Abstract

BACKGROUND: Herpes zoster is viral infection that occurs with reactivation of the varicella-zoster virus (VZV). It is usually a painful but self-limited dermatomal rash with cutaneous distribution. Although it’s usually a painful, self-limiting rash, it can be much more serious; In addition, acute cases often lead to postherpetic neuralgia (PHN) and seriously impair quality of life. It is important to recognize those at risk of developing postherpetic neuralgia, early treatment, and prevent complications.

AIM: Our aim is to determine the clinical features of our herpes zoster diseases and to review the treatments in patients with postherpetic neuralgia.

METHODS: A search for HZ and PHN was conducted in a general practice research database, comprising two general practices (dermatologist and physiatrist) and representing 5600 people. We analyzed a retrospective 170 case series of pediatric and adults admitted to the dermatology and physical therapy and rehabilitation outpatient clinic between October 2018 and October 2020.

RESULTS: A total of 170 new cases had been diagnosed with HZ in the dermatology and physical therapy and rehabilitation clinics over 2 years. Female-to-male ratio was 2:1 and the age ranged from 5 years to 88 years. The thoracic dermatomes were the most commonly involved. The risk of developing PHN 1 month after the start of the rash was 21%. Independent risk indicators for the occurrence of PHN were age [55–74] years.

CONCLUSION: The risk of developing PHN increases with age and with comorbidity. Preventive strategies such as vaccination should focus on patients with herpes zoster aged >55 years.

Introduction

Herpes zoster (HZ), is a viral disease characterized by a painful skin rash with blisters in a localized area. It is a viral disease caused by the reactivation of the chickenpox-zoster virus that is dormant in the sensory ganglia or dorsal root ganglia of the cranial nerve after chickenpox infection [1]. It is a common disease, with a reported incidence varying from 2.2 to 3.4/1000 patients/year [2]. While Varicella-zoster is more common in children as form as chickenpox, herpes zoster occurs in adults or the elderly [1].

The most common neurological complications associated with HZ is postherpetic neuralgia (PHN), defined as pain at least for 90 days after the onset of rash. PHN is characterized by persistent spontaneous sharp or paroxysmal burning sensation and neuropathic pain, including hyperesthesia, affecting the patient’s quality of life. PHN is estimated to affect 10–20% of all patients with HZ over the age of 50 and 30% of those aged 80 years [3].

Diagnosis of PHN requires consideration of known risk factors, including advanced age, severe prodromal pain, severe rash, and HZ location on the trigeminal dermatomes or the brachial plexus [4].

PHN patients have a poor quality of life and difficulty in daily living activities. Approaches to managing postherpetic neuralgia include preventing herpes zoster by vaccination and/or antiviral therapy and administering specific drugs to treat pain. Moreover, treatment of PHN due to HZ is particularly difficult in the elderly population [5].

Tricyclic antidepressants, gabapentin and pregabalin, and topical lidocaine 5% tape are categorized as first-line treatments for PHN in guidelines published by the American Academy of Neurology (2004) [6]. Opioids, tramadol, capsaicin cream, and 8% capsaicin patch are generally considered second or third-line treatments due to safety and/or efficacy disadvantages compared to first-line treatments [7].

In this study, we retrospectively determined the incidence of HZ and PHN in patients enrolled in the general practice research database and analyzed risk indicators for PHN.
Methods

Patients and setting

Data were collected from the General Practice Research Database. All HZ patients diagnosed between October 30, 2018, and October 31, 2020, were identified by searching the database for the ICPC code B0.09, B0.01 (HZ), and for free text ("zoster"). Patients admitted to the hospital and diagnosed with these ICD codes were included in the study. During the study, two authors, one of whom was a dermatologist and the other a physiatrist (took part in data collection and follow-up of patients who developed PHN), made general practices and examined the full-text medical records of the selected patients. The duration of pain was recorded for each HZ patient. In this study, PHN was defined as any pain that persists for at least 3 months after the diagnosis of HZ. Patients age, gender, localization, presence of prodrome pain, time between symptom and presentation, comorbidity pain severity, medication for HZ (systemic local) were questioned. Relevant comorbidity included diabetes mellitus (DM), Hypertension, cardiovascular disease, HIV, and Malignancy, at the time of HZ diagnosis. Topical or systemic antiviral treatments were applied according to the risk status of the patients and the severity and dermatomal location of the lesions.

