Singapore Med J 1997; Vol 38(11):471-474

Clinical Presentation of Herpes Zoster in a Singapore Hospital

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ABSTRACT

Background: There is a direct correlation between increasing age and incidence of herpes zoster. There is an increased risk of complications in the elderly and the immuno-compromised.

Objective: To study the clinical epidemiology of hospitalised patients with herpes zoster.

Methods: Medical records of all patients hospitalised with zoster were respectively analysed.

Results: Sixty-seven patients (3% of total admissions) were studied. There were 35 males and 32 females with a mean age of 50.35 ± 21.71. There was an increased proportion of older patients in the study cohort.

Nineteen patients (28.4%) were immuno-compromised with malignancy occurring in 9 patients. Thirteen had been on cytotoxic and/or steroid therapy. The commonest symptoms were rash, pain and fever. Eighty-five percent of the patients had complications (bacterial super-infection in (61%), dissemination (31%), ocular involvement (5%) and post-herpetic neuralgia (13.4%). There was an increasing frequency of duration of pain with increasing age in the patients with post-herpetic neuralgia.

Forty-three patients were treated with acyclovir. The median time to healing of lesions was 11 days. The 41 patients with bacterial super-infection received antibiotics with median time to healing of 12 days.

Conclusion: Increasing age and immuno-compromised state appear to be risk factors for developing herpes zoster in hospitalised patients.

Keywords: immuno-compromised, post-herpetic neuralgia, acyclovir

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INTRODUCTION

Herpes zoster occurs during the lifetime of 10% to 20% of all persons[1]. The zoster is caused by a reactivation of varicella-zoster virus which remains latent in the sensory ganglion after primary varicella infection.

There is a direct correlation between increasing age and incidence of zoster[1]. This age-related risk is believed to reflect the gradual senescence of immune containment of the virus. In the immuno-competent patients, the course may be benign. However, in the elderly and immuno-compromised patients, there is an increased risk of cutaneous or visceral dissemination and post-herpetic neuralgia[2,3].

The objective of our study was to review the clinical and therapeutic features of hospitalised patients with herpes zoster in a Singapore hospital.

MATERIALS AND METHODS

The Communicable Disease Centre (CDC) is a 130-bed tertiary referral centre. For this study, we retrospectively analysed the medical records of all patients with herpes zoster admitted to the CDC between 1 January 1993 and 30 June 1994. The patients were located from a computerised medical records system.

Medical records were analysed for clinical features, complications, treatment and outcome. Time to healing of the lesions was defined as the interval from the onset of the rash until complete crusting occurred. Post-herpetic neuralgia was defined as pain persisting for one month or more after the onset of the zoster rash. All the patients were followed up in the out-patient clinic for the development of post-herpetic neuralgia after discharge. Cutaneous dissemination is defined as the appearance of more than 20 lesions outside the primary or contiguous dermatomes. An immuno-compromised host is defined as a host with a condition, congenital or acquired, temporary or chronic, in which the response of the host to a foreign antigen is abnormal. This includes patients with solid tumours, hematologic malignancies, organ transplant recipients, collagen vascular disease and patients with congenital or acquired immunodeficiencies.

Significance testing between groups was done where applicable with Fischer's exact test.

RESULTS

A total of 2,262 patients were admitted to CDC during the 18-month study period. Herpes zoster accounted for 3% of all admissions to CDC (67 patients) and varicella accounted for 54% (1,218 patients).

The mean age of the hospitalised patients with zoster was 50.35 ± 21.71 years (range 23 months to 88 years). Thirty-nine of 67 patients (58%) in

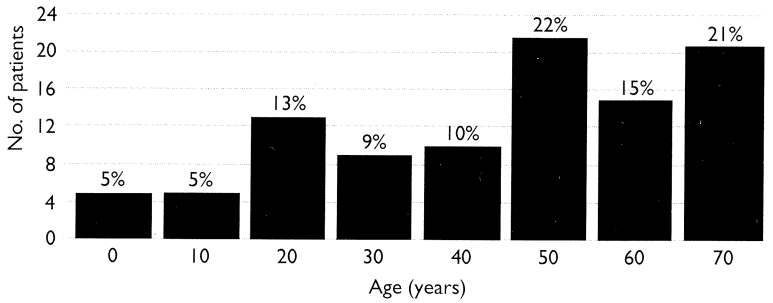

Fig 1 - Age distribution of herpes zoster

Table I - Demographic characteristics of the patients with herpes zoster

Characteristic		No. of patients n=67	[No. of patients on steroid/ No. of patients on cytotoxic therapy]
Age (years)			
Mean ± SD		50.35 ± 21.71	
Sex: M/F		35:32	
Race:	Chinese	49 (73.1%)	
	Malay	11 (16.4%)	
	Indian	4 (6.0%)	
	Others	3 (4.5%)	
Past History:	Varicella	18	
	Herpes zoster	0	
Median duration of rash at presentation (days)		5	
Immuno-compromised patients			
Renal transplant		4	[4/4]
Lymphoma		3	[1/3]
Leukaemia		2	[0/2]
Breast Carcinoma		3	
Medulloblastoma		1	
HIV Infection		2	
Systemic Lupus Erythematosus		2	[2/0]
Rheumatoid arthritis		2	[2/1]
Other underlying medical conditions			
Diabetes mellitus		11	
Hepatitis B carrier		1	
Chronic schizophrenia		1	
Hypertension		8	
Chronic obstructive airway disease		1	
Migraine		1	
Ischaemic heart disease		1	

