A Clinical Study of Herpes Zoster with Generalized Varicelliform Eruptions

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***Background*: Herpes zoster with generalized varicelliform eruptions occurs in 2 to 10% of patients with herpes zoster. It occurs mainly in old or debilitated persons especially those who have immunologic defects such as lymphoproliferative diseases, AIDS, or recipients of immunosuppressive therapy. The reported incidence of herpes zoster with generalized varicelliform eruptions is variable.**

***Objective*: The purpose of this study was to elucidate the incidence and clinical features of herpes zoster with generalized varicelliform eruptions.**

***Methods*: We reviewed the clinical data of 962 patients with herpes zoster by retrospective methods. The annual incidence, age, sex, seasonal variation, predilection sites, and associated conditions of herpes zoster with generalized varicelliform eruptions were analyzed from January 1990 to December 1996 (7 years).**

***Results*: 1. Among 962 patients, 8 patients with herpes zoster revealed generalized varicelliform eruptions (0.83%).**

2. The age ranged from 20 to 85 and the majority of cases occurred in the 6th decade. There were 4 females and 4 males.

3. Past histories of malignancy were observed in 2 patients. However, there were no signs of malignancy at the time of diagnosis of herpes zoster with generalized varicelliform eruptions.

4. The most common site of initial lesion was the thoracic dermatome, followed by the lumbar and the cervical ones.

***Conclusion*: From our observation, it is suggested that herpes zoster with generalized varicelliform eruptions may occur in patients without underlying malignancy or immunosuppressive disorders. Sudden incidental uprising of herpes zoster with generalized varicelliform eruptions was observed in 1996. (Ann Dermatol 10:(1) 1~5, 1998).**

Key Words : Herpes zoster with generalized varicelliform eruption

Herpes zoster with generalized varicelliform eruptions occurs in 2 to 10% of unselected patients with herpes zoster[1,2]. Merselis et al. reported that 65% of the patients with herpes zoster with generalized varicelliform eruptions had associated serious underlying diseases, such as leukemia, Hodgkin's disease, lymphosarcoma, multiple myeloma, etc[2]. In Korea, the incidence of herpes zoster with generalized varicelliform eruptions ranged from 0.1% to 1%[3,4]. In this article, we report the epidemiology and the clinical features of herpes zoster with generalized varicelliform eruptions.

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MATERIALS AND METHODS

Patients

We reviewed the medical records of 962 patients with herpes zoster, who visited the out patient

clinic of the Department of Dermatology at Ewha Womans University Tong-dae-mun Hospital between January 1990 and December 1996. In 954 patients, herpetic lesions were localized at the area of initial involvement. However, 8 of 962 patients had widespread varicelliform eruption which developed during the course of typical herpes zoster.

Clinical evaluation

We evaluated the clinical features including the annual incidence, age, sex, seasonal variation, predilection site and associated conditions of these 8 patients.

RESULTS

Age and Sex distribution of patients(Table 1)

Among the 8 cases of herpes zoster with generalized varicelliform eruptions, the age distribution varied from 20 to 85. The greatest incidence was observed in the 6th decade (4/8 cases). The sex ratio was 1:1 (4 male, 4 female). Of the 954 cases reviewed in this report without disseminated herpes zoster, 385 occurred in male patients and 569 in female patients. By far the greatest incidence was in patients between 50 and 59 years of age (259/954 cases, 27.14%).

Table 1. Age and sex distribution of patients with herpes zoster

Age(yr)	Male	Female	Total No.
< 40	0	1	1(273)
40~49	0	0	0(111)
50~59	2	2	4(259)
60~69	1	1	2(123)
70~79	0	0	0(107)
80~89	1	0	1(20)
Total No.	4(385)	4(569)	8*(954)**

* : number of patients with herpes zoster with generalized varicelliform eruption

**: number of patients with herpes zoster only

Onset & Seasonal variation(Table 2)

This disease occurred most commonly during the year 1996 (5 patients) and during the summer months (6 patients). Herpes zoster without dissemination also occurred in the summer months most frequently (284/954 cases, 29.8%).

Associated condition and Past history(Table 3)

Among our patients, 3 patients had underlying diseases. Patient 1 had hypertension, but she had not taken the medication. Patient 4 was diagnosed to have lymphoma 4 years before and received radiotherapy and chemotherapy. She was in the remission stage of lymphoma and had no signs of malignancy or immune deficiency at the time of the diagnosis of herpes zoster. Patient 7 was a hepatitis B carrier and he was diagnosed to have rectal cancer 12 years prior to this study. After the operation for rectal cancer, there was no evidence of other malignancy or recurrence.

