation

The lecture presents data on the etiopathogenesis, clinic, diagnosis and treatment of acute and recurrent herpetic stomatitis in children. Particular attention is paid to diagnostics and modern treatment protocols.

Keywords: herpetic stomatitis, children, etiology, pathogenesis, clinic, diagnosis, treatment. Herpes (from the Greek herpes - creeping) has been known for more than 2 thousand years. In total, about 80 representatives of the herpes virus have been discovered, 8 of the occurring pathogens for humans.

Introduction

Herpesviruses belong to the Herpesviridae family (DNA-genomic viruses) and, according to their biological properties, are part of 3 subfamilies Herpesviridae family Subfamily Alphaherpesvirinae representatives Herpes simplex viruses (HSV) types 1 and 2: Herpes simplex virus - 1, - 2 (HSV) -1, HSV-2). The varicella/shingles virus is the Varicella-Zoster virus (VZV). Betaherpesvirinae Cytomegalovirus - Cytomegalovirus (CMV). Herpes virus type 6 - Human herpes virus - 6 (HHV-6). Herpes virus type 7 - Human herpes virus - 7 (HHV-7). Gammaherpesvirinae Epstein-Barr virus - Epstein-Barr virus (EBV). Herpes virus type 8 - Human herpes virus - 8 (HHV-8, with Kaposi's sarcoma associated human virus - KSHV) The causative agent of acute and recurrent herpetic stomatitis, herpes lips is HSV. Characteristics and epidemiology of HSV was first discovered in the fluid of herpetic vesicles in 1912 by Grüther. In 1921, Lipschütz exhibits visible in ordinary light acidophilic inclusions ("Lipshütz bodies"), which Cowdry (1934) identified as HSV inclusions. The chemical composition of HSV is complex. The virion contains a linear continuous (non-fragmented) double-stranded DNA (6.5%), protein (70%), phospholipids (20%), carbohydrates (1.6%), spermine, spermidine, glycoproteins. The virion envelope contains a significant amount of lipids (more than 20%) [2]. HSV is highly sensitive to heat (it is inactivated at a temperature of 50–52 °C for 30 minutes, and at 37 °C for 10 hours). The virus stably holds on to temperature (at -24 °C for up to 2 years), includes ionizing radiation and ultrasound, freezing and thawing. Due to the fact that HSV virions are more than 20% part of the lipids that are present in the envelope of the virus, it is easily absorbed by ether. Alcohol, chloroforms, phenol, formalin, proteolytic enzymes, phosphatase, bile are also HSV inactivators [4]. UV exposure, exposure to reflective rays and photodynamically active dyes (Proflavin, Neutral Red) covers HSV even at low doses.



The virus has two antigenic types pathogenic for humans. HSV-1 usually occurs in the mouth, nasopharynx, eyes, skin responsible for infection above the waist); HSV-2 - urogenital tract (below the belt). However, in the course of recent observations, it was found that HSV, regardless of type, can affect all human organs and systems, cause acute, latent and chronic infection, cause diseases of the central and peripheral nervous system, parenchymal organs, eyes, skin, oral mucosa passengers, gastrointestinal tract, genitals. Viral intrauterine pathology of the fetus, diseases of newborns (with a frequent fatal outcome). HSV can manifest itself as a manifestation of carcinogenesis, induce atherosclerosis and Alzheimer's disease [1, 2, 4]. In recent years, the relevance of herpes infection with its spread in AIDS patients. It has been established that HSV can activate the HIV genome at the provirus stage and be a cofactor in the progression of HIV infection. According to WHO data, HSV-related mortality ranks second among viral diseases after discomfort [3]. Classification according to ICD-10: B 00. Infections caused by the herpes virus (herpes simplex). 00.9 Herpes infection, unspecified HSV infection is the most common among humans (80–95% of the population are lifelong carriers of the virus). Seroepidemiological studies have shown that by the age of 15, about 83% of children are infected with HSV, and at the age of 30 years and older, more than 90% of the population have antibodies to HSV of one type or another [2, 3, 4]. Most people are exposed to the virus in early childhood. A manifestation of primary herpes infection is often acute herpetic stomatitis (AHS), most common in children aged 6 months to 3 years [3]. This is due to the disappearance of antibodies obtained interplacentally from the mother, with structural features of the oral mucosa, high permeability of histohematological barriers, insufficient activity of local immunity, as well as with frequent natural violations of the integrity of the mucous membrane as a result of teething and microtrauma. Transmission of infection occurs by contact or airborne droplets. The disease is contagious (there are outbreaks of stomatitis in children's institutions, hospital children's wards, orphanages, families). The source of infection is a sick person or a virus carrier. The pathogenesis of herpetic stomatitis OGS, proceeding as an infectious disease, has 5 periods of development:

