JC POLYOMAVIRUS REACTIVATION IS NOT ASSOCIATED WITH HERPES ZOSTER

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Summary. – Herpes zoster (HZ) is a neurocutaneous disease caused by Varicella-zoster virus (VZV) as a consequence of declined cell-mediated immunity, immune suppression and immunodeficiency. As reactivation of JC polyomavirus (JCPyV) might be linked with immunodeficiency or immunosuppressive therapy, the relationship between HZ and JCPyV reactivation was investigated. The incidence of JCPyV in urine samples from 102 patients with HZ and 100 healthy individuals from South Korea was determined by PCR. The incidence values for HZ patients and control individuals did not differ significantly (24.5% vs. 20.0%, respectively, P = 0.5391). When different age groups were monitored, the positivity values of 21.1%, 20.0%, and 30% were found for 20–39, 40–59 and over 60 year-old patients, respectively. In order to determine the genotype of JCPyV isolates, their VP1-large T antigen (VT)-intergenic region was PCR amplified, sequenced and analyzed. Three distinct types, namely 1, 2A and 7B were found in 8%, 24%, and 68% of were found among 25 isolates from HZ patients. Using phylogenetic analysis, the type 1 isolates were assigned to the 1C subtype. These results indicate that HZ does not play an important role in JCPyV reactivation and is not associated with JCPyV.

Key words: JC polyomavirus; genotype; herpes zoster; Varicella-zoster virus; virus reactivation; phylogenetic analysis

Introduction

JCPyV (the species *JC polyomavirus*, the genus *Polyomavirus*) is the causative agent of progressive multifocal leukoencephalopathy (PML), a fatal demyelinating neurodegenerative disease. The incidence of PML among AIDS patients is about 5% based of neuropathological findings (Berger and Levy, 1993). JCPyV can be reactivated in individuals with immunological deficits such as AIDS patients, transplantation recipients and patients receiving immunosuppression therapy (Chesters *et al.,* 1983; Arthur *et al.,* 1986; Apperley *et al.,* 1987). This virus is widespread in the human population (Padgett and Walker, 1973), infecting children asymptomatically. It persists in the renal tissue (Chesters *et al.,* 1983) and is excreted in the urine of 40% of the general population above 30 years of age (Kitamura *et al.,* 1990; Agostini *et al.,* 1996).

The JCPyV genome consists of a circular double-stranded DNA of about 5.1 kb. Genotype analysis of JCPyV revealed at least 15 distinct types. VZV causes two clinically distinct diseases. Primary VZV infection typically causes childhood varicella (chicken pox), a common and extremely contagious acute infection, which is characterized by generalized vesicular rash. Reactivation of latent VZV from dorsal root ganglia results in herpes zoster (shingles), a localized

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Abbreviations: JCPyV = JC polyomavirus; HZ = herpes zoster; PML = progressive multifocal leukoencephalopathy; VZV = Varicella-zoster virus; HIV-1 and/or HIV-2 = Human immunodeficiency virus 1 and/or Human immunodeficiency virus 2; MS = multiple sclerosis;VT = VP1-large T antigen