Site of initial lesion

The thoracic dermatome was by far the most common site in this study (5 patients) as in other reports2,4. The cervical and lumbar dermatomes were the second in frequency (1 patient respec-

Table 2. Seasonal incidence of 962 cases of herpes zoster

	Spring	Summer	Autumn	Winter	Total No.	Annual incidence rate(%)
1990	—	1	—	—	1(173)	0.58
1991	—	—	—	—	0(138)	0
1992	—	1	—	—	1(138)	0.72
1993	—	—	—	—	0(117)	0
1994	—	—	1	—	1(144)	0.69
1995	—	—	—	—	0(117)	0
1996	—	4	—	1	5(127)	3.9
Total No.	0(221)	6(284)	1(222)	1(217)	8*(954)**	

* : number of patients with herpes zoster with generalized varicelliform eruption

**: number of patients with herpes zoster only

Table 3. The clinical features of the 8 cases of herpes zoster with generalized varicelliform eruptions

	1	2	3	4	5	6	7	8
Age(yr)	58	20	85	69	53	55	60	57
Sex	F	F	M	F	M	M	M	F
Onset	1990	1992	1994	1996	1996	1996	1996	1996
Season	summer	summer	autumn	winter	summer	summer	summer	summer
MH*	hypert-ension	—	—	—	—	—	Hepatitis B carrier	—
HM**	—	—	—	lymphoma	—	—	Rectal cancer	
Involved dermatome	C1 Lt.	T4 ?	T4 Lt.	T4,5 Rt.	T4,5 Rt.	L1,2 Rt.	T11 Rt.	T11,12 Rt.
IBD***	1	1	2	2	8	2	3	1
DT****	12	?	35	43	20	13	60	42

MH* : medical history
HM** : History of malignancy
IBD*** : interval before appearance of disseminated vesicles(day)
DT****: duration of treatment(day)

tively). The right side was more commonly affected than the left side (right side : left side = 5 : 2, unknown 1 case).

Interval before dissemination

The interval from the appearance of the initial herpetic lesion to dissemination ranged from 1 to 8 days. In 3 of 8 patients, the interval was 1 day. The mean interval before dissemination was 2.5 days.

Clinical course

All of the patients were afebrile and had no evidence of varicella pneumonia during the course of dissemination. They were treated with acyclovir, systemic steroids, human gamma globulin, antibiotics, topical wet dressing and triamcinolone intralesional injections. The duration of treatment ranged from 12 to 60 days. The mean duration of treatment was 32.1 days.

Laboratory findings

Complete blood counts with differential leukocyte counts, urinalysis with microscope, liver function tests, chest roentgenograms and electrocardiograms were performed in 7 patients. The erythrocyte sedimentation rate was elevated in 3 patients, but other results were within normal limits.

Outcome of the disease

All of the patients recovered without specific complications such as postherpetic neuralgia, secondary bacterial infection, keloid formation, and recurrent herpes zoster.

DISCUSSION

Herpes zoster is an acute localized infection caused by the varicella-zoster virus and is characterized by grouped vesicles on the erythematous base and distributed over the sensory dermatomes. Herpes zoster with generalized varicelliform eruptions occurs in 2 to 10% of patients with herpes zoster[1,2]. In Korea, the incidence was variable(0.1-1%)[3,4]. In the present study, the incidence of generalized varicelliform eruptions in 962 cases of herpes zoster was 0.83% during 7 years (January 1990 to December 1996), which is lower than the results of western countries[1,2].

Herpes zoster occurs frequently in the middle-aged or elderly in the general population, but it appears to be more common, extensive and severe in certain immunocompromised patients or particularly those with lymphoproliferative malignancies[5]. Merselis et al. reported that 65% of the patients with herpes zoster with generalized varicelliform eruptions had serious underlying diseases, for example, leukemia, Hodgkin's disease, lymphosarcoma,

multiple myeloma, etc[2]. In this study, the higher incidence was observed in patients between 50 and 59 years of age. None had the signs of malignancy or immunosuppression at the time of diagnosis of herpes zoster with generalized varicelliform eruptions, except two patients who had suffered from malignancy prior to the development of herpes zoster.

The clinical features of the varicelliform eruptions were widespread vesicular lesions developing during the course of typical localized herpes zoster. When vesicles are counted, at least 20 extradermatomal lesions are involved[6]. The interval before dissemination is about 2 to 12 days[2,7]. We found that the interval before dissemination in our cases was consistent with that of other reports.

There were no seasonal variation in the majority of reports of herpes zoster[8,9]. However, the incidence increased from March to September in some other reports[10,11]. The higher incidence was observed in summer in our cases (6 patients). Mazur et al. reported that distant lesions appeared to involve only the skin in two thirds of patients with dissemination, but the central nervous system involvement including encephalitis, cranial nerve palsies, and motor neuropathy developed in one third of patients[5]. In our cases, the visceral dissemination to the lungs, liver or gastrointestinal tracts on the basis of clinical symptoms, physical examination, chest film or liver function tests was not evidential. A recent study demonstrated that polymerase chain reactions (PCR) were helpful in diagnosing unusual manifestations of the varicella-zoster virus (VZV), such as nondermatomal, disseminated VZV, and PCR was clearly superior to viral cultures in identifying VZV infection[12,13]. Several studies have been described of cases of VZV-induced CNS disease occurring as the only sign of viral reactivation, with the diagnosis aided by PCR amplification[14,15].