- 1) incubation;
- 2) prodromal;
- 3) the period of development of the disease: a - catarrhal; b - rashes of elements of the lesion;
- 4) the period of extinction of the disease;
- 5) clinical recovery. The incubation period of the disease lasts from 2 to 17 days. After the virus enters the child's body, it multiplies in the cells of local tissues and nearby lymphatic formations, which is manifested by the occurrence of regional lymphadenitis (submandibular, sometimes cervical). Lymphadenitis in OHS precedes rashes of lesions in the oral cavity, accompanies the entire course of the disease and remains for 7–10 days after complete epithelialization of the elements. During the incubation period, primary viremia is observed. With a herpes infection, regardless of the mechanism of infection, viremia develops. Penetrating through the capillary barrier by diapedesis, HSV settles in the liver, spleen and other organs and multiplies rapidly. Tissue lesions appear as foci of necrosis. Secondary viremia corresponds to the prodromal and catarrhal period of the disease and is characterized by the appearance in the blood of a large amount of the virus, after its multiplication in these



organs. With viremia, HSV is found in leukocytes, erythrocytes, and platelets. During secondary viremia, viruses rush to the skin, mucous membrane, where their intracellular reproduction continues [2–4]. The catarrhal period is due to a generalized lesion of epithelial tissues and the reproduction of HSV in them. Depending on the degree of generalization, the mucous membranes of the oral cavity, pharynx, upper respiratory tract, eyes, and sometimes the genitals are involved in the pathological process. The more severe the disease, the more pronounced the viremia and the intensity of intracellular reproduction of HSV, the longer and brighter the manifestations of catarrh of the mucous membranes. Under the influence of this process, the formation of clinical symptoms in the form of laryngitis, runny nose, cough, conjunctivitis, vulvitis, etc. is possible. A special role in the occurrence of a catarrhal state of the mucous membranes is played by a violation of the blood coagulation system during herpetic infection, which increases the symptom of bleeding of the mucous membranes. Necrotic areas in organs and tissues during herpetic infection occur as a result of both direct destruction of cellular elements by the virus, and as a result of capillary thrombosis. In children who have undergone ACS, a clinical recovery occurs, but the release of HSV with saliva can last several weeks. The state of the immune system plays an important role in the occurrence and nature of the course of herpetic infection. The body's immune response to a virus consists of two phases. In the first phase, the production of interferons and the activation of natural killers are stimulated. In the early stages of a viral infection, under the influence of interferon, the activity of natural killers, their proliferation, and the formation on the cell surface of determinants involved in the binding of natural killers to virus-infected cells sharply increase. Interferon restores the activity of natural killers after they have delivered a lethal blow. Due to this, the pathological action of the virus is limited. In the second phase of the immune response, a number of immune reactions are triggered: the production of humoral specific antibodies, active T-cells (enhancing or suppressing the functions of other cells), T-cell immunity reactions. Factors of cellular immunity suppress the replication and dissemination of the virus in the body, cause lysis of infected cells, releasing the virus for subsequent neutralization by antibodies. Thus, primary infection stimulates both humoral and cellular immune responses. Specific antibodies after a primary infection may persist for a long time. However, they do not protect against recurrence of the disease. The leading factors in the pathogenesis of recurrent herpetic infection is the pathology of the cellular link of immunity and interferon formation. The pathogenesis of herpes infection is determined by the ability of HSV to persist in the nerve ganglia throughout a person's life. Once attached to the nerve endings, the virions are rapidly transported into the axons. Then the virus reaches the pseudounipolar neurons of the regional ganglion (Gasser node), where it persists throughout life. The virus resides in the ganglion in the form of viral DNA. The "silent" genome cannot be removed from ganglion cells by any known antiviral chemotherapy drugs. HSV, which is in a latent state, is protected from the human immune system, but at the same time it is able to infect other people who come into contact with the virus carrier. Asymptomatic isolation of the virus (detected in saliva) is observed in 5-10% of individuals who do not have clinical manifestations. HSV reactivation means the persistence of whole viral DNA molecules and its expression. The activated virus is carried along the axon to the site of its initial entry into the body. The clinical manifestation of



