THE TREATMENT OF NEUROCYSTICERCOSIS WITH PRAZIQUANTEL

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Abstract. Twenty-five patients with cerebral cysticercosis admitted to the Bangkok Hospital for Tropical Diseases from March 1987 to November 1989 were studied. The patients had a mean age of 41 ± 5 years with a mean body weight of 57 ± 4 kgs. Male to female ratio was 1.5:1. Eight patients (32%) gave a history of having taeniasis with a mean duration of 3.6 years before having symptoms of cerebral cysticercosis. Six patients (24%) also had subcutaneous cysticercosis with a duration of 20 ± 8 months. The important clinical symptoms were headache, focal seizure, epilepsy and dementia. Fourteen patients (56%) had headache, 12 patients (48%) had focal seizure and four patients (16%) had a mild degree of dementia. Baseline study included routine blood examination, biochemical tests, cerebrospinal fluid for routine examinations and immunological study. Biopsy of subcutaneous cysts, plain films of soft tissue and computerized tomography of brain. Praziquantel was given orally at a dosage of 45 mg/kg/day in 3 divided doses at 4-5 hour interval for 15 days. Patients who were taking anti-epileptic drugs before were permitted to continue their medications. The evaluation of results of treatment was done a year post treatment, ten patients (40%) were asymptomatic, 12 patients (48%) had much clinical improvement, their epileptic attack was controlled by 1-2 tablets of phenobarbital (1/2 g) at bedtime. Two patients (8%) had mild headache. One patient (4%) was not improved. Those patients with dementia were not improved. During treatment, strong inflammatory reactions occurred as evidenced by increased intracranial pressure, and increased protein and cell counts in cerebrospinal fluid in six patients (24%). Follow-up CT brain after a year found that the total number of active cysts had disappeared in 80%; 15% had discrete calcified spots around the previous cysts, and 5% had dense calcification. Our study indicated that praziquantel at a dosage of 45 mg/kg/day is effective in active cerebral cysticercosis.

INTRODUCTION

Cysticercosis is one of the common parasitic infections affecting the central nervous system and it is endemic in many developing countries, (Grisolia and Wiederholt, 1982). In Thailand, a dramatic rise in the number of cases observed after 1983 coincided with the introduction of computed tomographic (CT) scan. (Jitsukon and Towanabut, 1989). Cysticercosis is an infection with *Cysticercus cellulosae,* the larval stage of *Taenia solium,* encysted in the subcutaneous tissue, in the striated muscle, smooth muscle, internal organs. The most important clinicopathological affects were those located in the brain. The disorder produces a complex neurologic picture with various degree of severity depending on the number of cysts, site, tissue involved, and reaction of normal tissue to the organism. Involvement of the subcutaneous tissue is generally asymptomatic; however, those patients with extensive subcutaneous and muscle involvement may have generalized swelling or even pseudomuscular hypertrophy. (Xu *et al,* 1985). The presence of subcutaneous cysts and clinical symptoms of neurological disturbances aid in the diagnosis of neurocysticercosis. The usual symptoms are headache, vomiting, seizures, convulsion, and mental deterioration (Shanley and Jardan, 1980; McCormick *et al,* 1982; Sotelo *et al,* 1984; Vanijanonta and Bunnag, 1985). The definite diagnosis is by surgical biopsy of the tissue involved. Cerebral cysticercosis is often diagnosed from the patient's history, clinical features, the presence of pleocytosis with eosinophils in the cerebrospinal fluid and computerized tomographic brain scan. Clinical trials with praziquantel have shown its efficacy in human cysticercosis (Rim *et al,* 1980; Botero and Castano, 1982;

Sotello *et al,* 1984; Xu *et al,* 1985; Jitsukon and Towanabut, 1989).

Cases of cerebral cysticercosis admitted to the Bangkok Hospital for Tropical Diseases were treated with praziquantel and the results of the follow up studies are reported herein.

MATERIALS AND METHODS

Twenty-five patients with cerebral cysticercosis admitted to the Bangkok Hospital for Tropical Diseases from March 1987 to November 1989 were studied. These included 19 cases with cerebral cysticercosis and six with cerebral and subcutaneous cysticercosis. Ages ranged from 20 to 63 years; the mean age was 41 ± 5 years. The mean body weight was 57 ± 4 kgs. Male to female ratio was 1.5:1. The diagnosis of cysticercosis was based on history, clinical manifestations, soft tissue radiography, computerized axial tomography of the brain, enzyme-linked immunosorbent assay (ELISA), and passive hemagglutination antibody test (PHA) of the cerebrospinal fluid. Six patients with subcutaneous cysticercosis were confirmed by biopsy of subcutaneous cysts.

Laboratory studies included routine blood examination, biochemical tests, stool examination for *Taenia* proglottids and eggs, urinalysis, and cerebrospinal fluid examination. Follow-up laboratory tests were done at weekly intervals during treatment and hospitalization, and at monthly intervals for the first three months after treatment, and then repeated at six months and a year.

Total body radiography of the soft tissue were taken prior to treatment, and at two weeks and twelve months post-treatment.

CT scan of the brain was performed both with and without contrast medium. The CT scan was done on every patient prior to treatment and a year after treatment for evaluation of treatment.

Biopsy of subcutaneous cysts was performed prior to treatment for confirmation of the diagnosis and at the end of praziquantel treatment to study the pathological changes and effects of the drug on cysticerci inside the cysts.

Praziquantel was given orally at a dosage of 45 mg/kg/day in three divided doses at 4-5 hours intervals for 15 days. Patients who were taking anti-epileptic drugs were permitted to continue their medication as necessary.

RESULTS

The clinical features of the patients included epilepsy (80%), headache (56%), focal seizure (48%), and mild degree of dementia (16%).

