The varicella-zoster virus (VZV) is a single virus that causes two diseases. The primary VZV infection, known as chickenpox, typically occurs during childhood. Herpes zoster infection results later in life from reactivation of VZV in the dorsal root ganglia. Herpes zoster characteristically results in a rash with a unilateral dermatomal distribution, which usually resolves within 2 to 4 weeks. If the infection does not resolve after its acute phase, long-term complications, such as postherpetic neuralgia, may develop. The author discusses the natural history and incidence of primary VZV infection and herpes zoster and details the epidemiology, clinical manifestation, diagnosis, and complications of this disease.

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tion. Primary VZV is transmitted from person to person by direct contact, inhalation of aerosols from vesicular fluid of skin lesions, or infected respiratory tract secretions that are aerosolized. Herpes zoster is typically transmitted person to person by direct contact. Because of its respiratory transmission, VZV can cause an epidemic among susceptible hosts.

In the United States, more than 90% of adults are susceptible to herpes zoster infection, and there is no way to predict in whom the infection will reactivate.1 The lifetime risk for development of herpes zoster is estimated to be approximately 30%—meaning that the illness will occur in about one in three adults.2,4

An estimated 1 million new cases of herpes zoster occur each year in the United States,5 resulting in 50,000 to 60,000 hospitalizations. Recurrence of shingles is uncommon. Only an estimated 4% of patients will experience a second episode of shingles, and third episodes are even rarer.5

The incidence and severity of herpes zoster increase with advancing age (Figure 2).5 Approximately 40% to 50% of the 1 million new cases that occur each year develop in individuals who are at least 60 years of age.5 Among individuals who reach age 85 years, as many as 50% will have experienced at least one episode of herpes zoster.6,6 With each decade of life, the incidence rate of herpes zoster per thousand person-years steadily increases.

The increased risk of herpes zoster associated with advancing age is at least partly caused by immunosenescence, the gradual deterioration of the immune system that is part of the natural aging process. Specific age-related decline in cell-mediated immunity to VZV also contributes to this increased risk.7

In addition to the role played by advancing age, immunosuppression increases the risk for development of herpes zoster. In fact, herpes zoster is the earliest opportunistic infection observed in patients with human immunodeficiency virus (HIV)/AIDS as their CD4 T-cell count declines. Patients who are immunocompromised have earlier and increased manifestations of herpes zoster infection than those who are not immunocompromised.8–12

The management of HIV/AIDS or other immunocompromising diseases may also contribute to herpes zoster development. For example, one of the most powerful risk factors for herpes zoster infection is the use of systemic corticosteroids, which are part of the standard management of most autoimmune diseases.

Despite the increased risk of herpes zoster associated with immunosuppres-
Clinic Manifestations

As previously mentioned, herpes zoster is the consequence of the primary VZV infection reactivating after a period of dormancy in the dorsal root ganglia. Herpes zoster is characterized by a unilateral vesicular eruption in a dermatomal distribution, with thoracic and cranial and cervical distributions being the most common. Zoster lesions contain high concentrations of VZV, which can be spread to susceptible individuals by direct contact with the lesions. Localized herpes zoster is contagious from the time of rash eruption until the time of lesion crusting. The rate of transmission of herpes zoster infection is lower than that of primary VZV infection.8,12

Figure 3 displays the stages of clinical manifestation of herpes zoster. In the initial stage of herpes zoster infection, known as the prodromal phase, patients may report such symptoms as headache, pain, malaise, and acute photophobia before the rash appears. After the prodromal phase, the acute phase is characterized by the dermatomal rash. The herpes zoster rash is typically unilateral, not crossing the midline of the body.4,13

The rash may be accompanied by unbearable itching, altered sensitivity to touch, or allodynia (ie, pain at the site provoked by innocuous stimuli). Pain may also be felt before the rash develops. In some cases, patients experience the allodynia, pain, itching, and burning without a rash ever developing—a condition known as zoster sine herpete. Initially, the rash is erythematous and maculopapular, but it progresses to take the form of coalescing clusters of clear vesicles containing high concentrations of VZV.4,13

The rash typically lasts 7 to 10 days and fully heals within 2 to 4 weeks. However, permanent scarring and altered pigmentation occur in some cases. If the infection does not resolve after the acute phase, complications, such as postherpetic neuralgia (PHN), may develop.4,13