Table 1. JCPyV isolates subjected to phylogenetic analysis

JCPyV isolate/strain	Gender/age in years	Donor	Source	Country	Acc. No.	Reference
Mad-1	M/38	PML	B	USA	J02226	Frisque *et al.,* 1984
#123	M/55	MS	U	USA	AF015527	Agostini *et al.,* 1998a
#124	M/52	MS	U	USA	AF015526	
#402	M/63	MS	U	USA	AF015528	Agostini *et al.,* 1996
GS/B	?	PML	B	Germany	AF004350	Loeber and Dorries, 1988
#223	M/36	HIV-1	U	USA	AF015532	Agostini *et al.,* 1998b
#226	F/78	?	U	USA	AF015531	
#229	M/48	HIV-1	U	USA	AF015535	
Tokyo-1	M/70	PML	B	Japan	AF030085	
CY	?	H	U	Japan	AB038249	Kato *et al.,* 2000
MY	?	H	U	Japan	AB038250	
KR-1	M/49	H	U	S. Korea	AF320284	Jeong *et al.,* 2004
KR-2	M/44	H	U	S. Korea	AF320285	
KR-3	M/56	H	U	S. Korea	AF320311	
KR-4	M/35	H	U	S. Korea	AF320312	
KR-5	M/62	H	U	S. Korea	AF320284	
KR-6	M/64	H	U	S. Korea	AF320313	
KR-7	F/44	H	U	S. Korea	AF320284	
KR-8	F/45	H	U	S. Korea	AF320284	
KR-9	F/41	H	U	S. Korea	AF320284	
KR-10	F/62	H	U	S. Korea	AF320284	
KR-11	F/75	H	U	S. Korea	AF320314	
KR-12	M/68	H	U	S. Korea	AF320315	
KR-13	M/7	H	U	S. Korea	AF320316	
KR-14	M/29	H	U	S. Korea	AF320284	
KR-15	F/57	H	U	S. Korea	AF320284	
KR-16	M/57	H	U	S. Korea	AF320284	
KR-17	M/42	H	U	S. Korea	AF320284	
KR-18	F/69	H	U	S. Korea	AY050519	
KR-19	M/57	H	U	S. Korea	AY050520	
KR-20	M/60	H	U	S. Korea	AY050519	
KJC-1	M/63	HZ	U	S. Korea	AF320284	This study
KJC-2	F/60	HZ	U	S. Korea	AY583233	
KJC-3	F/79	HZ	U	S. Korea	AY583233	
KJC-4	F/38	HZ	U	S. Korea	AF320284	
KJC-5	F/59	HZ	U	S. Korea	AF320315	
KJC-6	F/65	HZ	U	S. Korea	AF320284	
KJC-7	F/78	HZ	U	S. Korea	AY583233	
KJC-8	F/22	HZ	U	S. Korea	AF320284	
KJC-9	F/74	HZ	U	S. Korea	AF320284	
KJC-10	M/68	HZ	U	S. Korea	AF320284	
KJC-11	F/62	HZ	U	S. Korea	AF320284	
KJC-12	M/54	HZ	U	S. Korea	AF320284	
KJC-13	F/66	HZ	U	S. Korea	AY583233	
KJC-14	M/38	HZ	U	S. Korea	AF320284	
KJC-15	M/85	HZ	U	S. Korea	AY583233	
KJC-16	F/58	HZ	U	S. Korea	AF320284	
KJC-17	F/76	HZ	U	S. Korea	AY050519	
KJC-18	F/85	HZ	U	S. Korea	AF320284	
KJC-19	F/57	HZ	U	S. Korea	AY583233	
KJC-20	M/53	HZ	U	S. Korea	AF320284	
KJC-21	M/65	HZ	U	S. Korea	AY583230	
KJC-22	M/31	HZ	U	S. Korea	AF320313	
KJC-23	F/65	HZ	U	S. Korea	AY583232	
KJC-24	F/68	HZ	U	S. Korea	AF320284	
KJC-25	F/50	HZ	U	S. Korea	AF320284	

B = brain; PML = progressive multifocal leukoencephalopathy; MS = multiple sclerosis; HIV-1 = HIV-1 infection; H = healthy individual; HZ = herpes zoster; U = urine; ? = unknown.

cutaneous eruption accompanied by neuralgic pain that occurs most commonly in older persons. The virus reactivates primarily in elderly individuals, organ transplant recipients and patients with cancer or AIDS (Gilden *et al.,* 2000). HZ correlates with specifically declined cell-mediated immunity, immunosuppression and immunodeficiency (Miller, 1980; Berger *et al.,* 1981). Tsai *et al.* (1997) have shown that the incidence of urinary excretion of JCPyV is increased in immunosuppressed autoimmune disease patients. However, other studies have shown contradictory results with human immunodeficiency virus-infected patients (Markowitz *et al.,* 1993; Sundsfjord *et al.,* 1994; Knowles *et al.,* 1999; Behzad-Behbahani *et al.,* 2004). Although it is known that immunosuppression may lead to HZ and JCPyV reactivation, their mutual relationship is still unknown.

Therefore the incidence of JCPyV in the urine of HZ patients as well as healthy individuals from South Korea was determined and the genotype of 25 JCPyV isolates from HZ patients was assessed.