Statistical analysis

All analyzes were performed on SPSS v15 (SPSS Inc., Chicago, IL, USA). Shapiro-Wilk test was used to determine whether variables are normally distributed. Number, percentage, mean, standard deviation (SD), median, minimum and maximum values were used in the evaluation of descriptive data. Categorical data were compared using the Chi-square test and continuous data were compared with Student’s t or Mann-Whitney U tests according to the distribution. Univariate and Multivariate Logistic Regression Analysis was performed to determine risk factors for postherpetic neuralgia and sequelae after shingles infection.

Results

A search of the database resulted in 6233 patients, 170 of whom were diagnosed as having HZ, equally distributed over the 2-year period. There were 170 patients, 76 (44.7%) male, 94 (55.3%) female, who had HZ infection in the study group. The ages of the patients ranged from 5 to 88 years, (the mean ± SD was 50.8 ± 19.2) years, and 2.4% (n = 4) of the patients were under 18 years old. The lesions were vesicles, papules, pustules, on erythematous bases, and crusts or present in various combinations (Figure 1).

In the study group, 37 patients with postherpetic neuralgia after HZ infection had significantly higher medians of age (p < 0.001), duration of HZ infection (p < 0.001), VAS-baseline (p < 0.001), LANSS-baseline (p < 0.001) than those without postherpetic neuralgia. In patients with postherpetic neuralgia, the frequency of comorbidity (p < 0.001), the frequency of prodromal findings (p < 0.001), and the frequency of receiving medical treatment (p = 0.002) were statistically significantly higher.
Table 1: Descriptive characteristics of the study group

| Age, Median (Min-Max) | Prodromal Duration of HZ infection (day) | Mean ± SD | Mean ± SD | VAS-Baseline, Median (Min-Max) | LANSS-Baseline, Mean ± SD, Median (Min-Max) |
|-----------------------|-----------------------------------------|-----------|-----------|-----------------------------|---------------------------------|
| Age, Mean ± SD, Median (Min-Max) | 50.8 ± 19.2, 48.5 (5.0–88.0) | 5.8 ± 5.5, 3.0 (1.0–25.0) | 6.7 ± 3.2, 8.0 (0.0–10.0) | 14.1 ± 10.4, 18.0 (0.0–24.0) |

Table 2: Comparison of patients with and without postherpetic neuralgia in terms of characteristics after HZ infection

| Postherpetic neuralgia | Absent | Present | p |
|-----------------------|--------|---------|---|
| Age, median (min-max) | 44.0 (5.0–88.0) | 70.0 (43.0–84.0) | <0.001 |
| Duration of HZ infection (day), median (min-max) | 3.0 (1.0–22.0) | 15.0 (1.0–25.0) | <0.001 |
| VAS-baseline, median (min-max) | 7.0 (0.0–10.0) | 9.0 (7.0–10.0) | <0.001 |
| LANSS-baseline, median (min-max) | 10.0 (0.0–24.0) | 24.0 (10.0–24.0) | <0.001 |

Discussion

Herpes zoster is caused by the reactivation of the varicella-zoster virus. Unlike chickenpox, the lifetime estimated incidence of herpes zoster ranges from about 10–20%. The incidence of herpes zoster increases sharply with advancing age, roughly doubling every decade beyond the age of 50. In a previous study, 1 patient over the age of 55 accounted for over 30% of herpes zoster cases, although they only represented 8 percent of the study population. In the same study, children younger than 14 years old represented only 5 percent of herpes zoster cases [2, 8]. Our results support a number of earlier studies, but the in our study HZ incidence found higher 21.8% (n = 37), which reported in other studies age was as a risk indicator of PHN. We thought our high rate was due to our average age (50.8 ± 19.2) and high rate of comorbidity 55.3% (n = 94). This higher risk of developing PHN with increasing age has often been explained by the decreasing immunity seen in older people. In addition, our absence of findings on PHN in patients under 18 years of age (n = 4) confirms the results of a study conducted on HZ in Iceland in children and adolescents [9] and shows that the risk of developing PHN increases with age.

One possible risk factor for HZ is exposure to ultraviolet radiation (UVR) from sunlight as it can suppress the cell-mediated immune response. Several observations support this hypothesis. The risk of HZ is higher in the summer than other seasons, possibly due to high UVR exposure. Especially in this literature, this rate was found to be higher in men [10]. Considering that the northern Cyprus region is sunny and hot for approximately 300 days, it was also an additional risk factor for our patients.