Although the precise pathogenesis of herpes zoster is unknown, indirect evidence suggests the activation of the latent virus in ganglia of nerves which innervate affected dermatomes[16]. The pathogenesis of herpes zoster with generalized varicelliform eruptions is thought to be hematogeneous dissemination of the virus from the usual site of multiplication in the skin or nervous tissue. The predisposing factor is not known yet. However, it is possible to regard that the defects in the cell mediated and humoral immunity in immunosuppressive patients may be considered as one of the predisposing factors[5,7,17]. Mazur et al. demonstrated the low level of serum antibody to herpes zoster[5] and Gallagher reported the finding of the depressed lymphocyte transformation and interferon response in these patients[7]. Such specific immune defects could not be analyzed in this retrospective series.

The aim of the management of herpes zoster with generalized varicelliform eruptions is to increase immune responses[18]. The treatment with systemic antiviral agents, human leukocyte interferon and human gamma globulin seem to have a favorable effect[19,20]. We treated the patients with systemic antiviral agents, systemic steroids, human gamma globulin, triamcinolone intralesional injections, calamine lotion and the application of cool compresses. All of the patients recovered without complications such as postherpetic neuralgia, secondary bacterial infection, keloid formation and recurrent herpes zoster.

From our observation, it is suggested that herpes zoster with generalized varicelliform eruptions could occur in patients without underlying malignancy or immunosuppressive disorders and the annual incidence increased dramatically in 1996. Interestingly, the cases of disseminated herpes zoster ocurred most commonly in summer, but we cannot exactly explain the causal relationship between the incidence and seasonal variation. Further precise definitions of predisposing factors for the dissemination of herpes zoster has to be studied in patients at high risk of these infections.

REFERENCES

1. Moragas JM, Kierland RR: The outcome of patients with herpes zoster. Arch Dermatol 75:193-196, 1957.
2. Merselis JG Jr, Kaye D, Hook EW: Disseminated herpes zoster: A report of 17 cases. Arch Intern Med 113:679-686, 1964.
3. Kim JW, Kim SY, Houh W: A clinical study on herpes zoster and chicken pox. Kor J Dermatol 20:69-76, 1982.
4. Lee HR, Lee MJ, Hahm JH: A clinical study and acyclovir therapy of herpes zoster. Kor J Dermatol 33(4):661-668, 1995.
5. Mazur MH, Dolin R: Herpes zoster at the NIH: A

20 year experience. Ann J Med 65:738-744, 1978.
6. Fitzpatrick TB, Eisen AZ, Wolff K: Dermatology in general medicine. 4th ed. McGraw-Hill Inc., New York, 1993, pp 2543-2567.
7. Gallagher JG, Merigan TC: Prolonged herpes zoster infection associated with immunosuppressive therapy. Ann Intern Med 91:842-846, 1979.
8. Goffinet DR, Glatstein EJ, Merigan TC: Herpes zoster-varicella infections and lymphoma. Ann Intern Med 76:235-240, 1972.
9. Stevens DA, Jordan GW, Waddell TF: Adverse effect of cytosine arabinoside on disseminated zoster in a controlled trial. N Engl J Med 289:873-878, 1973.
10. Schimpff S, Serpick A, Stoler B: Varicella-zoster infection in patients with cancer. Ann Intern Med 76:241-254, 1972.
11. Feldman S, Hughes WT, Kim HY: Herpes zoster in children with cancer. Am J Dis Child 126:178-184, 1973.
12. Nahass GT, Goldstein BA, Zhu WY: Comparison of Tzanck smear, viral culture, and DNA diagnostic methods in detection of herpes simplex and Varicella-zoster infection. JAMA 268:2541-2544, 1992.
13. Thomas CA, Smith SE, Morgan TM, White WL, Feldman SR: Clinical application of polymerase chain reaction amplification to diagnosis of herpes virus infection. Am J Dermatopathol 16(3):268-274, 1994.
14. Bergstrom T: Polymerase chain reaction for diagnosis of varicella zoster virus central nervous system infections without skin manifestations. Scand J Infect Dis Suppl 100:41-45, 1996.
15. Baringer JR, Pisani P: Herpes simplex virus genomes in human nervous system tissue analyzed by polymerase chain reaction. Ann Neurol 36:823-829, 1994.
16. Bastian F, Rabson A, Yee C: Herpes virus varicellae isolated from human dorsal root ganglia. Arch Pathol 97:331-333, 1974.
17. Dolin R, Reichman RC, Mazur MH: Herpes zoster-varicella infection in immuno- suppressed patients. Ann Intern Med 89:378-388, 1978.
18. Yaffe HS, Greenberg MS: Herpes zoster resembling acute varicella associated with multiple myeloma. JAMA 18:160-162, 1961.
19. Whitley RJ, Chien LT, Dolin R, Galaaso GJ, Alford CA Jr, and the collaborative study group: Adenine arabinoside therapy of herpes zoster in the immunosuppressed: NIAID collaborative antiviral study. N Engl J Med 296:1372-1377, 1977.
20. Merigan TC, Ranc KH, Pollard RB, Abdallah PS, Jordan GW, Fried RP: Human leukocyte interferon for the treatment of herpes zoster in patients with cancer. N Engl J Med 298:981-987, 1978.