Materials and Methods

Urine samples from 102 HZ patients were collected at Chunchon Sacred Heart Hospital, College of Medicine, Hallym University, Chunchon, South Korea. The patients were diagnosed for HZ on the basis of characteristic dermatomal or disseminated vesicles. Patients with previous antiviral treatment were excluded. Urine sample were collected before the starting of antiviral treatment and were kept at -70°C until used. The study was approved by the Ethical Committee of Chunchon Sacred Heart Hospital and all volunteers gave informed consent.

Total DNA. A 10 ml aliquot of urine was centrifuged at 142,000 × g for 90 mins at 4°C (Beckman SW 41 Ti rotor). The pellet was resuspended in 1 ml of distilled water and a 5 µl aliquot of the sample was mixed with 1 µl of a 10 × lysis buffer containing proteinase K (100 mmol/l Tris-HCl, 10 mmol/l EDTA pH 8.0, and 500 µg/ml proteinase K) and 4 µl of water. The mixture was incubated first at 50°C for 15 mins and then at 95°C for 10 mins, and centrifuged at 10,000 rpm for 3 mins. The supernatant was collected and used for PCR.

PCR amplified a 656 bp fragment from the VT-intergenic region of JCPyV genome using the primers P1 (5'-TTTTGGGA CACTAACAGGAGG-3', nts 2107–2127) and P2 (5'-AGCAGAA GACTCTGGACATGG-3', nts 2762–2742) (Frisque *et al.,* 1984).

The reaction mixture (50 µl) contained 50 pmoles of each primer, 1.5 mmol/l $MgCl_2$, 0.2 mmol/l dNTPs, 2.5 U of *Taq* DNA polymerase (Promega), and 5 µl of 10 × buffer. The PCR consisted of 94°C/5 mins (initial denaturation), 40 cycles of 94°C/45 secs, 60°C/45 secs, and 72°C/1 min, and 72°C/10 mins (final extension). The products were separated by electrophoresis in 1.2% agarose gel and stained with ethidium bromide.

Sequencing and sequence analysis. For sequencing, a PCR product was purified using a standard kit from Qiagen. The sequencing was carried out in an automatic ABI 377 sequencer using the Taq Dideoxy Terminator Cycle Sequencing Kit (ABI). Nucleotide sequences were assembled and edited using a combination of the ABI 377 DNA Sequencer Data Analysis Program and Sequence Navigator Software.

Phylogenetic analysis. The JCPyV isolates subjected to phylogenetic analysis are shown in Table 1. A neighbor-joining phylogenetic tree (Saitou and Nei, 1987) was constructed using the CLUSTAL W and TREEVIEW 1.4 programs (Thompson *et al.,* 1994; Page, 1996). Divergences were estimated by the two-parameter method (Kimura, 1980). The bootstrap test was employed to estimate the confidence of the branching of the tree (Felsenstein, 1985).

Statistical analysis. Significance of differences was evaluated by the X^2 test using the SAS 8.1 software (SAS Institute Inc.).

Results

Incidence of JCPyV in HZ patients and healthy individuals

Urine samples were screened for JCPyV by PCR. The results showed that the virus was detected in 25 (24.5%) of 102 samples from HZ patients (Table 2). In healthy

Table 2. Incidence of JCPyV in HZ patients and healthy individuals in South Korea

Group	Age (years)	Mean age ± SD	No. of samples examined	No. of positives (%)	No. of positives/No. of total (%)	
					Male	Female
Healthy individuals	0–19	5.7 ± 4.0	26	1 (4)	1/15 (6.67)	0/11 (0)
	20–39	32.0 ± 5.4	23	2 (9)	2/18 (11.11)	0/5 (0)
	40–59	48.6 ± 6.1	26	10 (38)	6/17 (35.3)	4/9 (44.44)
	≥60	67.0 ± 4.9	25	7 (28)	4/13 (30.77)	3/12 (25)
	Total	38.2 ± 23.4	100	20 (20)	13/60 (21.67)	7/37 (18.92)
HZ patients	0–19	7.0 ± 3.6	3	0 (0)	0/2 (0)	0/1 (0)
	20–39	30.4 ± 6.4	19	4 (21.1)	2/11 (18.2)	2/8 (25.0)
	40–59	51.6 ± 5.6	30	6 (20.0)	2/10 (20.0)	4/20 (20.0)
	≥60	69.1 ± 7.3	50	15 (30.0)	4/10 (40.0)	11/40 (27.5)
	Total	38.2 ± 23.4	102	25 (24.5)	8/33 (24.2)	17/69 (24.6)

