Herpes Zoster, Clinical Course and Associated Diseases: A 5-Year Retrospective Study at Ramathibodi Hospital

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Objective: *Herpes zoster was more frequently found in immunocompromised hosts and elderly persons than in general population. The aim of this study is to find out the distributions of skin lesions, treatments, complications of herpes zoster and associated diseases that occur in concomitant with or after herpes zoster infections.*
Material and Method: *The medical records of the patients diagnosed as herpes zoster between January 1995 - December 2000 were reviewed. Only the patients who were followed up regularly at Ramathibodi hospital for at least 3 years after the first diagnosis of herpes zoster were enrolled into the study. Demographic data, distribution of skin lesions, treatments, complications of herpes zoster and associated diseases were recorded.*
Results: *Three hundred and ninety-nine cases were enrolled in the study. Three hundred and ninety-eight patients (99.7%) had one dermatomal involvement. Sixty-seven patients (16.8%) had postherpetic neuralgia. Fifty-six patients had associated HIV infection. In 3 years followed up, 17 patients developed HIV infection, 3 patients developed acute leukemia, 2 patients developed mycosis fungoides.*

Keywords: *Herpes zoster, HIV infection, Leukemia, Mycosis fungoides*

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Herpes zoster represents reactivation of the latent varicella-zoster virus in the sensory ganglia. The cutaneous eruptions consist of painful vesicles with or without itchiness which tend to follow a unilateral dermatomal distribution. Prodromal pain may often precede the development of visible lesions. The entire course is usually 2-3 weeks in duration. The two most commonly involved areas for herpes zoster are thoracolumbar (T3-L2) and facial dermatomes (first branch of the trigeminal nerve)[1]. Anyone who has had varicella may develop herpes zoster. However, it usually develops in persons older than 50 years, and the incidence increases with advancing age. Herpes zoster is more frequently found in immunocompromised individuals and also as an early manifestation of HIV infection. Approximately 10-20% of patients with herpes zoster will experience a recurrence; such recurrence involves the same dermatome in about 50% of these patients[2].

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Disseminated herpes zoster is defined as the presence of more than 20 vesicles outside the primary and adjacent dermatomes. Disseminated herpes zoster is uncommon in immunocompetent patients, but 25-50% of immunocompromised patients may develop this complication[3].

Postherpetic neuralgia is the most common complication of herpes zoster. It is defined as the presence of pain after skin lesions have healed, or pain lasting more than 4-6 weeks after disappearance of cutaneous lesions[4]. The pain is often severe and debilitating. It occurs in 8-15% of patients[4], but the incidence increases dramatically with age.

The aim of this study was to find out the clinical course of herpes zoster and the associated diseases that occur in concomitant with or after herpes zoster infection.

Material and Method

Data gathering

Using the Ramathibodi Hospital computerized medical record database, the authors compiled a list of patients diagnosed with herpes zoster who attended

the Department of Medicine, Ramathibodi Hospital over a 5-year period between January 1995 - December 2000. Only the patients with at least 3 years of follow-up after the first diagnosis of herpes zoster were enrolled into the study. All available charts were reviewed.

The following data were recorded:

1. Demographic data (sex and age)
2. Underlying diseases at the onset of herpes zoster
3. Clinical manifestations (skin lesions, distribution of skin lesions)
4. Complication (postherpetic neuralgia)
5. Associated diseases that occurred within 3 years of the onset of herpes zoster

Results

There were 612 patients diagnosed as herpes zoster from January 1995 to December 2000. Only 399 records can be enrolled into the study. There were 297 males (74%) and 102 females (26%). Age range from 22-81 years (mean $\pm$ SD = 59 $\pm$ 7 years).

Three hundred and eighty-two patients (95.7%) experienced one episode of herpes zoster and only 17 (4.3%) patients had a recurrent episode. The duration from the first episode to the second episode ranged from 4 months - 5 years (mean $\pm$ SD = 2 $\pm$ 0.4 years).

Three hundred and ninety-eight patients (99.7%) had one dermatomal involvement and only one patient had disseminated herpes zoster. This patient had associated HIV infection.

Information regarding distribution of skin lesions was available in only 178 patients. The most common anatomic segment was the trunk (114 patients: 64%) followed by the face (64 patients; 36%) (Table1). Among this group, 25 patients (39%) had ophthalmic involvement.