Diagnosis

A diagnosis of herpes zoster is often made based on the localization and morphologic characteristics of the rash. However, the rash associated with herpes zoster is sometimes confused with that of herpes simplex virus (HSV). Physicians should keep in mind that a rash that is recurrent in the same dermatome is most likely HSV. A comparison of VZV and HSV is available elsewhere in this supplement to JAOA—The Journal of the American Osteopathic Association.14

The varicella-zoster virus can be collected from lesions and identified using tissue culture, but this is a time-consuming process, and false-negative results may occur because viable virus is difficult to obtain from cutaneous lesions. Polymerase chain reaction (PCR) can be used to detect the DNA of VZV from collected lesion material. However, this technique is not widely available.

Direct fluorescent antibody staining of VZV-infected cells obtained by scraping the base of the lesion is a rapid and sensitive method for diagnosis of herpes zoster. This technique is useful for evaluation of atypical skin lesions to guide early treatment decisions.

When the symptoms of allodynia, pain, burning, and itching manifest without the rash, herpes zoster is especially difficult to diagnose. As a result of its localization, pain is often misdiagnosed as a gallbladder attack or appendicitis and is mismanaged until a rash develops.

Results of recent studies15,16 suggest that PCR can be used to positively identify VZV DNA in patients’ blood before symptoms manifest. Thus, PCR has potential application as a diagnostic tool for identifying patients who are in the prodromal phase of herpes zoster and patients who have zoster sine herpete, allowing these individuals to receive treatment before rash and nerve damage develop.

Complications

Postherpetic neuralgia is a common and potentially debilitating complication of herpes zoster that is difficult to manage. It is characterized by pain or dysesthesia that persists after resolution of the rash. Postherpetic neuralgia occurs in 10% to 18% of patients with herpes zoster, and the risk for development of this complication increases with advancing age.17

The severity of pain in PHN ranges from mild to excruciating, and it can be constant, intermittent, or triggered by such stimuli as clothes touching the skin.
Although allodynia affects 45% to 55% of patients with herpes zoster, it may affect as many as 90% of those with PHN. The pain associated with herpes zoster or PHN may last for a few minutes or occur as chronic pain. The duration of PHN has been found to be inconsistent, ranging from 30 days to 6 months or longer after rash onset. In some cases, the pain persists for years.

Postherpetic neuralgia adversely affects the patient’s quality of life as a result of its potential to interfere with sleep, work, and other activities of daily living, leading to social withdrawal and depression. In a study by Katz and Melzack, in which patients were asked to compare the pain associated with PHN with other types of pain they had experienced, pain associated with PHN was ranked as more severe than labor pain, postsurgical pain, arthritis pain, and chronic cancer-related pain.

Pathologic mechanisms believed to cause the transition from uncomplicated herpes zoster to PHN include axonal and cell-body degeneration, atrophy of the spinal cord dorsal horn, scarring of the dorsal root ganglia, and loss of epidermal innervations in the affected region.

In addition to PHN, other neurologic complications that can result from herpes zoster include chronic sensory loss at the site of the rash, limb weakness, and autonomic dysfunction related to the site of the rash (eg, bladder dysfunction if the rash has sacral dermatomal distribution). More severe neurologic complications include encephalitis, meningitis, and myelitis. Bacterial “superinfection,” particularly with methicillin-resistant Staphylococcus aureus, can also occur. Disseminated disease, with a mortality rate as high as 40%, is a complication that is observed mainly in patients who are immunosuppressed.

Herpes zoster ophthalmicus, which is prevalent in 10% to 25% of patients with herpes zoster, can occur when reactivation of latent VZV involves the first division of the trigeminal nerve. Ophthalmic herpes zoster is a severe complication that is difficult to manage. Affected patients require admission to the hospital and administration of intravenous acyclovir and, in some cases, intravenous immunoglobulin. Even after aggressive management, patients may have long-term sequelae, including vision loss and pain related to the location of the rash, stemming from herpes zoster ophthalmicus. Keratitis occurs in approximately two-thirds of patients with herpes zoster ophthalmicus.

Conclusion
Herpes zoster infection results from the reactivation of VZV in the dorsal root ganglia. It typically results in a rash with a unilateral dermatomal distribution, which usually resolves within 2 to 4 weeks. Herpes zoster may or may not lead to PHN or other long-term complications, depending on the case.

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