A

JCPyV type	Strain /isolate	2161	2203	2239	2251	2278	2317	2369	2371	2401	2404	2416	2440	2455	2458	2518	2534	2535	2540	2574	2575	2584	2587	2592	2593	2604	2606	2621	2639	2642	2645	2663	2712	2723
2B	GS/B	C	A	T	C	A	A	C	A	G	G	C	T	G	A	G	T	C	G	G	T	C	C	G	A	T	T	C	T	A	G	A	T	T
2A	#226	·	T	·	A	G	G	T	G	·	·	T	·	·	·	A	·	·	·	·	·	·	T	T	·	C	·	T	·	·	·	·	A	·
2B	#223	·	·	·	·	·	·	T	·	·	·	·	·	·	·	·	·	·	·	·	·	·	·	·	·	·	·	T	·	·	·	·	G	·
2C	#229	·	T	·	A	G	G	T	G	A	·	T	·	·	·	A	·	·	·	·	·	·	T	T	·	C	·	T	·	·	·	·	A	·
2A	Tokyo-1	·	·	·	A	G	C	T	G	·	A	T	·	·	·	A	·	·	T	·	·	·	T	T	·	C	·	T	·	G	·	·	A	C
7B	CY	·	·	G	·	G	·	T	·	·	·	·	·	A	·	·	·	·	·	·	·	·	T	T	G	·	C	T	·	·	·	G	G	·
2A	MY	T	·	·	A	G	C	T	G	·	·	T	·	·	·	A	C	·	·	·	·	G	T	T	·	C	·	T	·	G	A	·	A	C
7B(CY)	KR-#, KJC-#	·	·	G	·	G	·	T	·	·	·	·	·	·	·	A	·	·	·	·	·	·	T	T	G	·	C	T	·	·	·	·	G	·
7B(CY)	KR-6, KJC-22	·	·	G	·	G	·	T	·	·	·	·	·	·	·	A	·	·	·	A	·	·	T	T	G	·	C	T	·	·	·	·	G	·
7B(CY)	KR-11	·	·	G	·	G	·	T	·	·	·	·	C	·	·	A	·	·	·	·	·	·	T	T	G	·	C	T	·	·	·	·	G	·
7B(CY)	KR-13	·	·	G	·	G	·	T	·	·	·	·	·	·	G	A	·	·	·	A	·	·	T	T	G	·	C	T	·	·	·	·	G	·
7B(CY)	KJC-21	·	·	G	·	G	·	T	·	A	·	·	·	·	G	A	·	·	·	A	·	·	T	T	G	·	C	T	·	·	·	·	G	·
7B(CY)	KJC-23	·	·	G	·	G	·	T	G	·	·	·	·	·	G	G	·	·	·	A	·	·	T	T	G	·	C	T	·	·	·	·	G	·
2A(MY)	KR-2	·	·	·	A	G	C	T	G	·	·	T	·	·	·	A	·	G	·	·	C	·	T	T	·	·	·	T	·	G	·	·	A	C
2A(MY)	KR-3	·	·	·	A	G	C	·	G	·	·	T	·	·	·	A	·	·	·	·	·	·	T	T	·	C	·	T	·	G	·	·	A	C
2A(MY)	KR-4	·	·	·	A	G	C	T	G	·	·	T	·	·	·	A	·	·	·	·	·	·	T	T	·	C	·	T	C	G	·	·	A	C
2A(MY)	KR-19	T	·	·	A	G	C	T	G	·	·	T	·	A	·	A	·	·	·	·	·	·	T	T	·	C	·	T	·	G	A	·	A	C
2A(MY)	KJC-§	·	·	·	A	G	C	T	G	·	·	T	·	·	·	A	·	·	·	·	·	·	T	T	·	C	·	C	·	G	A	·	A	C

