Good cognitive outcome of patients with herpes zoster encephalitis: a follow-up study [Letter]

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Sirs: Varicella zoster virus (VZV), a virus of the herpes group, causes chickenpox in 90–100 % of the population [14]. The virus remains latent in cranial nerves and dorsal-root ganglia and endogenous reactivation may cause herpes zoster. Severe neurological complications such as aseptic meningitis, myelitis or encephalitis are rare in immunocompetent patients but can occur in up to 35 % of immunocompromized individuals [5, 15]. Herpes zoster encephalitis (HZE) develops in approximately 5 % of patients hospitalised because of herpes zoster [9]. The diagnosis of HZE includes an encephalopathic state, clinical evidence of herpes zoster with or without virological confirmation and an inflammatory cerebrospinal fluid (CSF) [7]. Mental changes are a main neurological symptom in HZE [1, 7, 10] but specific neuropsychological sequelae after the acute stage of HZE have not been adequately studied.

We investigated the cognitive outcome of 8 patients with HZE (for clinical data of acute HZE and follow-up examination see Table 1). Headache and fever were common prodromal symptoms in the acute stage of the disease. The main neurological symptoms were confusion and somnolence as well as focal signs including hemihypaesthesia, hemiparesis and aphasia.

In most cases, the CSF showed a lymphocytic pleocytosis (WBC 18 to 800/μl) and an elevated protein level (600–1200 mg/l). The electroencephalogram (EEG), performed in 6 cases, was always abnormal, including generalised slowing of background activity and paroxysmal bilaterally synchronous slow waves. Magnetic resonance imaging (MRI) or computed tomography (CT) in 7 patients, revealed multiple enhancing lesions in the subcortial white matter related to HZE only in one patient.

All patients were re-examined 4–52 months after the onset of acute encephalitis and a comprehensive neuropsychological appraisal was carried out. The neuropsychological evaluation included Mini-Mental State examination (MMSE) [4], Rey-Osterrieth Complex Figure test [8] and the clock-drawing-test [11] for visuoperceptual function, Rey auditory verbal learning test and Rey visual design learning test [12] for verbal and visual memory, digit span [13] for short-term memory, Stroop test [2] for executive function and d–2-test [3] for attention. Patients' performance was compared with that of a control group matched in sex, age and education (Mann-Whitney-U-test). In aged patients with multiple concomitant diseases only a limited number of tests could be performed.

The neuropsychological data are summarised in Table 2. Apart from the Rey-Osterrieth Complex Figure copy our results show no significant differences between the patients and the controls. This would suggest impaired visuoconstructive abilities, but statistical interpretation must be with caution owing to the small number of patients ($n = 6$). In addition, the clock-drawing-test, a much simpler test assessing the visuoconstructive skills, showed no significant difference.

Our findings are in contrast to those of the only previous neuropsychological study investigating sequelae after acute HZE by Hokkanen et al. [6]. They described a subcortical impairment involving forgetfulness, slowing of thought processes, emotional and personality related changes and impaired cognitive ability in 9 immunocompetent patients. However, the examination was carried out directly after the patients could co-operate adequately after the acute stage of the infection and only one patient was evaluated for the first time 7 months after onset of HZE. Thus, except for one patient there was no long-term follow-up which may explain these contrasting findings. Neuropsychiatric sequelae have been described by Appelbaum et al. [1] in 3 of 9 patients who were studied up to 10 years after HZE but were not observed in our study group. However, none of the patients in Appelbaum's study received adequate virus inhibiting treatment which may account for this unfavourable outcome.

In conclusion, our data suggest that neuropsychological sequelae after HZE in immunocompetent patients are less frequently than previously assumed but larger studies are needed to confirm these findings.

Table 1 Clinical data of the patients during the acute stage of HZE and of the follow-up examination

no.	age/sex	shingles	fever	headache	concomitant diseases	acute neurological findings	EEG	cerebral MRI	CSF Findings				Aciclovir	follow up (months)	residual symptoms
									cells (/µl)	protein (mg/l)	VZV-PCR[1]	VZV AI[2]			
1	16/m	–	+	–	none	hypaesthesia of the right arm, aphasia	pathol.	normal	800	1199	+	1,2	no	35	none
2	45/f	sine he V2	–	+	none	hemihypaesthesia	pathol.	normal	400	770	+	4,3	yes[4]	4	headache, fatiguerpete
3	64/m	V1–3/ C2–3 left	–	+	diabetes mellitus	somnolence	n. d.	n. d.	18	650	n. d.	n. d.	yes[4]	52	postherpetic neuralgia
4	67/f	–	+	+	rheumatism, (methotrexate, cortisone)	somnolence, confusion	pathol.	few nonspecific WML	18	1032	–	9,9	yes[4]	41	none
5	70/f	V1/V2 right	+	+	none	confusion, paresis N. III/VI	pathol.	normal	82	710	n. d.	n. d.	yes[4]	51	postherpetic neuralgia
6	74/m	V1 right	+	+	none	somnolence, confusion, aphasia	pathol.	few nonspecific WML	129	839	+	0,8	yes[4]	10	none
7	82/f	V3 right	–	–	none	confusion	n. d.	few nonspecific WML	69	600	n. d.	n. d.	yes[5]	43	not evaluable[3]
8	92/f	–	+	–	none	hemihypaesthesia/ hemiparesis, aphasia	pathol.	enhancing WML	88	993	–	1,0 (plasma: IgM +)	yes[4]	13	none

[1] VZV-PCR varicella-zoster-virus polymerase chain reaction; [2] VZV AI varicella-zoster-virus antibody index; [3] The patient suffered from a stroke with onset after HZE; [4] 3 x 10 mg /kg body weight for 7–21d i. v.; [5] 5 x 400 mg oral for 7d
n. d. not done; *WML* white matter lesions

Table 2 Neuropsychological test performance of HZE patients compared with a healthy control group (n, median)

	encephalitis group (n = 8) average age: 66.1 years; SD 23.6 average years of education: 9; SD 1		control group (n = 8) average age: 63.1 years; SD 21.5 average years of education: 9.1; SD 1		Statistical difference (Mann-Whitney-U-test)
Verbal memory	n = 7	*46*	n = 7	*43*	p = 0.798
Visual memory	n = 5	*39.5*	n = 5	*36.5*	p = 0.917
Stroop colour naming (T-value)	n = 6	*54*	n = 6	*46.5*	p = 0.686
Stroop colour selection (T-value)	n = 6	*46*	n = 6	*51*	p = 0.226
MMSE	n = 8	*27.5*	n = 6	*28*	p = 0.595
Rey-Osterrieth Complex Figure (copy)	n = 6	*31.75*	n = 6	*34.75*	**p = 0.043***
Rey-Osterrieth Complex Figure (delay)	n = 6	*13*	n = 6	*15.75*	p = 0.258
Clock-drawing-test	n = 6	*1*	n = 5	*3*	p = 0.260
Digit span foreward	n = 6	*7.5*	n = 5	*6*	p = 0.165
Digit span backward	n = 6	*6*	n = 5	*7*	p = 0.443
d-2 test-celerity	n = 5	*332*	n = 5	*384*	p = 0.347
d-2 test-mistakes (%)	n = 5	*3.4*	n = 5	*6.52*	p = 0.602

SD standard deviation

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