



Review Article

Review of virus diseases in the nervous system

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Abstract

Viruses are important to the study of molecular and cellular biology as they provide simple systems that can be used to manipulate and investigate the functions of cells. The study and use of viruses have provided valuable information about aspects of cell biology. For example, viruses have been useful in the study of genetics and helped our understanding of the basic mechanisms of molecular genetics, such as DNA replication, transcription, RNA processing, translation, protein transport, and immunology. This Review focused on the neurological complications of the human herpes viruses (HHVs), and discusses optimal virological tests to identify the etiological agent, along with state-of-the-art treatments for these disorders.

Key words

Viruses, Encephalitis, Meningitis, Herpes, Infection, Latency, Neurological complications.

Introduction

The term "Slow virus infections" refers to the tempo of the disease, not to the growth rate of the virus. These diseases have a prolonged incubation period (which can be months or years), and a protracted, progressive clinical course. Slow virus diseases may be caused by conventional viruses or by the unconventional viruses (also known as the unconventional agents or typical viruses/agents). The symptoms

associated with slow viral diseases of the central nervous system tend to have multiple neurological manifestations. Different patients may present with very different symptoms. The brain and spinal cord are fairly resistant to infection, but when an infection affects the central nervous system (CNS), it can be very serious. There are numerous kinds of CNS infections, including rabies and botulism, and most can be categorized as 1 of 3 types: meningitis, encephalitis, and brain abscess. CNS infections are caused by bacteria, viruses, fungi,



or parasites. In response to one of these pathogens, the brain, and sometimes the spinal cord, becomes inflamed. Herpes viruses are large double-stranded DNA viruses [1]. Approximately 130 different herpes viruses have been identified, not only in mammals, but also in frogs, lizards, birds, fish and mosquitoes. There are eight human herpes viruses (HHVs): herpes simplex virus (HSV) - 1, HSV-2, Varicella zoster virus (VZV or HHV-3), Epstein–Barr virus (EBV or HHV-4), Cytomegalovirus (CMV or HHV-5), HHV-6, HHV-7, and HHV-8 [2]. A characteristic feature of all herpes viruses is their ability to become latent, primarily in ganglia of the nervous system and lymphoid tissue. For example, HSV and VZV become latent in neurons of ganglia, whereas EBV is latent in B lymphocytes. Most of the HHVs are neurotropic and infrequently cause serious acute and chronic neurological disease of the PNS and CNS that might be monophasic, recurrent or chronic [3]. Infection with each herpes virus produces different clinical features and imaging abnormalities and many HHV infections can now be treated.

What are some disorders of the nervous system?

The nervous system is vulnerable to various disorders. It can be damaged by the following:

- Trauma
- Infections
- Degeneration
- Structural defects
- Tumours
- Blood flow disruption
- Autoimmune disorders

Disorders of the nervous system

Disorders of the nervous system may involve the following:

- **Vascular disorders**, such as stroke, transient ischemic attack (TIA), subarachnoid hemorrhage, subdural hemorrhage and hematoma, and extra dural hemorrhage
- **Infections**, such as meningitis, encephalitis, polio, and epidural abscess
- **Structural disorders**, such as brain or spinal cord injury, Bell's palsy, cervical spondylosis, carpal tunnel syndrome, brain or spinal cord tumors, peripheral neuropathy, and Guillain-Barré syndrome
- **Functional disorders**, such as headache, epilepsy, dizziness, and neuralgia
- **Degeneration**, such as Parkinson's disease, multiple sclerosis, amyotrophic lateral sclerosis (ALS), Huntington's chorea, and Alzheimer's disease [4].

Signs and symptoms of nervous system disorders

The following are the most common general signs and symptoms of a nervous system disorder. However, each individual may experience symptoms differently. Symptoms may include:

- Persistent or sudden onset of a headache
- A headache that changes or is different
- Loss of feeling or tingling
- Weakness or loss of muscle strength
- Sudden loss of sight or double vision
- Memory loss
- Impaired mental ability
- Lack of coordination
- Muscle rigidity
- Tremors and seizures
- Back pain which radiates to the feet, toes, or other parts of the body
- Muscle wasting and slurred speech



The symptoms of a nervous system disorder may resemble other medical conditions or problems [5].

Encephalitis

Encephalitis is defined as inflammation of the brain due to an infection. This inflammation is commonly the result of a viral infection. Viruses can gain access to the central nervous system (CNS) through the blood or by travelling within nerve cells (neurons). The neuro-Intensive Care Unit (ICU) deals primarily with acute viral encephalitis. In the United States, the most common cause of acute viral encephalitis is the herpes simplex virus.

Meningitis

In order to better understand meningitis one must first have knowledge about the structures surrounding the brain. Beneath the inner surface of the skull the brain is surrounded by a membranous covering known as the meninges. A fluid known as cerebrospinal fluid (CSF) circulates around the brain and serves to cushion the brain against injury. Meningitis is an inflammation of the meninges due to infection. It occurs when a foreign pathogen invades the subarachnoid space and populates the CSF. The foreign microorganisms can either be bacteria or viruses. Accordingly, meningitis can be classified as either bacterial or viral. Since bacterial infection is much more serious, a neuro-ICU is specialized towards the treatment of this type of meningitis [6].