B

JCPyV type	Strain /isolate	2134	2227	2260	2269	2311	2320	2356	2369	2377	2431	2455	2472	2479	2494	2502	2553	2596	2661	2692
1A	Mad-1	A	C	A	T	G	G	C	T	C	C	A	G	A	C	A	T	G	A	G
1A	#124	·	·	T	A	T	·	·	C	·	T	·	·	·	T	·	C	T	·	T
1B	#123	G	·	T	·	T	·	·	·	·	·	·	·	·	·	G	·	T	·	T
4	#402	·	T	T	·	T	·	T	·	T	·	·	A	·	·	G	·	T	T	T
1	KR-12, KJC-5	·	·	·	·	T	A	·	·	·	·	G	·	G	T	G	·	T	·	T
1	KR-18, 20, KJC 17	·	·	·	·	T	A	·	·	·	·	·	·	G	T	G	·	T	·	T

Fig. 1

Comparison of JCPyV isolates from HZ patients and healthy individuals from South Korea and standard JCPyV strains based on VT-intergenic region

A: 23 isolates from HZ patients and 17 isolates from healthy individuals compared to standard strains of types 2 and 7B. The GS/B strain of type 2B used as reference. B: 2 isolates from HZ patients and 3 isolates from healthy individuals compared to standard strains of types 1 and 4. The Mad-1 strain of type 1A was used as reference. KR-# indicates KR isolates 1, 5, 7, 8, 9, 10, 14, 15, 16, and 17. KJC-# indicates KJC isolates 1, 4, 6, 8, 9, 10, 11, 12, 14, 16, 18, 20, 24, and 25. KJC-§ indicates KJC isolates 2, 3, 7, 13, 15, and 19. The nucleotide numbering is based on that of Mad-1 strain (Frisque *et al.,* 1984).

individuals, the incidence of the virus was similar (P = 0.5391). When different age groups were monitored, the positivity values of 21.1%, 20.0%, and 30% were found for 20–39, 40–59, and over 60 year-old patients, respectively. There was no significant correlation between the virus incidence and gender, as 24.2% of men and 24.6% of women were virus-positive (P = 0.973). These results suggest that HZ does not play an important role in JCPyV reactivation.

Genotyping of the JCPyV isolates from HZ patients

In order to genotype the JCPyV isolates from HZ patients, a 656 bp VT-intergenic region of their DNAs was sequenced. We identified 3 distinct JCPyV isolates belonging to types 7B (KJC-21 and -23) and 2A (KJC-2) (Fig. 1) The 7B type was dominant (68%), while the types 2A and 1 occurred in 24% and 8%, respectively. There was no significant

difference in the distribution of the virus types in HZ patients and healthy individuals (P = 0.7464). A significant correlation was not found between the virus type and the age within the group of HZ patients (Table 3). These results suggest that HZ is not associated with a particular type of JCPyV .

Phylogenetic analysis of the JCPyV isolates from HZ patients

A phylogenetic tree, based on the VT-intergenic sequence described above, was constructed for the JCPyV isolates from HZ patients from South Korea and other JCPyV isolates/strains described earlier (Fig. 2). The tree revealed that out of the 25 isolates from HZ patients 17 belonged to

Table 3. Incidence of individual types of JCPyV in HZ patients and healthy individuals in South Korea

Group	Age (years)	No. of JCPyV isolates examined	No. of JCPyV isolates		
			Type 7B	Type 2A	Type 1
Healthy individuals	0–19	1	1	0	0
	20–39	2	1	1	0
	40–59	10	7	2	1
	≥ 60	7	4	1	2
	Total	20	13	4	3
HZ patients	0–19	0	0	0	0
	20–39	4	4	0	0
	40–59	6	4	1	1
	≥60	15	9	5	1
	Total	25	17	6	2