this is the appearance of HSV in saliva, the occurrence of a repeated lesion [5, 7]. Clinically, the disease proceeds according to the type of acute infectious process in the form of mild, moderate and severe forms. The severity of the pathology is determined by the severity of general symptoms and the prevalence of lesions of the oral mucosa. The clinical course of the disease, its forms and periods are presented Scheme of the evolution of the elements of the lesion in the oral cavity: a spot - a vesicle with cloudy (fibrinous) contents - erosion with uneven scalloped edges (formed as a result of the opening of the vesicle. Grouped erosions, often merging into erosive areas) - erosion in the epithelialization stage (covered fibrinous plaque, a corolla of hyperemia appears around) - a spot. Clinical recovery The temperature is normal. Feeling good. Gingivitis absent (or untreated gingivitis). Lymphadenitis persists for 7 days. Duration 7 days Lymphadenitis 7 days Residual effects of gingivitis. Lymphadenitis. The duration of the period is 7–10 days. Criteria for the early clinical diagnosis of ACS should be highlighted: submandibular lymphadenitis, catarrhal gingivitis, symptoms of acute respiratory viral infections. When these symptoms appear, early antiviral therapy should be initiated. The virus remains in the body for life. Children who have had ACS become carriers of the virus or suffer from recurrent herpetic stomatitis (RGS), herpes lips. Every 7–8th child develops a relapsing form of the disease after suffering from ACS. Moreover, in most children, a relapse occurs within the first year after ACS. Factors contributing to the activation of HSV. In small amounts, HSV can be activated spontaneously. However, this mainly occurs as a result of various factors: hypothermia, overheating, insolation, febrile conditions, respiratory viral infections, diseases of internal organs, stress, hormonal changes, diseases with a defect or with a decrease in immunity, taking drugs that cause immunosuppression. Under the influence of such factors, an imbalance in the "organism-virus" equilibrium occurs in favor of the virus. Along with this, great importance is attached to the change in the physiological state of the skin and mucous membranes: microtrauma of the oral mucosa, microtrauma as a result of bad habits ("biting, chewing lips, cheeks, tongue", "the child puts everything in his mouth", "constantly hands in mouth"), microtrauma after dental intervention or cosmetic procedures. As a result, nerve endings are irritated, productive replication in neurons is turned on, and favorable conditions are created for the reproduction of the virus in the skin and mucous membranes. Clinical course of CHD The severity depends on the frequency of relapses of the disease, the duration of recurrence, the severity of general and local symptoms. The mild form of CHD is characterized by rare (from 1-2 times in several years to 2 times a year) relapses of the disease. In the moderate form of CHD, relapses of the disease are observed 3-4 times a year. The severe form of CHD is characterized by frequent (5 or more times a year) relapses of the disease and a permanent (continuously relapsing) form of the disease. In preschool children, the first relapses occur mainly with general symptoms of varying severity. For children of the older age group, generally weak severity or absence of general symptoms are characteristic (since relapses occur in the presence of high titers of antiviral antibodies). Methods for laboratory diagnosis of HSV:

1. Virological.
2. Electron microscopy.



3. Cytological.

4. Serological: - immunofluorescent (IF); – enzyme immunoassay (ELISA).

5. Indication and identification of nucleic acids (molecular biological methods). Used to detect the viral genome in the test material: the method of molecular hybridization of nucleic acids (MG), polymerase chain reaction (PCR). B The percentage of positive results of diagnostic methods increases when material is taken in the first 2-3 days of the disease Treatment of herpetic stomatitis. Unfortunately, there are currently no treatments that can eliminate HSV from the human body. Therefore, the purpose of therapeutic measures is: a) suppression of the reproduction of HSV in the acute period; b) the formation of an adequate immune response and its long-term preservation in order to block the reactivation of HSV in the persistence foci. There are two main directions in the treatment of herpes simplex:

1. The use of antiviral chemotherapy, the main place in which is given to acyclic nucleosides and, first of all, acyclovir.