HZ disease has prodromal symptoms before the lesion develops. these; it includes symptoms such as alodynia, pain, itching, and burning. Some patients have these symptoms without a rash, also known as “zoster sinus herpes” [11].

Symptoms typically include prodromal sensory phenomena during 1 or more skin dermatomes lasting 1–10 days (average 48 h). In a study investigating the prodromal pain and severity of HZ, the prodromal symptom rate was found to be 74% [12]. In our study we found that a painful prodrome in our patient was 68.8% (n = 117), which could be considered a sign of more severe HZ, was associated with an increased risk of PHN. In the same study prodromal pain was associated with more severe acute pain (Initial Zoster Impact Questionnaire. 6.2 vs. 4.3, p = 0.0001). Similar with these results our patients with postherpetic neuralgia after HZ infection had significantly higher medians VAS-baseline (p < 0.001), LANSS-baseline (p < 0.001) than those without postherpetic neuralgia.

The dermatomal distribution of HZ in this study is shown in Table 2 and is comparable to other studies [13, 14]. These studies reported an involvement of thoracic dermatomes (44%–56.4%), trigeminal dermatomes (11.8%–25%), cervical dermatomes (11%–20%), and lumbosacral dermatomes (11%–17%). PHN developed in all dermatomes except cervical involvement in our patients.
Skin damaged primarily by viruses may be susceptible to a secondary skin lesion. Skin physically deformed by the previous disease may be a result of the response. In contrast, skin scars are not often reported after herpes zoster (HZ). Risk factors for post-HZ scarring remain undetermined. In a study investigating the incidence and risk factors of cutaneous scars after herpes zoster, it was reported that 11 (9.7%) of 113 patients developed postinflammatory scar (hypo/hyperpigmentation, atrophy, keloid) in a 6-month follow-up. Immunosuppression and severe herpes zoster were identified as risk factors [15]. In our study the frequency of post-infective sequelae (atrophy, hypo/hyperpigmentation) among the patients was found to be 26.5% (n = 45), This risk was too high in patients with malignancies, weak immune system, and severe widespread rash.

Current treatment of HZ with antiviral drugs and analgesics gives good results in younger patients where the disease is generally milder and is effective against acute pain and skin rashes. However, it is much less effective against PHN, which occurs more frequently and more severely in elderly patients. Once PHN develops, current treatments offer only limited benefits and side effects need to be reviewed [16].

Ideal treatment for herpes zoster should be initiated within 72 h after the rash appears, but if new skin lesions are developing or ophthalmic or neurological complications are present, this treatment can be applied outside the 72-h window [17].

The standard treatment is acyclovir (800 mg 5 times a day). If the disease is severe, the intravenous application is warranted [18] Valaciclovir (1000 mg) and famciclovir (500 mg) can be given 3 times a day. These agents are as effective as acyclovir possibly due to better absorption and higher blood levels. In recent studies, valaciclovir, 1.5 g orally twice daily, was found to accelerate the resolution of the HZ rash, associated pain, and reduce the duration of PHN in immunosuppressed patients [19].

Controversial a study conducted by Alakloby et al. In Eastern Arabia there was no significant difference between patients with PHN who received systemic acyclovir and those who did not receive it. Likewise, no significant difference was observed in the disease duration between patients who used systemic treatment and those who did not use it [20]. Based on the previous literature, there are no data on the development of PHN in patients receiving topical antiviral therapy [18]. In contrast to this result, in our study patient, those who received topical treatment had a lower risk of developing PHN. In addition, PHN was developed in 37 of 141 patients who received systemic therapy. Frequency of receiving medical treatment (p = 0.002) was significantly higher in the PHN group. Management approaches include treatment of herpes zoster infection and associated pain, prevention of postherpetic neuralgia, and control of neuropathic pain until the condition is resolved.

Conclusion

As a result, the incidence of herpes zoster is increasing every year due to the increasing life expectancy and the addition of various comorbid diseases. Unfortunately, this situation puts a serious burden on the health system. Based on these studies, we have compiled 170 patients with herpes zoster in our hospital. Females were more affected than males. The thoracic dermatomes were the most commonly involved. The most common coexisting disease was hypertension, diabetes mellitus, and the most common complication of HZ was PHN. Prevention strategies, such as vaccinating those at greatest risk, can offer the best option for the future.

Ethical approval

Approval was provided by local ethics committee.

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