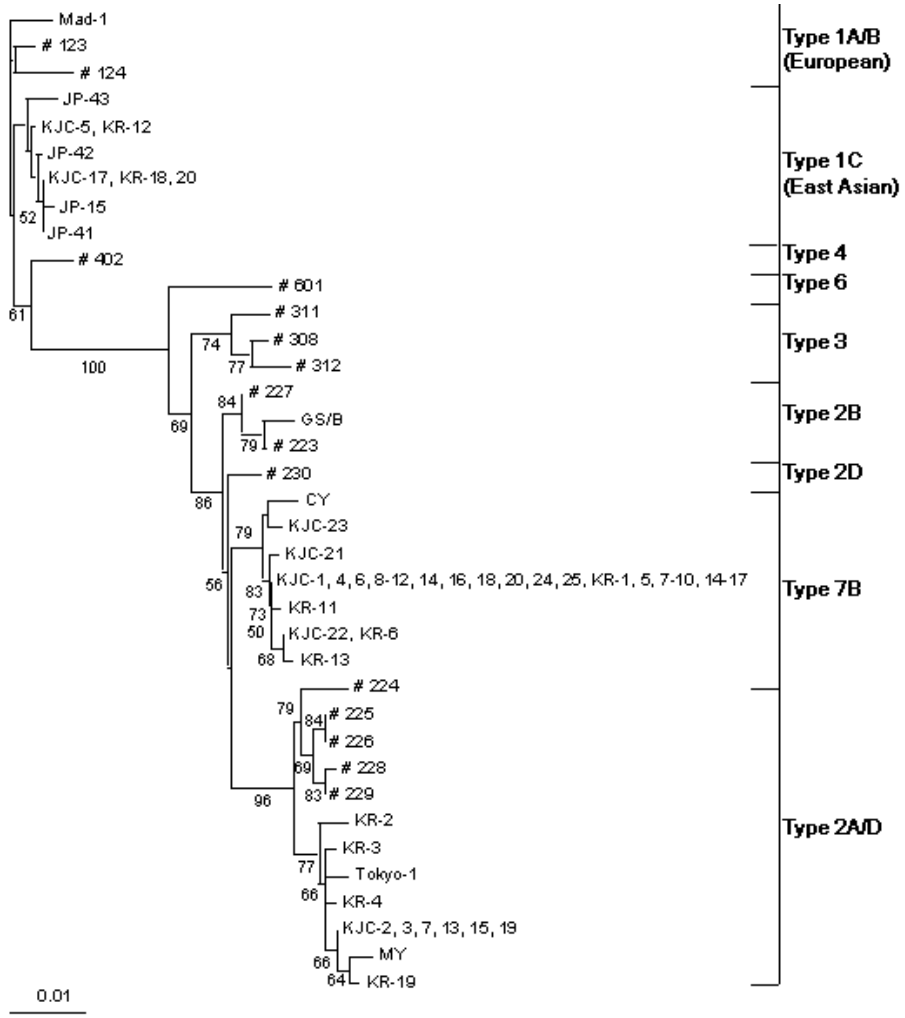

Fig. 2

Phylogenetic tree of JCPyV isolates from HZ patients from South Korea and standard JCPyV strains based on VT-intergenic region

The neighbor-joining phylogenetic tree was constructed from the isolates and strains (Table 1) using the CLUSTAL W and TREEVIEW 1.4 programs. The numbers at the nodes indicate bootstrap confidence levels obtained from 100 replicates. Only values exceeding 50% are shown. The isolates from HZ patients from South Korea (KJC-#) are in bold.

the type 7B cluster, 6 to the 2A cluster, and 2 to the type 1 cluster. The analysis also showed that 5 South Korean isolates from 2 HZ patients and 3 healthy individuals clustered with the type 1C (East Asian) group located separately from the 1A/B (European) group.

Discussion

Previously, the incidence of JCPyV in the urine of immunocompetent individuals in the South Korean population has been reported (Jeong *et al.,* 2004). It was found that 20% of immunocompetent individuals were JCPyV-positive. There are reports showing that JCPyV DNA is detectable in the urine of 13.2–80.0% of human population as whole (Kitamura *et al.,* 1990; Agostini *et al.,* 1996; Chang *et al.,* 1996a,b, 1999; Tsai *et al.,* 1997). In this study, we followed JCPyV in the urine of HZ patients as well as healthy individuals from South Korea. We found that the virus incidence in general population and in individual age groups, and the virus genotype were not associated with HZ

