기 생 충 학 잡 지 제24권 제 2 호
The Korean Journal of Parasitology
Vol. 24, No. 2, 159-170, December, 1986

Serologic follow-up Study in neurocysticercosis patients by ELISA after praziquantel treatment*

Seung-Yull Cho, Suk-Il Kim and Shin-Yong Kang

Department of Parasitology, College of Medicine, Chung-Ang University, Seoul 151 Korea

INTRODUCTION

The efficacy of praziquantel in human neurocysticercosis has been evaluated on the bases of sequential changes in findings of brain computed tomography (CT) (Rim *et al.*, 1980; Brink *et al.*, 1980; Rim *et al.*, 1982; Botero and Castano, 1982; Spina-Franca *et al.*, 1982). Brain CT has been very useful not only in diagnosis but for evaluating the progress of the parenchymal lesions in neurocysticercosis (Sotelo *et al.*, 1984). The effectiveness of praziquantel for cysticercosis is now unquestionable (Groll, 1982).

Although praziquantel is effective for cysticercosis, the therapeutic effects in chronic patients were reported to be extremely variable (Rim *et al.*, 1982). Excellent results were observed mostly in patients of early infection, especially within a year. Therefore, in this usually chronic and clinically protean neurocysticercosis, the long-term benefits from praziquantel administration cannot always be guaranteed in every patient. In addition, even the proper evaluation of the effectiveness of the treatment has been sometimes difficult. Since clinical symptoms were frequently masked by antiepileptics/steroid treatment or ventriculo-peritoneal shunt operation, the progress of the lesion itself can not be properly evaluated based on symptomatology. Follow-up brain CT also may not evaluate the progress of hidden lesions.

* This study was supported in part by a research grant from the Korea Science and Engineering Foundation

In this context, it appeared that serologic follow-up might provide additional information concerning the result of the treated lesions. As Flisser and Larralde (1986) mentioned, the advent of the sensitive and specific immunoserology in neurocysticercosis makes it possible to monitor serologically the post-treatment progress. By using cystic fluid (CF) of *Taenia solium* metacestodes as antigen in enzyme-linked immunosorbent assay(ELISA), highly reproducible measurement of the specific antibody levels is now possible in both serum and cerebrospinal fluid(CSF) (Cho *et al.*, 1986; Larralde *et al.*, 1986). The measurement of antibody levels to parenchymal antigens such as scolex antigen (SC) or bladder wall antigen (BW) of *T. solium* metacestodes are also possible by ELISA (Choi *et al.*, 1986).

In this communication, we report results of the serologic follow-up by ELISA in neurocysticercosis patients who received the praziquantel treatment, trying to elucidate the significance of serological monitoring after praziquantel treatment.

SUBJECTS

From January 1984 to June 1986, a total of 69 cases of confirmed neurocysticercosis was referred to us for follow-up tests. All of them were the registered patients of teaching hospitals in Seoul and provinces, and were examined by brain CT and cysticercus-specific IgG antibody levels in serum and CSF by ELISA using CF as antigen. Out of them 63 cases were positive for IgG antibody in both or either pre-treatment

samples while the remaining 6 cases were negative for the antibody in both samples.

All patients received praziquantel treatment, and symptomatic management or life-saving procedures were performed depending on the symptoms they manifested. Dexamethasone was given in 28 of 69 patients during praziquantel treatment, and in 4 cases during the episodes of acute encephalitic attack. Dexamethasone was administered in doses of 5-15mg/day from a day before to the last day of praziquantel treatment.

The dose schedule of praziquantel differed by institution, but was one of the followings: (1) 3×25mg/kg for 4 days, (2) 3×25mg/kg for 7 days and (3) 3×25mg/kg for 14 days (Rim *et al.*, 1982). In this study all the above doses were regarded simply as praziquantel treatment because comparative evaluation of different doses was not an objective of this study.

Because follow-up was determined by clinical necessity, the intervals and numbers of follow-up examinations were highly irregular and variable by patient. Long-term follow-up of regular interval was almost impossible. Most of long-term follow-up was done because of reattack of symptoms. Since the lumbar puncture was sometimes not allowed due to intracranial hypertension or poor cooperation of patient, the number of follow-up cases made with CSF was smaller than that with serum samples.

The patients included in this study were categorized into 5 groups as shown in Table 1. The factors considered in the grouping patients were: (1) IgG antibody levels before praziquantel treatment, (2) duration between praziquantel treatment and the last sampling (3) number of sampling and (4) concomitant dexamethasone administration during praziquantel treatment.

METHOD

Three antigens of *T. solium* metacestodes, namely CF, SC and BW, were used in this study. Antigens were prepared as described by Choi *et al.* (1986), and diluted in 2.5 μg/ml of protein concentration in carbonate buffer (pH9.6), and 200 μl of them were applied for the coating wells of polystyrene plate overnight at 4°C.

All the sera and CSF were stored at −40°C after collection and simultaneously tested to minimize technical error between tests. Sera were tested to all of 3 antigens while CSF were tested to CF and SC.

