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Herpes zoster as a systemic disease

Ivan Staikov, MD, PhD[a,*], Neyko Neykov, MD[a], Branka Marinovic, MD, PhD[b], Jasna Lipozenčić, MD, PhD[b], Nikolai Tsankov, MD, PhD, MSc[a]

[a]*Departments of Neurology and Dermatology, Tokuda Hospital Sofia, Bulgaria*
[b]*Department of Dermatology, Medical Faculty, Zagreb, Croatia*

Abstract Herpes zoster (shingles, zona) is a viral infection commonly afflicting the skin and the nervous system with an overall occurring rate of 3 to 5 cases per 1000 persons per year, with higher rates in middle or later life. With the advancement of medicine, more and more case reports have started to emerge showing different incidences of VZV, some new localizations, clinical presentations, and complications, which break the well-known fact that "VZV affects the skin and nervous system."

Skin lesions are the most important ones for the early and exact diagnosis of herpes zoster (HZ), due to its visibility and well-defined clinical picture of lesions. The most frequent condition following the acute herpes zoster eruption is postherapeutic neuralgia (PHN). There have been other reports of the disease with otorinolaryngologic complications and ophthalmologic ones, such as ophthalmoparesis/plegia. There have also been reports of delayed contralateral hemiparesis/hemiplegia following the infection, as a manifestation of vaculitis due to a direct VZV invasion of the cerebral arteries. Encephalitis and destructive myelitis is similarly rare, but a serious complication. Some authors found that patients with inflammatory bowel disease are at a significantly increased risk for herpes zoster. As a gastroenterologic complication, there have been several instances of HZV infection with symptoms resembling an acute abdomen. The diagnosis is hard to pinpoint, and a vast array of examinations are required to identify it, sometimes even posthumously. Nephrologic representations and complications have also been reported.

With more and more skin diseases being acknowledged as systemic ones, this viral infection is a more likely candidate for the same title.

Introduction

Herpes zoster (shingles, zona) is a viral infection commonly afflicting the skin and the nervous system with an overall occurring rate of 3 to 5 cases per 1000 persons per year, with higher rates in middle or later life.[1] Especially at risk are immunocompromised patients, the incidence in whom is about 20 times higher.

Some historical features of herpes zoster show that the neurologic implications of the segmental distribution of the eruption were recognized in 1831. The first description of the inflammatory changes in the ganglia and related portions of the spinal nerves were made in 1862. In 1909, the concept that varicella and zoster are caused by the same agent was introduced.[1]

The virus that causes herpes zoster is the varicella zoster virus (VZV), the causative agent of varicella.[2] VZV is a large, double strained DNA-containing virus, enclosed in a protein envelope that is similar in structure to the virus of herpes simplex.[1,2] The infection is usually clinically characterized by a skin eruption preceded and followed by pain in the distribution of the affected root ganglia. Primary VZV infection, which usually occurs in childhood, results in chickenpox (varicella), after which the virus becomes latent in the cranial nerve ganglia, dorsal root ganglia, and

* Corresponding author. Tel.: +359 88 49 33 001; fax: +359 2 403 44 03.
E-mail address: ivanstaikov@hotmail.com (I. Staikov).

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autonomic ganglia along the entire neuraxis. Later, as cell-mediated immunity to VZV declines with age or is caused by immunosuppression (such as in organ-transplant recipients or in patients with cancer or HIV), VZV can reactivate and cause zoster.

With the advancement of medicine, more and more case reports have started to emerge, showing different incidences of VZV, some new localizations, clinical presentations, and complications that break the well-known fact that "VZV affects the skin and nervous system."

Skin lesions are the most important ones for the early and exact diagnosis of herpes zoster (HZ) due to its visibility and well-defined clinical picture of lesions. Varicella zoster virus (VZV) moves down the nerve axon and causes skin lesions in the corresponding dermatome. Basically, skin lesions are determined as a dermatome eruption with pain, but clinically they are characterized with different phases[3]:

- Preeruptive phase
- Acute eruptive phase
- Chronic phase

Preeruptive phase (preherpetic neuralgia)

This prodromal period is characterized by sensory nerves phenomena, including paresthesias, pain, burning, or itching in the affected area. Usually, this period lasts 48 to 72 hours but could be extended to a week. Pain may resemble headache, brachial neuritis, cardiac pain, appendicitis, etc. Malaise, myalgia, headache, photophobia, and fever can be present along with the main neurologic symptoms.

Acute eruptive phase

After the prodromal period, typical skin lesions appear involving one or a few neighboring dermatomes. At first, erythematous macular, papular or urticarial-like lesions become visible on the skin, but they quickly turn to vesicles. The typical vesicles are grouped in a herpetiform pattern on the erythematous skin. The size of the vesicles is between 1 to 2 mm, but some of them can become confluent. Skin lesions are always distributed unilaterally in a stripe or beltlike pattern. They do not cross the midline. In the beginning, the vesicles are clear, filled with serous fluid. After 3 to 5 days, the vesicles become hemorrhagic and thereafter dry out with brownish crusts. A new eruption may appear over a period of 3 to 4 days. These new lesions appear in the same area and have the same evolutionary polymorphism. Patients are infectious until the vesicles convert to crusts. Enlarged regional lymph nodes can be observed. The eruption heals within two to four weeks. Scarring is rare, usually only if there is a superinfection. The subjective symptoms are usually pain, pruritus, and/or hyperesthesia localized in the same area as the skin lesions. Pain can be mild to severe often with a burning sensation and can last for a long period after the eruption has disappeared. Pain is described as stinging, tingling, aching, or burning. Pruritus is usually mild.

Clinical forms

Disseminated herpes zoster

The eruption in disseminated herpes zoster is localized within the borders of one or more primarily affected dermatomes.[4] These extradermatomal vesicles occur a week after the onset of classic dermatomal herpes zoster. Disseminated herpes zoster occurs in approximately 2% of the zoster cases. This clinical form often develops in patients with depressed cell-mediated immunity, which can be caused by various underlying clinical situations, including malignancies, radiation therapy, cancer chemotherapy, organ transplants, and long-term use of systemic corticosteroids.

Recurrent herpes zoster

In one study, the frequency of herpes zoster (HZ) recurrence in a community population was higher than previously reported.[5] In this study, 1669 patients with a medically documented episode of HZ were investigated. Out of a total number of patients, 95 of them had 105 recurrences. The Kaplan-Meier estimate of the recurrence rate at 8 years was 6.2%. With a maximum follow-up of 12 years, the time between HZ episodes in the same person varied from 96 days to 10 years.

Zoster sine herpete

Patients with this clinical form represent the entire symptom characteristic for herpes zoster except the typical eruption. Patients experience pain and weakness in a dermatomal distribution, but they have no skin signs, or in rare cases only erythematous macules or plaques with no vesicles.

Herpes zoster and immunodeficiency

HZ rates of 29.4 to 51.5 per 1000 person/year have been reported among adults infected with the human immunodeficiency virus. In this form, due to severe immunodeficiency, the eruption often crosses the midline (Figure 1). In addition, higher rates have also been reported in persons with systemic lupus erythematosus, rheumatoid arthritis, granulomatosis with polyangiitis (Wegener), and inflammatory bowel disease.[6]