To investigate the effects of immunosuppressed conditions on the incidence of JCPyV, several studies have been undertaken on immunocompromised and immunocompetent subjects (Markowitz *et al.,* 1993; Sundsfjord *et al.,* 1994; Tsai *et al.,* 1997; Knowles *et al.,* 1999; Wang *et al.,* 2000; Behzad-Behbahani *et al.,* 2004). Tsai *et al.* (1997) have detected JCPyV in 13.3% of immunocompetent individuals and in 37.5% of immunosuppressed patients with autoimmune disease. Wang *et al.* (2000) have found an increased incidence of JCPyV in Taiwanese immuosuppressed patients compared with immunocompetent individuals ($P = 0.036$). In addition, the incidence of JCPyV DNA in the cytotoxic immunosuppresed group was significantly higher than that in the non-cytotoxic group ($P < 0.05$). These results indicate that immunosuppression may play an important role in JCPyV reactivation. However, in other studies, JCPyV DNA has been found in similar percentage in the urine of immunosuppressed patients and healthy individuals (Markowitz *et al.,* 1993; Sundsfjord *et al.,* 1994; Behzad-Behbahani *et al.,* 2004). The JCPyV-positivity of British HIV-1-infected patients and healthy individuals was about 16.4% and 26.7%, respectively. ($P = 0.1156$) (Behzad-Behbahani *et al.,* 2004). In Norwegian and Danish populations, it was about 16% and 20% for HIV-1-infected patients and immunocompetent healthy individuals, respectively ($P = 0.4887$) (Sundsfjord *et al.,* 1994). In an American population, it was 22.7% and 26.5% for HIV-1-infected patients and immunocompetent control subjects and, respectively ($P = 0.7342$) (Markowitz *et al.,* 1993). These results suggest that the immunosuppression caused by HIV-1 infection has little effect on the incidence of JCPyV in general population.

VZV infection is serious condition in immunosuppressed patients, particularly those with defects in cell-mediated immunity (Winston *et al.,* 1988; Wingard, 1993; Anaissie *et al.,* 1998). Little is known about the correlation between the immunity and the reactivation of JCPyV. The reactivation of JCPyV is associated with the depression of cell-mediated immunity in PML patients and can be suppressed in glial cells by the soluble factors secreted from T lymphocytes (Willoughby *et al.,* 1980; Chang *et al.,* 1996). It is believed that the cell-mediated immunity may be involved in the reactivation of JCPyV. However, several results including ours suggest that the incidence of JCPyV is not associated with the HIV-1-immunodeficiency and the cell-medicated immunity.

The results of this study showed that there was no significant difference in the JCPyV prevalence between men and women. These results are in accord with those reported earlier (Kitamura *et al.,* 1990; Agostini *et al.,* 1996; Jeong *et al.,* 2004).

Different JCPyV types are located in various geographic regions in the world (Sugimoto *et al.,* 1997; Yogo *et al.,* 2004). It is possible that different JCPyV strains possess variable neurotropic properties. Some earlier reports have shown that the proportion of type 2 among at least 4 different genotypes of JCPyV is significantly increased in the brain or cerebrospinal fluid of PML patients compared to the urine from healthy individuals. However, the proportion of type 1 was the same in these two groups (Agostini *et al.,* 1997, 1998; Ferrante *et al.,* 2001). These results suggest that a specific JCPyV genotype could be important risk factor for the PML development. In this study, the distribution of different genotypes of JCPyV in South Korean HZ patients did not differ from those of healthy controls. The genotyping revealed among others also type 1 in urine samples from HZ patients. The same type was found in two South Korean PML patients with AIDS (Jeong *et al.,* 2002) and in three healthy subjects (Jeong *et al.,* 2004). The phylogenetic analysis assigned the recent isolates to the 1A/B (European) subtype, separately from the 1C (East Asian) subtype.

In conclusion, this study showed that there was no difference in the incidence of JCPyV in HZ patients and that in healthy individuals. Thus it appears that there is no association between HZ and JCPyV reactivation. Furthermore, regarding the distribution of different genotypes of JCPyV, there is no difference between HZ patients and control subjects.

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