After washing the wells, 200 μl of either sera, diluted by 1 : 100 in phosphate buffered saline (PBS)/Tween 20 (pH 7.2), or undiluted CSF were reacted for 2 hours at 36°C. After washing, 200 μl of the conjugate (peroxidase conjugated anti-human IgG, heavy and light-chain specific, goat IgG, Cappel), diluted in PBS/Tween 20 by 1:5,000 was incubated at 36°C for 2 hours. Then after the final washing, 200 μl of substrate, made of 99ml of distilled water, 10 μl of 30% H_2O_2 and 1ml of 1% *o*-phenylene diamine, was reacted for 30 minutes at 25°C. The reaction

Table 1. Grouping the cases of follow-up study

Group	No. of cases	Result of ELISA before treatment	Duration of follow-up	Total No. of F/U* with		Steroid therapy**
				serum	CSF	
I	6	Negative in both samples	4 weeks	6	6	not done
IIa	12	Positive in both or either samples	4 weeks	14	12	not done
IIb	11	*Ibid*	4 weeks	12	9	done
III	16	*Ibid*	1-3 months	33	28	done/not done
IV	9	*Ibid*	4-16 months	9	6	done/not done
V	15	*Ibid*	6-22 months	62	53	done/not done
Total	69			136	114	

* F/U : Follow-up

** Steroid therapy during praziquantel administration

Table 2. Mean and standard deviation (SD) of absorbance in ELISA measuring IgG antibody to 3 antigens in serum and CSF of 6 patients in Group I

Test sample	Antigen used*	Before treatment		After treatment	
		No. positive	mean±SD of absorbance	No. positive	mean±SD of absorbance
Serum	CF	0	0.09±0.05	0	0.08±0.05
	BW#	0	0.06±0.03	0	0.05±0.02
	SC#	0	0.07±0.05	0	0.06±0.03
CSF	CF	0	0.08±0.07	1**	0.09±0.12
	SC#	1#	0.08±0.12	1	0.09±0.12

* CF: Cystic fluid antigen of *T. solium* metacestodes, BW: Bladder wall antigen, SC: Scolex antigen
** Positively converted # Not routinely examined before this study

was stopped by adding 20 μl of 8N H_2SO_4. The absorbance was read at 492nm using Gilford spectrophotometer. To standardize the absorbance, all the read value were corrected by dividing them with an absorbance of a reference serum which gave absorbance around 1.0 in every run.

The cut-off value of positive range was absorbance 0.18 or higher as determined by Cho *et al.* (1986). This differential value was applied to absorbance of serum and CSF obtained before treatment as well as follow-up samples.

RESULTS

1. Changes of antibody levels within 4 weeks after praziquantel treatment

(1) Cases who were antibody-negative before the treatment

Six patients in Group I were negative for the specific IgG antibody in both serum and CSF when measured by ELISA using CF as antigen. Later ELISA using SC revealed an antibody positive case in CSF (Table 2).

The mean absorbance of IgG antibody to CF, BW and SC were not changed following the treatment in both serum and CSF (Table 2). But antibody level in a case became positive in CSF when CF was used as antigen (Fig. 1).

(2) Cases who were antibody-positive before the treatment

(a) Cases treated with praziquantel only

A total of 12 cases was included in Group IIa. In serum the mean absorbance to CF was

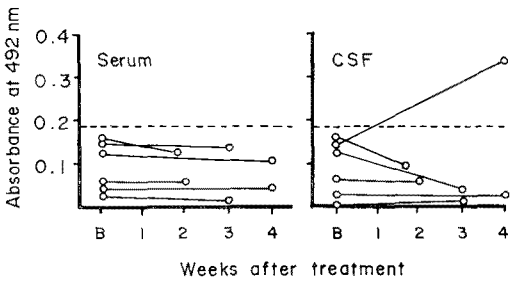

Fig. 1. Changing patterns of specific IgG antibody levels to CF in sera and CSF as shown by individual patient in Group I. Transverse dotted line at absorbance 0.18 is differential criterion. B: Before treatment.

elevated to 142% of the pre-treatment mean while the mean to BW was increased to 137% and that to SC to 129%. In CSF, the mean absorbance to CF was increased to 114% of the pre-treatment mean, while that to SC to 118% (Table 3).

As shown in Fig. 2, the patterns of increases of IgG antibody to CF in serum and CSF differed apparently case by case. Among them, there observed a case in which antibody conversion to positive occurred after the treatment.

(b) Cases concomitantly treated with both praziquantel and dexamethasone

A total of 11 cases (Group IIb) was treated with praziquantel together with dexamethasone to minimize adverse reactions. The mean absorbance of IgG antibody in serum decreased when compared with the mean of pre-treatment absorbance; the post-treatment mean to CF was 92% of pre-treatment mean, 90% to BW and 93% to

Table 3. Absorbance in ELISA measuring IgG antibody to 3 antigens in serum and CSF of patients in Group IIa and IIb before and within 4 weeks after praziquatel treatment

Group/ Test sample	No. of cases	No. of followed cases	Antigen used	Mean±SD of absorbance	
				before treatment	after treatment
IIa (without concomitant dexamethasone)					
Serum	12	12	C F	0.52±0.23	0.74±0.17
			B W	0.27±0.09	0.37±0.11
			S C	0.28±0.11	0.36±0.11
CSF	12	10	C F	0.91±0.26	1.04±0.12
			S C	0.56±0.19	0.66±0.20
IIb (with dexamethasone)					
Serum	11	11	C F	0.64±0.31	0.59±0.30
			B W	0.26±0.12	0.23±0.11
			S C	0.30±0.12	0.28±0.14
CSF	11	10	C F	0.81±0.40	0.81±0.41
			S C	0.51±0.29	0.53±0.30

