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Epidemiology of Herpes Zoster Ophthalmicus

Recurrence and Chronicity

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Purpose: A hospital-based epidemiology study to describe herpes zoster ophthalmicus (HZO) prevalence and risk factors for recurrent and chronic disease.

Design: Retrospective, hospital-based cohort study.

Participants: All patients evaluated in the Broward and Miami Veterans Administration Healthcare System (MIAVHS) during the study period.

Methods: Retrospective medical record review of patients seen in the MIAVHS from January 1, 2010, through December 31, 2014, with a HZO clinical diagnosis. Assessment of the patient's clinical course was defined by the following: an acute episode of HZO was defined as quiescence of disease within 90 days of initial presentation, HZO recurrence was defined as any recurrent eye disease or rash 90 days or more after quiescence of disease was noted off therapy, and chronic HZO was defined as active disease persisting more than 90 days from initial presentation.

Main Outcome Measures: Main outcome measures included the frequency of HZO with and without eye involvement, HZO recurrence rates, and risk factors for recurrent or chronic HZO.

Results: Ninety patients with HZO were included in the study. The mean age at incident episode of HZO was 68±13.8 years (range, 27–95 years). Most patients were white (73%), immune competent (79%), and did not receive zoster vaccination at any point during the follow-up (82%). Patients were followed for a mean of 3.9±5.9 years (range, 0–33 years). The period prevalence of HZ in any dermatome was 1.1%, the frequency of HZ involving V1 (HZO) was 0.07%, and the frequency of HZO with eye involvement was 0.05%. The overall 1-, 3-, and 5-year recurrence rates for either recurrent eye disease or rash were 8%, 17%, and 25%, respectively. Ocular hypertension (hazard ratio [HR], 4.6; 95% confidence interval [CI], 1.3–16.5; odds ratio [OR], 6.7; 95% CI, 1.5–31.2) and uveitis (HR, 5.7; 95% CI, 1.7–19.0; OR, 6.7; 95% CI, 1.5–31.2) increased the risk of recurrent and chronic disease.

Conclusions: This study supports newer data indicating that a significant proportion of patients experience recurrent and chronic HZO. Further study is needed to guide preventative and therapeutic approaches to recurrent and chronic HZO. *Ophthalmology 2016;■:1–7 © 2016 Published by Elsevier on behalf of the American Academy of Ophthalmology.*

Herpes zoster (HZ) is defined as the emergence from latency of the varicella zoster virus (VZV). Because HZ is not a reportable condition in the United States, its incidence is inferred. When age adjusted to the 2000 United States population, the Centers for Disease Control and Prevention estimates that there are 1 million cases of HZ annually and that 32% of persons in the United States will experience HZ during their lifetime.[1] Observed rates have varied across individual studies, ranging from 3.2 to 4.2 per 1000 population per year.[2–7] Immunosuppression and the immunosenescence of aging have been associated with an increased risk of HZ developing.[8–10] The most common long-term complication of HZ is postherpetic neuralgia (PHN), or persistent neuropathic pain lasting beyond 3 months after initial presentation of HZ. Postherpetic neuralgia can have a negative effect on quality of life to a degree similar to congestive heart failure, depression, acute myocardial infarction, and diabetes. Postherpetic neuralgia is a leading cause of suicide in patients older than 70 years with chronic pain.[11,12]

Herpes zoster ophthalmicus (HZO) is defined as HZ within the ophthalmic division of the fifth cranial nerve (V1).[12] Herpes zoster ophthalmicus accounts for 10% to 20% of HZ cases[12] and can be categorized further as HZO with or without eye involvement. The most common presenting ophthalmic manifestations in HZO are keratitis, uveitis, and conjunctivitis. Other presentations include episcleritis and scleritis, acute retinal necrosis, cranial nerve involvement, meningoencephalitis, or a combination thereof.[13] Long-term structural complications, including glaucoma, cataract, corneal scarring, and PHN, can have devastating outcomes on visual function, quality of life, or both. In the preantiviral era,

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approximately 50% of patients with HZO demonstrated ocular involvement.[14] With antiviral therapy, lower frequencies of eye involvement have been reported, ranging from 2% (4 of 202)[15] to 29% (25 of 85).[16]