our study were above 50 years of age (Fig 1). The youngest patient with herpes zoster was 23 months old. His mother had chickenpox during her pregnancy. There was no sex or racial predominance in the patients studied (Table I).

The mode of presentation was analysed in the 67 patients with herpes zoster. The median duration of rash was 5 days. Eighteen patients (27%) had a past history of varicella. None of the patients had zoster previously. Eleven patients had underlying diabetes mellitus (Table I).

Nineteen out of 67 patients (28.4%) were immuno-compromised; 4 were renal transplant recipients, 3 had lymphoma and 3 had breast carcinoma. Three patients were receiving steroids, 4 were on cytotoxic chemotherapy and 6 were on combination of steroids and cytotoxic chemotherapy (Table I).

Table II shows the clinical features of the patients at presentation. The predominant symptoms were rash (100%) and pain (76%). Thoracic dermatome was the most commonly involved. Sixteen patients had multiple dermatomal involvement (≥ 3 dermatomes) of which 6 were immunocompromised. At presentation, only 6 patients were leukopenic and 9 were thrombocytopenic.

Fifty seven of 67 patients (85%) developed complications. Twelve patients had 3 complications and 23 patients had 2 complications. Bacterial super-infection occurred in 41 (61.2%), cutaneous dissemination in 21 (31.3%), ocular involvement in 10 (14.9%) and neurologic complications in 13 (19.4%) of the patients. Of the 21 patients with cutaneous dissemination, only 4 were immuno-compromised. Of the 13 patients with neurologic complications, 9 patients (13.4%) had post-herpetic neuralgia, 3 had neuropathy and 1 patient had encephalitis.

Fig 2 shows the increasing frequency of duration of pain with age in the patients with acute zoster-associated pain and post-herpetic neuralgia.

In this study, 43 of our 67 patients were treated with acyclovir (Table III). The immuno-compromised patients were treated with intravenous acyclovir 10mg/kg 8 hourly for 7 days and the immuno-competent patients were given oral acyclovir 800 mg 5 times daily (adults) or 20 mg/kg qid (children) for 7 days. The median time to healing of the lesions was 11 days. Nine out of the 19 immuno-compromised patients received oral acyclovir for 7 days while the rest received intravenous acyclovir for 7 days.

Table II - Clinical and laboratory findings at presentation in patients with herpes zoster

Feature	No. of patients (%)
I Clinical symptoms:	
Rash	67 (100)
Pain	51 (76.1)
Headache	8 (11.9)
Fever	17 (25.4)
Itch	6 (9.0)
Dysesthesiae	1 (1.5)
Signs:	
Dermatomal involvement -	
Cervical	16 (23.8)
Thoracic	28 (41.8)
Lumbar	7 (10.4)
Trigeminal	16 (23.8)
II Laboratory	
Leukopenia (<4,000 WBC/mm^3)	6 (9.0)
Thrombocytopenia (<150,000 platelets/mm^3)	9 (13.4)

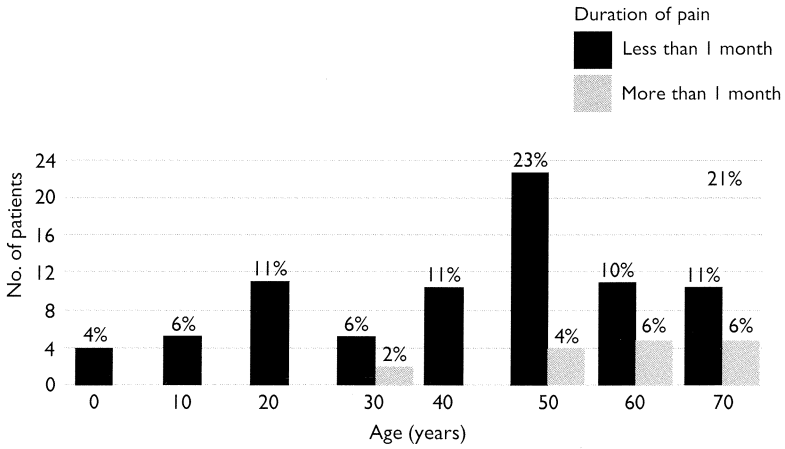

Fig 2 - Frequency of duration of pain among 52 patients with zoster by age

Table III - Treatment and outcomes of herpes zoster

	No. of patients (%)
I Treatment	
Acyclovir	43 (64.2)
Antibiotics	41 (61.2)
Analgesics:	
Paracetamol	31 (46.3)
NSAIDS	29 (43.3)
Carbamazepine	6 (9.0)
Amitriptylline	3 (4.5)
Temgesic	1 (1.5)
Morphine	1 (1.5)
II Outcome	
No. of days of hospitalisation (mean)	5.7
Time to healing of the lesions (median days):	
- Infected HZ lesions	12
- Non-infected HZ lesions	10
Recurrence	0