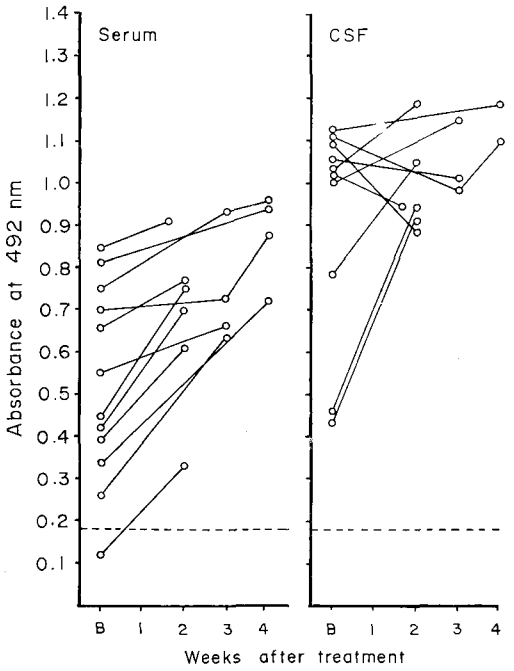

Fig. 2. Changing patterns of specific IgG antibody levels to CF antgen as shown by individual patient in Group IIa who were treated without concomitant dexamethasone.

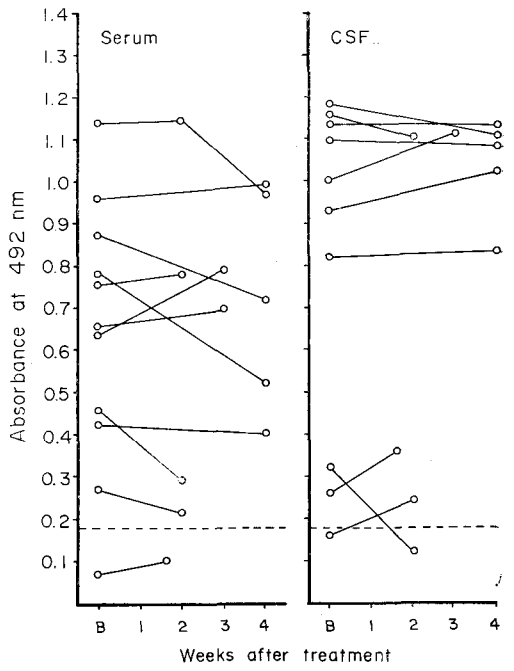

Fig. 3. Changing patterns of specific IgG antibody levels to CF antigen as shown by individual patient in Group IIb who were treated with dexamethasone during praziquantel treatment.

SC. In CSF, the mean either did not change (to CF) or slightly increased (104% to SC).

Of them, positive conversion of antibdy level to CF occurred in a case (Fig. 3).

2. Changes of antibody levels during 1-3 months following the praziquantel treatment

In Group III, the period of follow-up varied case by case ranging from 1 to 3 months (Mean

Table 4. Absorbance in ELISA measuring IgG antibody to 3 antigens in serum and CSF of 16 patients in Group Ⅲ before and 1～3 months after praziquantel treatment (last follow-up)

Test sample	No. of followed cases	Antigen used	Mean±SD of absorbance	
			before treatment	after treatment
Serum	16	C F	0.49±0.27	0.68±0.33
		B W	0.21±0.08	0.33±0.22
		S C	0.24±0.12	0.37±0.24
CSF	13	C F	0.76±0.23	0.81±0.20
		S C	0.43±0.21	0.46±0.23

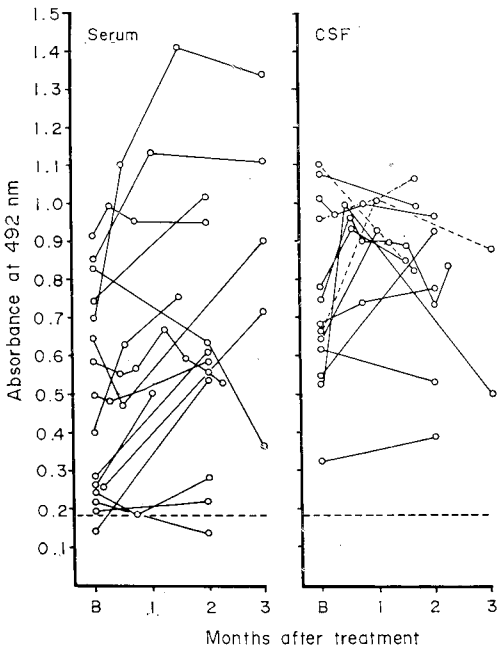

Fig. 4. Changing patterns of specific IgG antibody levels to CF antigen as shown by individual patient in Group III.

and standard deviation, 2.1±0.5 months). The effect of dexamethasone on antibody levels was considered to be waning in this period. Therefere, the results in 16 followed-up cases were presented together in Table 4 and Fig. 4, disregarding whether steroid was used or not.

In serum, the mean absorbance to CF was elevated to 139% of pre-treatment mean, while it was 157% to BW and it 154% to SC. In CSF, the mean absorbance to CF was increased to 107% of pre-treatment mean and was to 107% to SC, respectively.

During this period of follow-up, the changing patterns of IgG antibody levels to CF were highly variable by individual patient (Fig. 4). In serum, increases in the levels of antibody were apparent in 10 cases, decreases, in 2 cases while the levels in the remaining 4 cases showed minimal differences (changes less than 10%). In CSF the antibody levels to CF were increased in 7 cases, decreased in 3 cases and no difference was recognized in 3 out of 13 patients.

