EDUCATIONAL COMMENTARY – HERPES SIMPLEX VIRUS

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LEARNING OUTCOMES

On completion of this exercise, the participant should be able to

- describe the symptoms related to herpes simplex 1 (HSV-1) and HSV-2 infections.
- discuss the transmission of HSV.
- list the drugs used to treat HSV infection.
- discuss laboratory testing related to HSV.

Introduction

Eight of the herpes viruses cause infection in humans. Herpes simplex virus (HSV) is one of these. The others include varicella zoster and herpes zoster, associated with chickenpox and shingles, respectively; Epstein-Barr virus, which causes infectious mononucleosis; and cytomegalovirus, human herpesvirus 6 and human herpesvirus 7, associated with roseola. Once a person is infected with any of these viruses, the infection continues for life.

There are two serotypes of HSV: HSV-1 and HSV-2. HSV-1 is responsible for most cases of oral cold sores or fever blisters and, in some cases, results in serious infection of the cornea. It is usually contracted in early childhood. According to the Centers for Disease Control and Prevention (CDC), approximately 56% of males and 60% of females between the ages of 14 and 49 test positive for HSV-1.\(^1\) Its seroprevalence in adults in Western countries is 50% to 80%. HSV-2 is the common cause of genital herpes, although HSV-1 may also cause a genital infection. There are approximately 776,000 new cases of HSV-2 infection in the United States annually.\(^2\)

Symptoms

HSV causes an eruption of small, fluid-filled blisters on the skin, predominantly in the mouth, lips, or genitalia. The primary infection may cause fever, malaise, and muscle aches. The symptoms persist for 2 to 4 weeks. After the blisters disappear, the virus remains dormant in the ganglia that serve the area of the infection. The virus may reactivate chronically after the initial infection. In reactivations, the virus replicates and travels along the nerve, returning to the skin or mucous membranes in the area of the
primary infection. The reactivation produces a milder disease that includes the blisters but not the other symptoms customary in the primary illness. Approximately 12 to 24 hours before the eruption of blisters, the patient often experiences tingling in the affected area. Reactivation may be triggered by another infection, stress, fever, or any condition or drug that causes immunosuppression. Complications of HSV infection include herpes simplex keratitis (corneal infection) which can lead to blindness, and herpes encephalitis which may lead to brain damage or death.

Transmission

Contact with the blisters or sores produced during the infection may result in transmission of the virus. Shedding of the virus occurs during symptomatic episodes but may also occur during asymptomatic periods. The virus is very contagious during viral shedding. There is no cure for HSV infection, and the virus remains in the body for life.

HSV-2 is transmitted sexually and may be transmitted at birth to a neonate. The risk for prenatal transmission is high in mothers who acquire the infection late in the pregnancy. Caesarian delivery may prevent transmission of the virus to the neonate. Women with recurrent disease before the pregnancy are unlikely to transmit the virus to the neonate. Treatment is often ineffective; approximately two-thirds of neonates who contract HSV develop brain damage or die.

Treatment

Although latent HSV cannot be eradicated, treatment with antiviral drugs often reduces the severity and speeds the resolution of the symptoms. Acyclovir, valacyclovir, and famciclovir are administered and, if introduced within 72 hours of the onset of symptoms, are effective in reducing the severity of the symptoms. Antivirals reduce viral shedding, but because they do not totally eradicate the virus, transmission remains possible. Intravenous acyclovir is used in cases of severe infection. Prophylactic treatment is often prescribed for persons with genital HSV infection. The long-term use of antiviral medications in transplant recipients and patients with HIV has resulted in mutations of the virus and produced antiviral-drug resistance in some patients. The prevalence of drug resistance in immunocompromised patients is 5%. The prevalence in allogeneic bone marrow transplant recipients is greater, reaching up to 30%.

Laboratory Testing

In most cases, the physician is able to diagnose the patient as having HSV-1 or HSV-2 infection by visual examination of the lesions. When symptoms are more severe, as in encephalitis or keratitis, laboratory testing to identify the causative organism may be necessary. Laboratory assays are performed on fluids
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from scrapings of the lesions to detect the virus or its DNA, and on serum to detect antibodies produced against the virus.

Enzyme-linked immunosorbent assay (ELISA) techniques for IgM and IgG for HSV-1 and HSV-2 are available. The presence of IgM in a patient’s serum indicates an acute infection. HSV IgG remains positive for life in persons who have been infected. Diagnosis of an acute infection can also be accomplished using an IgG ELISA assay. Serial IgG determinations on serum samples collected approximately two weeks apart must show at least a two-fold rise in the titer to consider the patient positive for a current infection. A titer that remains the same or only changes by one dilution indicates that the IgG antibodies were produced in an earlier infection.

The virus can be cultured from scrapings of a lesion collected within 48 hours of the onset of symptoms. After the virus is isolated, the subtype can be identified by direct immunofluorescence using monoclonal antibodies specific for HSV-1 or HSV-2 antigens conjugated with fluorescent dye.

HSV DNA testing is performed using polymerase chain reaction (PCR) to detect the presence of genetic material of the virus in a patient’s blood, cerebrospinal fluid, or fluid from a lesion. The HSV serotype is also identified when using this method. DNA testing is the preferred method for evaluating patients with encephalitis or keratitis, because its high sensitivity allows detection of very small amounts of the virus.

Antiviral drug resistance can be detected using molecular diagnostic techniques. Phenotypic and genotypic methods are performed. Phenotypic methods require several days to perform. Genotypic assays are more common, less time-consuming, and can identify the specific mutation. Resistance testing is not standardized and is only available in a few laboratories across the nation.4

Conclusion

HSV infection is common but in most cases not fatal. In cases in which the eye or brain is affected, laboratory testing can be important in identifying the cause of infection and the serotype involved. Treatment varies according to the serotype involved. Drug-resistant HSV occurs in patients who have undergone long-term antiviral therapy. Resistant HSV can be problematic in immunocompromised or transplant patients. Availability of testing for antiviral drug resistance in HSV is limited.

References

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