Forty-one patients with bacterial super-infection also received antibiotics (ampicillin, amoxicillin, cloxacillin or erythromycin). The most common analgesics utilised in the treatment of pain was paracetamol and NSAID. Carbamazepine, amitriptylline, temgesic and morphine were given in 6 patients. The mean duration of hospitalisation was 5.7 days. There were no recurrences of herpes zoster in the patients studied over a follow-up period of 18 months (Table III).

There was no significant difference in time to healing of the lesions between the immuno-compromised and the immuno-competent patients, and those treated with acyclovir and those who were not treated with this anti-viral agent.

DISCUSSION

Herpes zoster occurs in individuals previously infected by varicella-zoster virus. Unlike chickenpox, herpes zoster occurs for the most part in older individuals. In our study, 39 of 67 patients (58%) were above 50 years of age.

There appears to be no influence of sex or race on disease incidence[4]. There was no sex or racial predominance in our study. Herpes zoster can occur within the first 2 years of life in children whose mothers had chickenpox during pregnancy. This was observed in our youngest patient who was 23 months old and whose mother had chickenpox during her pregnancy, probably reflecting in utero chickenpox with reactivation early in life.

In immuno-competent hosts, herpes zoster is usually self-limiting, resolving within 4 weeks of onset of rash. Herpes zoster in immuno-compromised hosts results in more severe disease, which can be life-threatening in the absence of treatment. In our study, 19 of 67 patients (28%) of our patients were immuno-compromised, 4 were renal transplant recipients, 5 had haematologic malignancies (including one bone marrow transplant recipient) and 3 with breast carcinomas. Only 4 of the immuno-compromised patients developed cutaneous dissemination and 6 had multiple dermatomal involvement (3 or more dermatomes).

The predominant presenting symptoms in our patients were rash (100%) and pain (76%). About 25% of the patients had multiple dermatomal involvement. The complications of herpes zoster add significantly to the morbidity of these patients. Eighty-five per cent of the patients in our study developed complications. This high complication rate is to be expected as CDC is a tertiary referral centre for infectious diseases. The 3 commonest complications observed were bacterial super-infection (61%), cutaneous dissemination (31%) and neurologic complications viz post-herpetic neuralgia, neuropathy and encephalitis (19.4%). The frequency of cutaneous dissemination is almost similar to that reported by other studies. Post-herpetic neuralgia occurred in 13.4% of the patients studied. Other studies have noted the incidence of post-herpetic neuralgia to be 9% to 14%[7,8]. In our study, there was an increased frequency of duration of pain with advancing age in the patients with acute zoster-associated pain and post-herpetic neuralgia. This finding concurs with that reported by Da Margas et al[9].

The current mainstay of treatment for herpes zoster is acyclovir. Acyclovir can greatly increase the rate of resolution of the rash and decrease the virus shedding[9]. In this study, 43 out of 67 patients were treated with acyclovir. The median time to healing of the lesions was 11 days compared to 6 to 7 days in the other trials. This is probably due to the delayed initiation of treatment in our study, with the median duration of rash at presentation being

5 days. New anti-herpes agents like famciclovir and valaciclovir appear to be effective in the treatment of herpes zoster and zoster-associated pain[10,11].

About 60% of the patients received antibiotics for bacterial super-infection. However, the time to healing in this group of patients was not significantly longer than the non-infected group (median 12 days compared to 10 days). We recognise the limitations to the interpretation of the data due to the retrospective nature of this study.

The most common analgesic utilised in the treatment of pain was paracetamol and non-steroidal anti-inflammatory drug eg mefenamic acid. Carbamazepine, amitriptylline and temgesic/morphine had to be given for zoster-associated pain in 11 patients. Amitriptylline blocks neuronal uptake of norepinephrine and serotonin, potentiating their inhibition of spinal neurons involved in pain perception[12]. Carbamazepine can significantly reduce the lancinating pain arising from post-herpetic neuralgia. To date, it has not been possible to demonstrate a consistent benefit of treatment with acyclovir on post-herpetic neuralgia[13,14]. There have been no recurrences of herpes zoster in the patients studied over a 18-month follow-up period.

Increasing age and immuno-compromised state (ie post-transplant and malignancies) appear to be risk factors for developing herpes zoster. There was an increased frequency of pain with age, with post-herpetic neuralgia occurring in 13.4%. The cost effectiveness of treatment with other newer anti-virals, for example famciclovir and valaciclovir, compared with acyclovir in decreasing the frequency of post-herpetic neuralgia need to be studied.

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