3. Changes of antibody levels later than 4 months after the praziquantel treatment

In Group IV, 9 patients were included. They

Table 5. Absorbance in ELISA measuring IgG antibody to 3 antigens in serum and CSF of 9 patients in Group Ⅳ before and 4～16 months after praziquantel treatment

Test sample	No. of followed cases	Antigen used	Mean±SD of absorbance	
			before treatment	after treatment
Serum	9	C F	0.50±0.27	0.60±0.29
		B W	0.24±0.12	0.35±0.17
		S C	0.25±0.14	0.37±0.20
CSF	6	C F	0.71±0.35	0.67±0.36
		S C	0.49±0.31	0.41±0.32

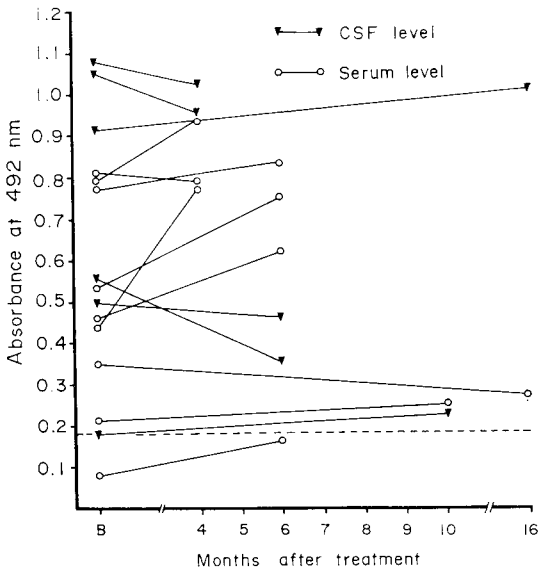

Fig. 5. Changing patterns of specific IgG antibody levels to CF antigen as shown by individual patient in Group IV.

Table 6. Case summaries of patients in Group V

Case No.	Sex and age (year)	Main symptoms	Onset of symptoms	Subcutaneous nodules	Brain CT findings	Dexamethasone*	Follow-up duration (months)	Follow-up No.	Remarks
1	M 38	Headache, seizures	6 years	(+)**	MLD*** with calcifications	+	6	3	
2	F 19	Seizures	1 year	—	MLD	—	7	3	
3	M 51	Memory loss, dysphasia	15 years	(+)	Multiple calcifications	+	7	3	Surgical treatment done
4	M 38	Headache	6 months	—	4th ventricular dilatation	—	7	4	Clinically cured
5	M 59	Dysphasia, weakness of lower limbs	3 months	—	Multiple nodular densities with a cystic mass	—	6	2	Surgical treatment done
6	F 54	Headache, psychotic behavior	6 months	—	Cystic mass with calcifications	+	10	4	Associated with racemose cysticercosis
7	M 35	Seizures	1 month	(+)	MLD	+	13	5	
8	F 49	Seizures, weakness of lower limbs	3 years	—	MLD with nodules	+	14	5	AEA# on 11th months after praziquantel treatment
9	M 15	Seizures, weakness of lower limbs	1 year	—	a low density and an enhanced nodule	+	6	3	Cured clinically and on brain CT
10	M 32	Seizures	5 years	—	Nodular and calcific spots	+	8	2	Cured on brain CT
11	M 47	Seizures	12 years	(+)	Calcified lesions	—	18	2	
12	F 37	Headache, seizures, amenorrhea	2 years	++	MLD with a cystic lesion	+	17	7	Associated with a racemose cysticercus, AEA
13	M 44	Headache, seizures	5 years	++	MLD with calcifications	+	22	7	AEA
14	F 39	Personality change, memory loss, seizures, headache	13 years	++	MLD with a cystic lesion	+	22	6	AEA
15	M 55	Headache, seizures	5 years	—	MLD	—	20	4	

* Dexamethasone administration during praziquantel treatment

** (+) means the presence of subcutaneous nodules in the past, but spontaneously disappeared without praziquantel treatment

*** MLD: Multiple low densities in brain CT

\# AEA: Acute encephalitic attack

were followed up once during 4~16 months after the treatment because of reattack of symptoms. As shown in Table 5 and Fig. 5, their mean absorbance in serum was increased to 120%, 145% and 148% to CF, BW and SC when compared with pre-treatment means. But the levels in CSF were decreased to 94% and 86% of pre-treatment mean to CF and SC respectively.

4. Changes of antibody levels in patients with long-term follow-up

In Table 6, the case summaries were presented who were followed-up for 2 or more times during longer than 6 months after the treatment. IgG antibody levels to CF, SC and BW in serum and CSF were presented in Fig. 6-1 and