2. A complex method of treatment, including antiviral therapy in combination with immunotherapy. The list of drugs used in the treatment is presented below. Means of therapy and prevention of herpetic infection

1. Antiviral drugs: a) abnormal nucleosides: Acyclovir (Zovirax), Valaciclovir (Valtrex), Famciclovir (Famvir), Vidarabine, Trifluorothymidine, Ribavirin, Cytarabine, Idoxuridine, Penciclovir, Foscarnet; b) specific inhibitors: Bonafton, Riodoxol, Florenal, Tebrofen, Deoxyribonuclease, Flacoside, Helepin, Alpizarin, Panavir, Oksolin. 2. Means of immunoreplacement, immunostimulating and interferon replacement therapy:

a) specific immunoglobulins: immunoglobulins with an increased titer of antiherpetic antibodies, human immunoglobulin, Cytotect, Intraglobin, Pentaglobin, Vezikbulin;

b) interferons and their inducers: human leukocyte interferon, Reaferon, Reaferon-A, Viferon, Leukinferon, Amiksin, Neovir, Cycloferon, Ridostin, Poludan, Megosin, Larifan; c)

immunomodulators acting on macrophages: Polyoxidonium, Likopid, Galavit; d)

immunomodulators acting on T-lim- (22) VESTNIK VolGMU 2007 16 2 focytes: Imunofan, Roncoleukin. Thymus hormone preparations: thymalin, thymosin, thymogen. e)

immunomodulators of a mixed mechanism of action: Derinat, Glutoxim, Ferrovir, Gepon, Imudon, Prodigiosan. 3. Herpetic vaccines.

4. Adaptogens of plant origin: eleutherococcus, ginseng root, yarrow, aloe.

5. Natural antioxidants (vitamins E and C). Currently, the main antiherpetic drugs with efficacy proven in randomized clinical trials include drugs from the group of nucleoside analogues: acyclovir, valaciclovir, penciclovir, famciclovir. In humans, valaciclovir is converted to acyclovir and famciclovir to penciclovir. Penciclovir and famciclovir are used to treat herpes infections in adults. Acyclovir is the ancestor of drugs blocking the synthesis of viral DNA, the "gold" standard of antiherpetic therapy. The drug acquires activity only under the influence of the virus enzyme - thymidine kinase, turning into acyclovir triphosphate, which becomes a defective substrate for the viral DNA polymerase. Thus, viral DNA polymerase is inhibited, viral DNA synthesis is blocked. The drug acts exclusively in cells affected by the virus, does not act on the DNA polymerase of human cells and is inactive in healthy cells. Therefore, it has high specificity and low toxicity. General treatment of acute herpetic stomatitis.



1. Antiviral drugs (prescribed for all degrees of severity of the disease): acyclovir: children over 2 years and adults 200 mg orally 5 times a day for 5 days. For children under 2 years of age, the dose is half the adult dose; valaciclovir (Valtrex): for adults and adolescents (from 12 years old) 500 mg 2 times a day for 3-5 days.
2. Preparations of interferons and their inducers: additional therapy according to indications in severe, complicated form of acute hepatitis C.
3. Immunoglobulins (immunoglobulin with an increased titer of antiherpetic antibodies, human immunoglobulin) are prescribed according to indications in severe ACS with severe symptoms of intoxication.
4. Detoxification: drinking plenty of water, multivitamin preparations.
5. Antipyretic drugs (at temperatures above 38 ° C).
6. Antihistamines.
7. Special nutrition and feeding. Plentiful drink. Food that does not irritate the affected mucous membrane: fresh vegetable broths, meat and fish broths, to which ground boiled meat is added after readiness; non-irritating juices and purees from vegetables and fruits (carrot, apple, rosehip broth). It is recommended to give lactic acid products (kefir, cottage cheese), warm low-fat milk; eggs boiled and mashed with broth, milk. General treatment of CHD There are several treatment regimens for recurrent herpes infection that have shown their effectiveness. In Russia, the program developed in 1991 by a group of virologists headed by V. A. Isakov is the most thoughtful and theoretically substantiated [2]. Its essence lies in the fact that patients with herpes infection require treatment both in the acute phase of the disease and in the period of remission. Local treatment is carried out 5-6 times a day for 5-10 days until complete epithelialization of the lesions. 5. Physical methods of local treatment (laser physiotherapy - an additional method according to indications).

Conclusion

Our own experience of long-term observation of patients with acute and recurrent herpetic stomatitis, herpes lips allows us to recommend the use of local therapy only in combination with general antiviral treatment (for all forms and degrees of severity of the disease) in order to prevent early recurrence and prevent an increase in the frequency of relapses.

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