Postherpetic neuralgia was found in 67 patients (16.7%). There were 59 patients aged > 60 years and 8 patients aged between 40-60 years. The duration of postherpetic neuralgia ranged from 1-9 months (mean $\pm$ SD = 2 $\pm$ 0.3 months). Thirty-eight patients (56.7%) were treated with tricyclic anti-depressants (amitriptyline). Twelve patients (17.9%) were treated with gabapentin. Seven patients (10.4%) were treated with tramadol. The recovery time ranged from 2 weeks to 4 months (mean $\pm$ SD = 3.4 $\pm$ 2 weeks) after treatment, There was no difference in recovery times between each treatment.

The underlying diseases of the patients were as follows: HIV in 56 patients (14%) dyslipidemia in 22 patients (5.5%) hypertension in 16 patients (4%), diabetes mellitus in 10 patients (2.5%) and breast cancer in 3 patients (0.75%) (Table2).

After a 3-year follow-up, HIV infection was detected in 17 patients (4.2%), other diseases were erythema nodosum in 5 patients, acute leukemia in 3 patients, mycosis fungoides in 2 patients, pyogenic granuloma at the same area of herpetic infection in 1 patient, squamous cell carcinoma on the upper lip in 1 patient and molluscum contagiosum at the lesion in 1 patient (Table 3).

Table 1. Distribution of skin lesions

Anatomic segment	No. of patients	% of patients
Trunk	114	64
Face	64	36

Table 2. Underlying diseases at the onset of herpes zoster

Underlying disease	No. of patients	% of patients
HIV	56	14.0
Dyslipidemia	22	5.5
Hypertension	16	4.0
Diabetes mellitus	10	2.5
Breast cancer	3	0.75

Table 3. Associated diseases detected during 3 years after onset of herpes zoster

Diseases	No. of patients	% of patients	Duration detected after onset of herpes zoster (months)
HIV	17	4.2	1-7
Erythema nodosum	5	1.2	4-24
Acute leukemia	3	0.75	2-7
Mycosis fungoides	2	0.5	8-24
Pyogenic granuloma	1	0.25	6
Squamous cell carcinoma at upper lip	1	0.25	24
Molluscum contagiosum	1	0.25	unknown

Discussion

Herpes zoster is caused by reactivation of latent varicella-zoster virus (VZV), a double stranded DNA virus in the Alphaherpesvirus family, which is also the causative virus of primary varicella[4]. After initial infection with clinical manifestation of chickenpox, VZV remains latent in dorsal root or cranial nerve ganglion for life. Declining virus-specific cell-mediated immune response, which occurs naturally as a result of aging or by immunosuppressive illness or immunosuppressive drugs increased the risk of herpes zoster[5].

In the present study, which retrospectively gathered information on 399 patients diagnosed as herpes zoster, affirms previously reported information regarding sex, age and distribution of the skin lesions[1,2,5], but extends and adds to those observations. Specifically, the present study is the first study to find out the associated diseases with herpes zoster at the time of onset of herpes zoster and three years afterwards.

Eye involvement was found in 39% of the patients who had facial lesions so ophthalmologic consultation is recommended in this group.

Postherpetic neuralgia is the most painful manifestation in these patients. Both the incidence and duration of postherpetic neuralgia are directly correlated with the age of the patients. The reported incidence of postherpetic neuralgia range from 8 to 70% and increased with advancing age. In patients over 50 years, 20% of patients continued to report pain six months after the onset of the rash despite treatment with valacyclovia or famcyclovia[6]. In the present study, postherpetic neuralgia occurred in 16.8% of the patients, most of the patients were more than 60 years old. This is in agreement with other studies that postherpetic neuralgia mostly occurred in old age[6,7].

Treatment of postherpetic neuralgia is difficult. Clinical trials have shown that opioids, tricyclic antidepressant and gabapentin reduced the severity and duration of postherpetic neuralgia, either as a single agent or in combination[6,7]. In the present study the authors found tricyclic antidepressants were most commonly used (56.7%). But there was no difference in terms of recovery among all pain-relieving medications.