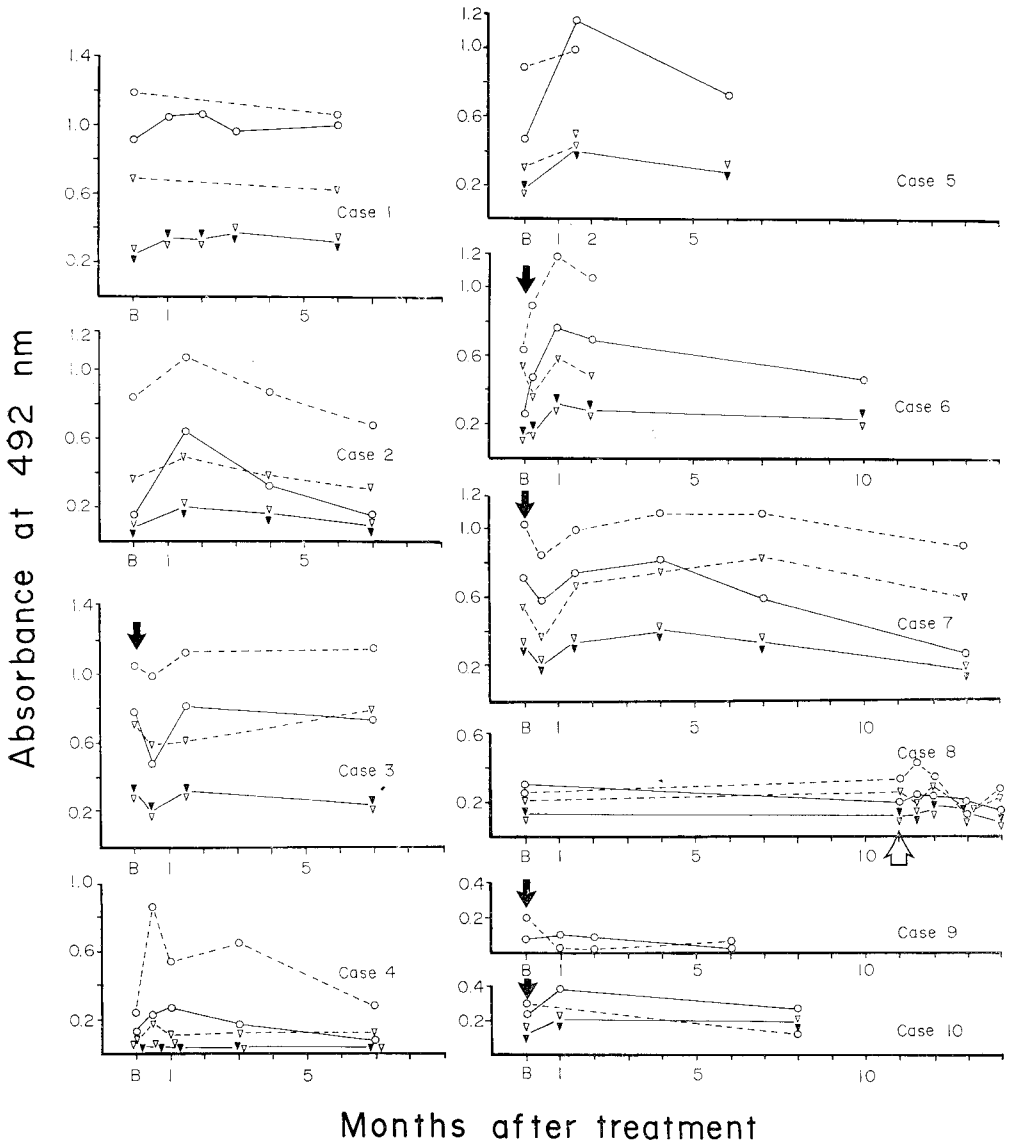

Fig. 6-1. Changing patterns of specific IgG antibody levels to CF(○), BW(▾) and SC(▽) antigens in serum (—) and CSF(···) before and after the treatment as shown by individual patient in Group V (Cases 1-10). ↓ : Concomitant dexamethasone treatment, ⇑ : Acute encephalitic attack. —4YB in Case 11 means the antibody level in a serum secured 4 years before.