Brain abscess

A brain abscess is a circumscribed region of infection within the substance of the brain. The abscess is initially characterized by an area of necrotic brain tissue surrounded by a zone of

cerebritis (local inflammation of brain cells). As the abscess develops the necrotic area becomes filled with pus and a ring of cells surrounds the area [7]. A mature abscess is characterized by a necrotic puss-filled region of brain tissue, surrounded by an area of cerebritis.

What causes a brain abscess to form?

A brain abscess forms as the result of the spread into brain tissue of an infection elsewhere.

There are three possible origins of this infection:

1. An abscess most commonly arises via the direct extension into the skull of a local infection in the paranasal sinuses or in the middle ear.
2. Microorganisms can also be spread by the blood during a systemic infection. In this case bacteria are carried to the site of abscess from a distant source, typically the skin, lungs, mouth, or heart valves. Under these circumstances there is not a solitary abscess but rather multiple abscesses in the brain.
3. Lastly, a brain abscess can result from head trauma. An infection can arise from a wound penetrating the skull. In this case inoculation with bacteria occurs from infected bone fragments or debris from the penetrating instrument [8].

Herpetic infections

Cold sores or fever blisters - those annoying purplish-reddish-whitish blisters that tend to pop up around people's mouths - are the most familiar sign of herpes, one of the world's commonest viral infections. Its full name is herpes simplex infection, and it occurs around the globe, even among remote Indian tribes in Brazil. Herpes simplex is best known for causing cold sores or genital blisters that go away on their own, only to break out again weeks or months or even years later. While these can be



painful and upsetting, they usually are not serious, and outbreaks get milder as time goes on. When herpes causes genital sores, it is considered a sexually transmitted disease [9].

In rare cases, herpes simplex can infect the eyes or internal organs, including the brain, where it may cause an infection called viral encephalitis. If the virus spreads to newborn babies, or to people with weakened immune systems, it can be serious, even fatal. Most often, however, herpes causes no symptoms at all or symptoms so mild that people do not realize they are infected with the virus. There are two types of herpes simplex virus. Both types can infect the mouth or the genitals. Usually, however, mouth blisters are caused by herpes simplex virus 1 (HSV-1), and genital blisters are caused by herpes simplex virus 2 (HSV-2) [10].

HSV-1

HSV-1 is common in children, and more than 90 percent of Americans become infected with it. It is spread by direct contact with an infected area - kissing a person with a cold sore, for instance - or by saliva. Although it does not usually spread on objects, some experts advise washing an infected person's eating utensils and towels before others use them [11].

HSV-2

HSV-2 usually is spread by sexual contact with an infected person. About 22% of adult Americans, or 1 in 5, have it. That number has risen sharply since 1980, with the fastest increase occurring among teenagers. HSV-2 spreads most easily when blisters are visible, or just before they appear. But it can be contagious even when there are no symptoms, and infected people often pass it on without knowing they have it. For this reason, genital herpes is sometimes called a silent epidemic. If a woman becomes newly infected with genital herpes during pregnancy, the infection can spread to the baby, who may be born prematurely,

become very sick, or even die [12]. Contagious means transmittable from one person to another. People can avoid infection by not engaging in sexual activity. For sexually active people, having few sexual partners and using latex condoms can reduce the chances of infection. Difficult as it may be, people with genital herpes should tell any potential sexual partner that they are infected. They should not have sex during an outbreak or if they feel an outbreak coming on.

What happens during the first herpes outbreak?

In herpes of the mouth or of the genitals, the first signs are usually itching, fever, and aches. Within hours or days, the skin breaks out in clusters of small blisters filled with fluid. In a week or two, the blisters begin to heal, drying into a yellowish crust. After three weeks, they usually are gone. The first time symptoms occur, they usually are more severe, especially in young children, who may have many painful mouth sores, swollen gums, fever, and aching muscles. When the symptoms recur, they usually are milder [13, 14]. Although the first outbreak usually starts within 10 days of infection, sometimes people do not notice blisters until years after they were infected. The nervous system is a complex, sophisticated system that regulates and coordinates body activities. It is made up of two major divisions, including the following:

- **Central nervous system (CNS).** This consists of the brain and spinal cord.
- **Peripheral nervous system (PNS).** This consists of all other neural elements.

In addition to the brain and spinal cord, principal organs of the nervous system include the following:

- Eyes
- Ears
- Sensory organs of taste



- Sensory organs of smell
- Sensory receptors located in the skin, joints, muscles, and other parts of the body [15].

Conclusion

Viruses affect the central nervous system in two ways. They can directly infect and destroy cells in the central nervous system during the acute illness. After recovery from an infection - in the central nervous system or elsewhere in the body - the immune response to the infection sometimes causes secondary damage to the cells around the nerves. This secondary damage (post infectious encephalomyelitis or acute disseminated encephalomyelitis) results in the child having symptoms several weeks after recovery from the acute illness. Most HHVs can cause serious neurological disease of the PNS and CNS through primary infection or following virus reactivation from latently infected human ganglia or lymphoid tissue. The neurological complications include meningitis, encephalitis, myelitis, vasculopathy, acute and chronic radiculoneuritis, and various inflammatory diseases of the eye. Disease can be monophasic, recurrent or chronic. Recognition of the clinical patterns and imaging characteristics of disease produced by different herpes viruses is important, because infection by many of the herpes viruses can be treated successfully. Early diagnosis and proper treatment are essential to a favourable outcome.

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