In the present study, the authors found that 56 patients (14%) had HIV infection at the time of diagnosis of herpes zoster. Seventeen patients (4.2%) were detected to have HIV during the follow-up periods. There were three possibilities for the detection of HIV in these 17 patients: 1) some of them might really be new cases 2) some might be in the window period 3) the physician did not request for a laboratory investigation for HIV at the time of onset of herpes zoster. Unfortunately, the information in the medical record was inadequate to clarify these possibilities. From the previous studies herpes zoster affected about 8-11% of patients with AIDS[4,8]. HIV patients commonly have cell counts between 200-400 cells/mm^3 when they had the first episode of herpes zoster[9-13]. Unfortunatedly, the authors did not have cell count records of the presented patients. The high percentage of HIV patients in the present study points out the importance of HIV screening in all herpes zoster patients, especially those who in the recognized risk group for HIV infection.

Herpes zoster has been reported to be associated with malignancy, especially in elderly persons. The patients who had Hodgkin's disease, non-Hodgkin's lymphomas, and leukemia possess a high risk for herpes zoster[14,15]. The patients with solid tumors have a lesser risk for herpes zoster, but treated patients with lung, breast or gynecologic cancers of any age are more likely to have herpes zoster than patients with other solid tumors[15]. In the present study, herpes zoster occurred in 3 patients who had underlying breast cancer. After a 3 year follow-up of these patients with herpes zoster, three patients developed acute leukemia, two patients developed mycosis fungoides, and one patient developed squamous cell carcinoma, although herpes zoster is not a risk factor for cancer[16,17].

Long term follow up for at least 2 years should be considered in patients with herpes zoster, especially in the older age group.

In conclusion, the incidence of herpes zoster is increasing nowadays. Old age and immunocompromised host are important predisposing factors and herpes zoster is a frequent early manifestation of HIV infection.

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งูสวัดและโรคที่พบร่วมด้วย: การศึกษาย้อนหลัง 5 ปี ที่โรงพยาบาลรามาธิบดี

สุธาสินี ตันสุริยวงษ์, ศิริเพ็ญ พัววิไล

วัตถุประสงค์*: งูสวัดเป็นโรคที่พบในผู้ที่ภูมิคุ้มกันต่ำและผู้สูงอายุบ่อยกว่าคนปกติ วัตถุประสงค์ของการศึกษานี้เพื่อศึกษาดูการดำเนินโรคของงูสวัดและโรคที่พบร่วมด้วยในขณะที่เป็นงูสวัด รวมทั้งโรคที่พบหลังจากเป็นงูสวัดแล้ว*

วัสดุและวิธีการ*: คณะผู้วิจัยได้ศึกษาเวชระเบียนของผู้ป่วยที่เป็นงูสวัด ซึ่งมาตรวจที่โรงพยาบาลรามาธิบดี ในระหว่างเดือนมกราคม พ.ศ.2538 ถึงเดือนธันวาคม พ.ศ. 2543 และเลือกศึกษาเฉพาะผู้ป่วยที่ได้รับการตรวจติดตามอย่างต่อเนื่องหลังจากได้รับการวินิจฉัยว่าเป็นงูสวัดแล้วเป็นเวลาอย่างน้อย 3 ปี ได้บันทึกข้อมูลของผู้ป่วยด้านอายุ เพศ ตำแหน่งของรอยโรค การรักษา ผลแทรกซ้อน รวมทั้งโรคที่พบร่วมด้วย*

ผลการศึกษา*: ผู้ป่วยในการศึกษานี้มีจำนวน 399 ราย ผู้ป่วย 398ราย (99.7%) เป็นงูสวัดที่ผิวหนังซึ่งจำกัดอยู่เฉพาะแนวเส้นประสาทเส้นเดียว ผู้ป่วย 67 ราย (16.8%) มีอาการปวดปลายประสาทหลังจากรอยโรคที่ผิวหนังหายแล้ว และมีผู้ป่วย 56 รายที่ผลตรวจ HIV เป็นบวกในขณะที่เกิดอาการของงูสวัด หลังจากติดตามผู้ป่วยอย่างต่อเนื่องเป็นเวลา 3 ปี พบผู้ป่วย 17 รายเป็นโรคติดเชื้อ HIV ผู้ป่วย 3 รายเป็นมะเร็งเม็ดเลือดขาวชนิดเฉียบพลัน และผู้ป่วย 2 รายเป็นโรคมัยโคซีส ฟังกอยดีส (Mycosis fungoides)*