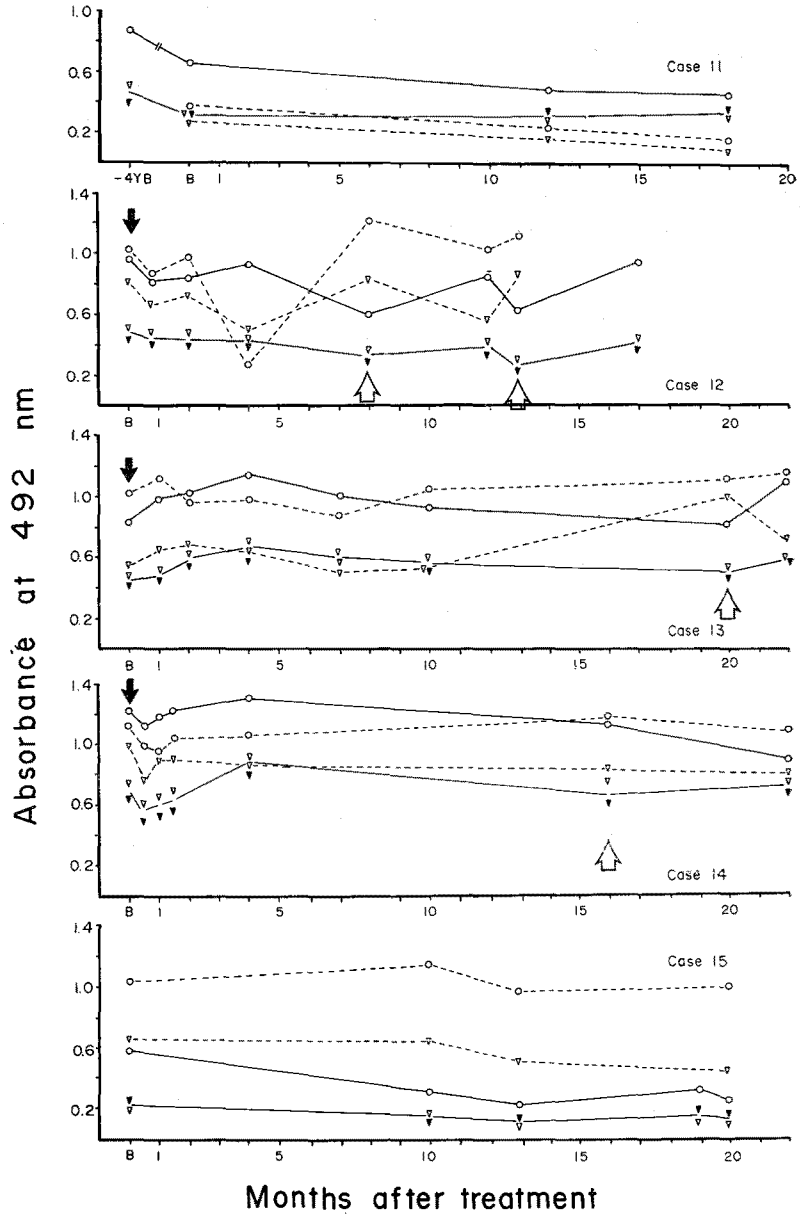

Fig. 6-2. Changing patterns of specific IgG antibody levels to CF(○), BW(▼) and SC(▽) antigens in serum (—) and CSF (···) before and after the treatment as shown by individual patient in Group V (Cases 11-15). ↓ : Concomitant dexamethasone treatment, ⇑ : Acute encephalitic attack.

Fig. 6-2 by individual patient.

During 3 months after the treatment, antibody levels changed as described in the above sections of this paper. The effect of concomitant administration of dexamethasone on the antibody levels were repeatedly found in these patients.

Among them, Case 9 was remarkable because its IgG antibody levels declined below the negative range within a month. Cases 2 and 4, who manifested their first symptoms within a year, showed evident declining tendencies of antibody level after a post-treatment spiking of

antibodies for 3-4 months period. However, these 2 cases could not be followed-up any further. Unlike the above 2 cases, Case 7 who was treated with praziquantel within a month after the first seizure, showed delayed decline of antibody levels especially in CSF. In Cases 5 and 6, who were also treated within a year after their first development of symptom, also showed delayed declining of the antibody levels. In these cases the course of infection appeared to be longer than their symptomatic period as evidenced in multiple calcifications in brain CT.

In patients with long history of cysticercosis (Cases 1, 3, 8, 12-15), the antibody levels in serum and CSF did not show any significant change even after the praziquantel treatment. Cases 10 and 11 who also had long history, however, showed a declining antibody levels in CSF.

There were 4 patients (Cases 8, 12, 13 and 14) who exhibited acute encephalitic attacks long after the praziquantel treatment. During the attacks, antibody levels to SC were elevated in CSF.

DISCUSSION

This study showed that in most of neurocysticercosis patients, the specific IgG antibody levels in both serum and CSF were elevated temporarily after praziquantel treatment when measured by ELISA. The levels reached their peak during 1-4 months after the treatment, then began to return to pre-treatment levels thereafter. The occurrence of fluctuation of antibody levels after chemotherapy were also known in other tissue helminthiases. For example, in schistosomiasis the level of antibody rose in 6 weeks after curative therapy with hycanthone when measured by ELISA (Salih *et al.*, 1978). In paragonimiasis, serum IgG antibody levels measured by ELISA were elevated in 1-2 months after chemotherapy with praziquantel, then decreased below pre-treatment levels (Knobloch *et al.*, 1984). However, when measured by complement fixation test (Yokogawa *et al.*, 1962) or by immunoelectrophoresis (Rim *et al.*, 1981) such a temporary elevation of antibody levels had not been recognized.

The antibody level in neurocysticercosis was found to be depressed in cases who were treated with simultaneous administration of dexamethasone with praziquantel. But in no case the levels dropped below the negative range of absorbance. The mode of action of steroid is known to be not related directly with depression of B-lymphocytes, but at the dose of 5-15 mg/day of dexamethasone the concomitant effect of immune depression was likely to be elicited. Exactly after the tapering stop of steroid administration, the antibody levels rebounded over the pre-treatment levels as shown in this study (Figs. 4, 6-1, 6-2).

The elevation of antibody levels after praziquantel treatment may be used as a complementary tool in serologic diagnosis of neurocysticercosis. It is well known that about 5-10% of the patients were negative for IgG antibody levels even when examined by sensitive ELISA (Mohammad *et al.*, 1984; Cho *et al.*, 1986; Larralde *et al.*, 1986). Our study also revealed that at least 6 out of 69 patients of confirmed neurocysticercosis were antibody negative. In one of these 6 cases, the level in CSF was elevated to positive range after praziquantel treatment. In some cases whose antibody levels in either serum or CSF were positive, the level in previously negative sample of antibody became positive after the treatment. The shifts of antibody level to positive range were found in cases with old, calcified brain lesions. But the provocation of antibody production may not be impossible in hitherto silent, newly established infections. Our results indicates that one month appeared to be sufficient interval to observe the elevated level of antibody in the provocation test.

The rate of change in IgG antibody levels (as mean absorbance) was smaller in CSF than in serum after the treatment. Even by dexamethasone administration, the antibody level changed less in CSF than in serum. Further-

more, the antibody levels in CSF returned to the pre-treatment level earlier than those in serum. These results suggested that the metacestodes in central nervous system (CNS) were affected less by praziquantel than those in extracranial location due to lower concentration of drugs in CSF; and the immune responses to the infecting parasites may be weaker in CNS even if the metacestodes in CNS could be damaged equally as in extracranial location.