What is less understood is the course of HZ after its initial presentation. Traditionally studied and treated in the acute phase,[17–19] recent data suggest that some patients experience a chronic or recurrent disease course. In a population-based study of individuals living in Olmsted County, Minnesota, from 1996 through 2001, a total of 1669 cases of HZ were identified, with an incidence of 3.6 per 1000 person-years.[2] To evaluate for recurrence, these patients then were followed up through 2007, and 105 recurrences of HZ, defined as a characteristic vesicular rash accompanied by pain or dysesthesia in a dermatomal pattern 3 months or more from the index episode, were identified. The Kaplan-Meier estimated recurrence rate of HZ at 8 years was 6% overall. Interestingly, 86% (90 of 105) of HZ recurrences were immunocompetent individuals,[20] and in 45% of the recurrences, the site of the recurrence was in a different region of the body than the site of the index episode.[20] Recurrences were more likely in persons with zoster-associated pain of 30 days or longer, immunocompromised status, female gender, and older age (≥50 years) at initial presentation.[20] Data on ocular manifestations of HZO likewise are available for an Olmsted County cohort. In a medical record review from 1980 through 2007, 2035 patients with HZ in any dermatome were identified, and of these individuals, 9% (12 of 84) had HZO with eye involvement.[13] Of these 184 patients, 6.5% were immunocompromised at time of eye involvement and 6.6% had permanent vision decrement at the 8-year follow-up. Recurrent eye disease 3 months or more from initial presentation of HZO was observed in the form of keratitis (6.9%) and iritis (7.4%) at the 8-year follow-up.[13] In more recent studies of HZO, even higher frequencies of recurrent eye disease have been suggested. In a retrospective review of 45 patients with HZO and eye involvement, recurrent disease was observed in 51% of patients over a mean follow-up of 24.9±18.2 months (range, 12–72 months) in the form of stromal (n = 9) and epithelial (n = 3) keratitis, keratouveitis (n = 4), and anterior uveitis (n = 6).[21] In a survey of 100 ophthalmologists, 87% reported treating recurrent or chronic cases of ocular disease in the setting of HZO in the previous year.[22]

Based on these data, it is clear that more information is needed on the long-term clinical course of HZO. The purpose of this study was to characterize the epidemiologic features of recurrent and chronic HZO in a unique South Florida population with an ethnically and racially mixed, predominately male population.

Methods

Study Methodology

This retrospective review of medical records examined all patients in the South Florida Veterans Administration Healthcare system (MIAVHS) seen between January 1, 2010, and December 31, 2014, with a clinically documented HZO diagnosis, defined as characteristic vesicular rash and dermatomal pain in the V1 dermatome. Miami Veterans Administration Institutional Review Board approval was obtained to allow the retrospective evaluation of charts. The study was conducted in accordance with the tenets of the Declaration of Helsinki and complied with the requirements of the United States Health Insurance Portability and Accountability Act.

Setting

The MIAVHS provides an excellent hospital-based study population because of its age and racial and ethnically diverse constituency. The electronic medical records system in place incorporates all notes from providers, including details of every visit to a clinic or emergency department, all hospitalizations, and all correspondence concerning each patient, providing an accurate and comprehensive view into a patient's disease course.

Subjects for Potential Inclusion

Between January 1, 2010, and December 31, 2014, a total of 119 569 patients were evaluated at the MIAVHS. Of these, 1358 patients had International Classification of Diseases, 9th Edition, codes of 53.0 through 53.9 designating HZ infection anywhere in the body. One hundred twenty-four patients had International Classification of Diseases, Ninth Edition, codes of 53.20 through 53.29 designating HZO, defined as HZ involvement of the V1 dermatome. Of that group, 90 patients had a clinically documented episode of a vesicular rash and dermatomal pain involving V1 in the medical record. Sixty-two of these patients had documented HZO with eye involvement diagnosed by a treating ophthalmologist based on characteristic ophthalmic findings in patients with typical dermatomal pain and vesicular rash.

Data Collected

The information collected from each HZO ophthalmic-related visit included recorded diagnoses, procedures, medications, and where possible, the extent of HZO ophthalmic involvement (e.g., episcleritis or conjunctivitis; epithelial, stromal, or endothelial disease; uveitis), pain (e.g., PHN); and ophthalmic complications (e.g., ocular hypertension, corneal scar, cataract). Patients were split into 2 groups based on whether signs of ocular involvement were present within 30 days of initial presentation of V1 rash (HZO with versus without eye involvement).

Demographic data included age, gender, and race. The patient's immune status at the time of initial presentation with HZ was assessed, and patients were deemed immunocompromised if they had human immunodeficiency virus, had actively treated malignancies (systemic chemotherapy), had hematologic malignancies, had end-stage renal disease, were taking immunosuppressive drug therapy, or had a combination thereof. Corticosteroid medications were considered immunosuppressive if they were given at levels equivalent to 10 μg or more of prednisone daily. If none of the conditions were documented at the time of or during the year before the HZ eye diagnosis, the patient was assumed to be immunocompetent.

Clinical Course

Assessment of the patient's clinical course was defined by the following: An acute episode of HZO was defined as quiescence of disease within 90 days of initial presentation and complete termination of all antiviral and anti-inflammatory treatment. Chronic HZO was defined as active disease requiring antiviral therapy, anti-inflammatory therapy, or both for more than 90 days from initial presentation. Herpes zoster ophthalmicus recurrence was

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