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CLINICAL VIGNETTE

Recurrent Herpes Zoster – VZV All Over Again

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Case

A 49-year-old otherwise healthy woman presented to an outside emergency department with a 2-day history of right sided abdominal pain. Examination was benign and urine and blood tests showed only a “slight” urinary tract infection. She was given an antibiotic and discharged home. She presented to clinic 3 days later with continued pain described as achy, with rare “inside burning” localized over her right lower ribs. She denied trauma or strain. Examination was unrevealing. X-rays were negative and repeat urinalysis showed no evidence of infection. She was advised to continue conservative management, however, returned 3 days later after noting a red, bumpy, pruritic, mildly painful rash over her right lower ribs. She reported a similar rash in the same area two years prior but had not sought medical evaluation. Examination was consistent with herpes zoster involving dermatomes T9-10, with a few lesions along T11. She was started on antiviral therapy and had an uneventful recovery.

Discussion

Herpes zoster (HZ) infection, commonly called shingles, is characterized by a painful vesicular rash typically presenting in a unilateral dermatomal distribution. It results from reactivation of the varicella zoster virus (VZV, “chickenpox”) that remains latent in the dorsal root or cranial nerve ganglia after primary infection, which usually occurs in childhood. While 90% of adults in the United States show serologic evidence of VZV and are at risk for HZ,¹ the actual incidence remains small, though increasing from 2.5 per 1000 person-years in 1993 to 7.2 per 1000 person-years in 2016.² Herpes zoster can occur at any age, but it is more frequent in older adults, presumably because of immunosenescence,³ with an incidence greater than 10 cases per 1000 person-years among persons older than 75 years. Overall, the lifetime risk of HZ is estimated to be 10-20 percent.¹ Herpes zoster generally is considered to occur only once in a lifetime with recurrence limited to immunocompromised individuals. Few studies have explored recurrence in immunocompetent persons or factors associated with that recurrence.

The presentation of herpes zoster is typically a prodrome of localized abnormal skin sensations, including itching, tingling, and pain of 1-5 days, prior to development of an erythematous maculopapular rash that progresses to pustules, ulceration, and crusting over a healing period of two to four weeks.¹ In some cases pain may precede rash up to 18 days.⁴ The rash is almost

always unilateral, involving a single dermatome, less commonly several contiguous dermatomes, and does not cross the midline. Diagnosis of herpes zoster is usually based on the clinical presentation of rash, however when the prodromal period is long, herpes zoster infection may be mistaken for another disease. Other vesicular lesions such as herpes simplex virus (HSV) infection may be mistaken for herpes zoster (“zosteriform herpes simplex”).^{5,6} This is more likely to occur on the face or genital and buttock areas, which are common locations for HSV, and there is often history of prior episodes in the same area.⁵

Age is the greatest risk factor for HZ, with a dramatic increase in occurrence after age 50. Twenty percent of cases occur between ages 50-59 and 40% after age 60. By age 85 it is estimated that 50% of individuals will have had an episode of herpes zoster.⁵ Other risk factors include immunocompromised status and reduced T cell-mediated immunity; transplant patients; patients with autoimmune disease, primarily related to the use of immunosuppressive therapies; gender (incidence is greater in women, even when controlling for age); race (lower incidence in black versus white persons); physical trauma; and comorbid conditions (underlying malignancy and chemotherapy, disorders of cell-mediated immunity, and chronic lung and kidney disease).⁵

Approximately 1 to 6 percent of individuals will experience a second episode of herpes zoster.^{3,5,7,8}

A cohort of 1669 adults in Olmsted County, Minnesota, with a confirmed previous episode of HZ reported population-based recurrence rate of HZ of 6.2% after 8 years of follow up.³ After adjustment for age and sex, the rate of recurrence was similar to the incidence rate of HZ, suggesting that the risk of HZ recurrence is about the same as that of a first HZ episode in the general population. Although recurrences were more common among individuals who were immunocompromised at time of the index HZ episode, most recurrences occurred in individuals who were immunocompetent at initial episode (recurrence rate 5.7%). Zoster associated pain lasting 30 or more days after the index episode was a strong predictor of recurrence, suggesting a possibly greater severity of the initial HZ episode. Timing of first HZ recurrence varied from 96 days to 10 years after the index episode. In 45% of recurrences the site was in a different body region than the index episode.

In a population-based study of 746,816 adults taken from the Korean National Health Insurance Service database, Kim et al (2019) identified 39,441 initial episodes of HZ with an incidence rate of 5.1 per 1000 person-years (60% women; 67% older than 50; 14% immunocompromised).⁹ During a mean follow up period of 4.4 years the recurrence rate was 12.0 per 1,000 person years, or 5.3%. The mean time between initial and recurrent HZ episodes was 1, 063 days. Risk factors for recurrence included older age (51-70 years), female gender, and zoster-related pain (ZRP) longer than 30 days. Concurrent hematologic malignancies, autoimmune diseases, dyslipidemia, and hypertension were also significant risk factors.

A Japanese study of 16,784 patients with an initial episode of herpes zoster, reported recurrence rate of 6.4% (7.8% in women; 4.5% in men).⁷ The peak age at initial episode was 50-59 years and 60-79 years for recurrent episodes. Men were 10 years older than women at time of initial and recurrent HZ episodes. The interval between initial and recurrent episodes peaked at 3-11 years and decreased gradually with time. Episodes within 8 years occurred more commonly in a different dermatome (38%) than in the same dermatome (29%), indicating that the recurrence of HZ was not a recrudescence of the same sensory ganglion but was independent of the initial episode. Right and left dermatomes were similarly affected in patients who experienced recurrence in different dermatomes, while left dermatomes were more affected than right in patients with a recurrence in the same dermatome.

These studies suggest that herpes zoster is not a once-in-a-lifetime experience and that recurrence is not uncommon. Associated risk factors for recurrence include increasing age, female gender, longer duration of zoster-associated pain, immunocompromised status, and comorbid conditions. However, it remains unclear how to predict recurrence risk an individual level. In addition, the efficacy of antiviral treatment and vaccination, particularly the relatively new HZ/su (Shingrix) vaccine¹⁰ has not yet been well studied.

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