After the praziquantel treatment, antibody levels to parenchymal antigens (BW and SC) were expected to be elevated, maybe higher than that to CF, because of increased exposure of the damaged tissue of parasite to immune recognition. The antibody levels to BW and SC were actually increased but rarely above the level to CF. The rate of increase of antibody levels to BW and SC was higher than that to CF, but the absolute differences between pre- and post-treatment antibody levels were greater in antibody to CF. Particularly in patients who showed the tendency of negative conversion in long-term follow-up (Cases 2 and 4 in Group V), the antibody to CF was elevated markedly during 1-4 months after the treatment. This initial up-spiking of antibody level to CF may be interpreted as a result of massive release of cystic fluid from damaged metacestodes. Contrarily, antibody levels to BW and SC were elevated temporarily in CSF as seen in cases with acute encephalitic attacks of chronic neurocysticercosis (Cases 8, 12, and 13 in Group V). Even in those cases of acute edematous complication of chronic brain lesions, the absolute level of antibody was not higher than that to CF.

Antibody levels were not always elevated in every follow-up case. Some exceptional patients showed steady decrease of their antibody levels in serum and CSF and in one example, to level below the positive criterion within a month (Case 9 in Group V). Similar observation was made by Robles and Chavarria (1980) in which antibody level declined steadily to negative after chemotherapy.

Persistence of high antibody level after chemotherapy would not necessarily mean that the lesions around the worm were not affected at all by the treatment. The diagnosis by ELISA is such sensitive that cure evidenced by serologic evaluation can hardly be expected unless all the pathologic lesions were resolved or calcified completely.

Serologic follow-up in this study indicates that it takes a considerable time for negative conversion in chronic neurocysticercosis. Some cases in this study (Cases 2 and 4 in Group V) could have been stated as cured serologically but they were not followed-up sufficiently long.

Our data suggest that it seems desirable to perform serologic follow-up of neurocysticercosis patients every year after the treatment. By such interval it may be possible to differentiate the cured from the chronically ill patients with slowly calcifying lesions.

SUMMARY

A total of 69 patients of confirmed neurocysticercosis was followed serologically by ELISA up to 22 months after praziquantel treatment. The intervals and numbers of follow-up were variable by patient. Serially collected samples of serum and CSF were examined simultaneously for their specific IgG antibody levels by ELISA, using cystic fluid, saline extracts of bladder wall and scolex as antigen.

Within 4 months after praziquantel treatment, the antibody levels were elevated temporarily in both serum and CSF in most patients. In some cases antibody levels exhibited steady declining tendency after the treatment. Concomitant administration of dexamethasone appeared to suppress the elevation of antibody levels. The rate of mean absorbance of antibody changed more in serum than in CSF. The rate of elevation was greater in antibodies to parenchymal antigens than that to cystic fluid, but absolute difference of antibody levels was greater in antibody to cystic fluid. Previously negative samples for IgG antibody may become positive

after the praziquantel treatment, which could be used as a complementary tool (provocation test) in serodiagnosis. One month was considered to be sufficient interval for the follow-up test for that purpose.

In the follow-up of up to 22 months, only few cases of chronic neurocysticercosis showed declining tendency of IgG antibody levels below negative range. During acute encephalitic attacks in chronic patients, IgG antibody to parenchymal antigen were elevated in CSF temporarily.

These results indicated that serologic follow-up of every year was recommendable to differentiate the cured patients from chronic patients with slowly calcifying lesions.

ACKNOWLEGEMENT

The authors of the present paper express their thanks to neurologists and neurosurgeons who referred their patients for serologic follow-up. They are grateful to Professor Y.T. Yang, Department of Microbiology, Chung-Ang University, Professor J.G. Chi, Department of Pathology, and Assoc. Professor C.Y. Cha, Department of Microbiology of Seoul National University for their review of the manuscript. Miss H.S. Kang, Department of Parasitology, Chung-Ang University retested the samples by ELISA.

REFERENCES

Botero, D. and Castano, S. (1982) Treatment of cysticercosis with praziquantel in Colombia. *Am. J. Trop. Med. Hyg.*, **31**(4):810-821.

Brink, G., Schenone, H., Diaz, V., Parra, M. and Corrales, M. (1980) Neurocysticercosis: Treatment with praziquantel; a preliminary study. *Bol. chileno Parasit.*, **35**:66-71.

Cho, S.Y., Kim, S.I., Kang, S.Y., Choi, D.Y., Suk, J.S., Choi, K.S., Ha, Y.S., Chung, C.S. and Myung, H. (1986) Evaluation of enzyme-linked immunosorbent assay in serological diagnosis of human neurocysticercosis using paired samples of serum and cerebrospinal fluid. *Korean J. Parasit.*, **24**: 25-41.

Choi, B.K., Kim, S.I., Kang, S.Y. and Cho, S.Y. (1986) Evaluation of antigens from different parts of *Cysticercus cellulosae* in serological diagnosis of human cysticercosis. *Chung-Ang J. Med.*, **11**(2): 135-146.

Flisser, A. and Larralde, C. (1986) Cysticercosis. In: Walls, K.W. and Schantz, P.M. (Eds.) *Immunodiagnosis of parasitic diseases Vol. 1, Helminthic diseases*, 109-161, Academic Press, Orlando.

Groll, E.W. (1982) Chemotherapy of human cysticercosis with praziquantel. In: Flisser, A. *et al.* (Eds.) *Cysticercosis: Present state of knowledge and perspectives*, 207-218, Academic Press, New York.

Knobloch, J., Pan, G., Feldmeier, H., Wegner, D. and Voelker, J. (1984) Serum antibody levels in human paragonimiasis before and after therapy with praziquantel. *Trans. Roy. Soc. Trop. Med. Hyg.*, **78**:835-836.

Larralde, C., Laclette, J.P., Owen, C.S., Madrazo, I., Sandeval, M., Bojalil, R., Sciutto, E., Contreras, L., Arzate, J., Diaz, M.L., Govezensky, T., Montoya, R.M. and Goodsaid, F. (1986) Reliable serology of *Taenia solium* cysticercosis with antigens from cyst vesicular fluid: ELISA and hemagglutination tests. *Am. J. Trop. Med. Hyg.*, **35**(5):965-973.

Mohammad, I.N., Heiner, D.C., Miller, B.L., Goldberg, M.A. and Kagan, I.G. (1984) Enzyme-linked immunosorbent assay for the diagnosis of cerebral cysticercosis. *J. Clin. Microbiol.*, **20**:775-779.

Rim, H.J., Won, C.R. and Chu, C.W. (1980) Studies on the cysticercosis and its therapeutic trial with praziquantel (Embay 8440). *Korea Univ. Med. J.*, **17**(3):459-476.

Rim, H.J., Chang, Y.S., Lee, J.S., Joo, K.H., Suh, W.H. and Tsuji, M. (1981) Clinical evaluation of praziquantel (Embay 8440; Biltricide) in the treatment of *Paragonimus westermani*. *Korean J. Parasit.*, **19**(1):27-37.

Rim, H.J., Lee, J.S., Joo, K.H., Kim, S.J., Won, C.R. and Park, C.Y. (1982) Therapeutic trial of praziquantel (Embay 8440; Biltricide) on the dermal and cerebral human cysticercosis. *Korean J. Parasit.*, **20**(2):169-190.

Robles, C. and Chavarria, M. (1980) Un caso de cisticercosis cerebral curado medicamente. *Gac. Med. Mex.*, **116**:65(cited by Groll, 1982).

Salih, S.Y., Bartlett, A. and Voller, A. (1978) Detection of antibodies by enzyme immunoassay in human *Schistosoma mansoni* infections: A clinical and chemotherapeutic study. *Tropenmed. Parasitol.*,

29:409-412.

Sotelo, J., Escobedo, F., Rodriguez-Carbajal, J., Torres, B. and Rubio-Dannadieu, F. (1984) Therapy of parenchymal brain cysticercosis with praziquantel. *New England J. Med.*, **310**:1001-1007.

Spina-Franca, A., Nobrega, J.P.S., Livramento, J.A. and Machado, L.R. (1982) Administration of praziquantel in neurocysticercosis. *Tropenmed. Parasitol.*, **33**:1-4.

Yokogawa, M., Tsuji, M. and Okura, T. (1962) Studies on the complement fixation test for paragonimiasis as the method of criterion of cure. *Jpn. J. Parasit.*, **11**(2):117-122.

=국문요약=

프라지퀀텔 치료후 효소면역측정법에 의한 뇌 유구낭미충증 환자의 혈청학적 추적검사

중앙대학교 의과대학 기생충학교실

조 승 열·김 석 일·강 신 영

1984년 1월부터 1986년 6월까지 30개월간, 확진된 뇌 유구낭미충증 환자 69명에 대하여 혈청학적 추적검사를 실시하였다. 환자는 모두 치료전에 뇌전산화 단층 촬영을 실시하였고 효소면역측정법에 의하여 혈청 및 뇌척수액의 특이 IgG 항체가를 측정하였다. 프라지퀀텔에 의한 약물 치료는 3×25mg/kg의 용량으로 4~14일간 실시하였다. 추적기간 및 회수는 환자마다 달랐으며 최대 추적기간은 22개월이었다. 추적검사용 혈청 및 뇌척수액은 −40°C에 보관한 후 낭액항원, 낭벽항원 및 두절항원에 대한 IgG 항체가를 일시에 측정하였다.

프라지퀀텔 투여후 1~4개월 사이에 환자의 대부분에서 혈청 및 뇌척수내 특이 IgG 항체가는 일시적으로 상승하였다. 치료 직후부터 항체가가 저하하는 환자가 있었으나 소수이었다. 프라지퀀텔 투여시의 부작용을 줄이기 위해 덱사메타손을 투여하면 항체가 상승은 억제되었다. 프라지퀀텔 치료후 혈청내 항체가 평균치의 변동이 뇌척수액내 항체가 평균치의 변동보다 심하였고, 항체가의 변화율은 낭벽항원이나 두절항원에 대한 항체에서 낭액항원에 대한 항체에서 보다 컸으나 항체가 변동폭은 낭액항원에 대한 항체가 더 컸다. 대상 환자 69명중 혈청학적으로 음성이었던 6명중 1명은 치료후 뇌척수액내 낭액항원에 대한 항체가가 양성범위로 전환하였다. 프라지퀀텔 투여후 항체가의 상승은 뇌 유구낭미충증의 혈청학적 진단에서 보조적으로 이용할 수 있다고 생각하였으며 추적기간으로는 투여후 1개월이 적합하다고 생각하였다. 치료후 6개월내지 22개월까지 추적검사한 환자 15명중 혈청과 뇌척수액에서 모두 음성으로 전환한 예는 1례뿐이었고 혈청이나 뇌척수액 어느 하나에서라도 음성으로 전환한 예도 3례에 불과하였다. 만성 경과를 취한 심한 뇌 유구낭미충증 환자에서의 혈청학적 음성전환은 관찰 기간중 없었다. 추적 검사중 급성 뇌염증상이 나타난 만성환자에서는 일시적으로 두절항원에 대한 항체가가 상승하고 있었다.

이상의 결과에서 뇌 유구낭미충증 환자를 프라지퀀텔로 치료한 다음 면역효소측정법으로 혈청학적 추적검사를 실시할 경우 투약후 매 1년에 한번씩 실시하면 완치된 환자를 감별할 수 있을 것으로 생각하였다.