Clinical response was seen in one month after treatment and a final evaluation was made at a year after treatment. Ten patients (40%) was asymptomatic, 12 patients (48%) had much clinical improvement, two patients (8%) had mild headache, one patient (4%) was not improved.

During treatment six patients (24%) had increased intracranial pressure, protein and cell counts in the cererospinal fluid.

Hematological study showed a normal leukocyte count with a slightly increased total mean eosinophil count (503 ± 78 / mm^3). There were abnormal total eosinophil counts during and post-treatment (Fig 1). There were biochemical or urine abnormalities; 21 patients (84%) had negative stool examination, three patients (21%) had hookworm ova and one patient (4%) had *Opisthorchis viverini* ova.

Cerebrospinal fluid showed a pre-treatment

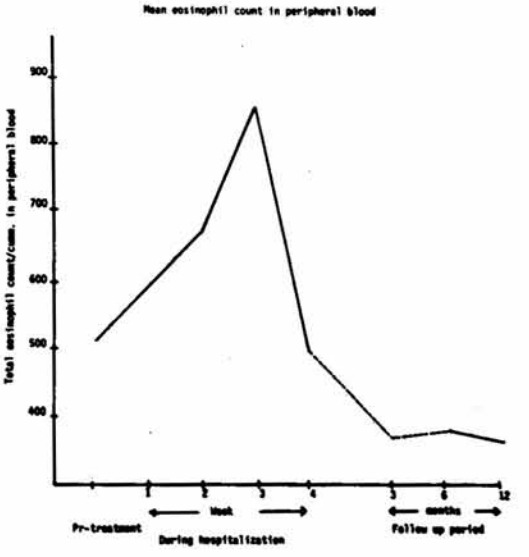

Fig 1—Show increased total eosinophil count in peripheral blood.

mean pressure of 206 ± 0.9 mm H_2O (115-420 mm H_2O); a day after treatment it was 169 ± 19 mm H_2O (132-270 mm H_2O), and a year after treatment was 176 ± 19 mm H_2O (130-290 mm H_2O). There was eosinophilic pleocytosis of the cerebrospinal fluid. It was found that the pretreatment eosinophil count was 3 ± 1 cells/ mm^3 (0-5 cells/mm^3), 10 ± 2 cells/ mm^3 (1-18 cells/mm^3) at a day after treatment and negative finding at a year after treatment. No protein, sugar, or chloride changes were detected

The pre-treatment histopathological findings consisted of characteristic fibrous capsules with live *T. solium* in fresh specimens. Most of the post-treatment biopsy specimens showed chronic inflammatory cell and plasma cell infiltration of degenerated larval structures. There were varying degrees of destruction of the cuticle and internal structures of the larvae.

Most of the partially calcified subcutaneous tissue cysts showed distorted appearances and a decrease in size when compared to the pre-treatment radiographs. Those with completely calcified lesions remained unchanged.

The pre-treatment CT scan findings showed active parenchymal cysts of 0.3-1.2 cm in diameter with no other intracranial abnormalities. There were 260 active cysts, mean 10 ± 2. At one year post-treatment, 80% of the cysts had dissolved, 15% had discrete calcified spots around the previous cysts, and 5% had dense calcification.

Six patients (24%) had increased intracranial pressure presented by severe headache, nausea and vomiting. The rest of the patients had mild and transient side effects, headache, nausea, myalgia, abdominal pain. No death occurred in this study.

Two patients (8%) had asymptomatic sinus bradycardia at D7, D15, detected by electrocardiogram. Passive hemagglutination test and enzyme-linked immunosorbent assay (Larralde *et al,* 1986) gave a positive result of 28% and 80% respectively. Post-treatment findings showed no changes.

DISCUSSION

The present study showed that praziquantel at doses of 45 mg per kilogram body weight daily for 15 days is effective for the treatmcnt of newly formed parenchymal cerebral cysticercosis. The patients with partially calcified subcutaneous cysts also responded to treatment, as shown by distorted cysts in post-treatment soft tissue radiographs.

Administration of praziquantel in healthy volunteers did not produce adverse reactions in the central nervous system (Leopold *et al,* 1978). Pharmacological studies had also shown that praziquantel at doses of 50mg per kilogram is safe. Therefore, the secondary reactions during treatment with praziquantel in patients with cerebral cysticercosis may be due to the death of parasites in the host. In our study, six patients (24%) showed strong reactions during treatment and shortly after treatment, and we thought this was due to secondary reactions. Two out of six of the patients with secondary inflammatory reactions were treated with 5 mg dexamethasone intravenously, followed by 0.5 mg dexamethasone tablets thrice daily for three days; the patients responded very well to the treatment. Other patients were treated by analgesics, phenytoin and phenobarbital. The role of steroids in the treatment or prevention of complications arising from the death of parasites is controversial. From our experience, the decision to administer steroids with praziquantel must be made on an individual basis in relation to the patients's response to praziquantel during treatment.

The clinical response correlated with CT scans. We found that patients with completely dissolved cysts had better clinical responses when compared to those with residual calcified spots in the brain.

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REFERENCES

Botero D, Castans S. Treatment of cysticercosis with praziquantel in Colombia. *Am J Trop Med Hyg* 1982; 31 : 811-21.

Grisolia JS, Wiederholt WC. CNS cysticercosis. *Arch Neurol* 1982; 39 : 540-4.

Jitsukon N, Towanabut S. Neurocysticercosis at Prasat Neurological Hospital. *Bull Dept Med Serv* 1989; 14 : 289.

Larralde C, Laclelte J, Owen CS, *et al.* Reliable serology of *Taenia solium* cysticercosis with antigens from cyst vesicular fluid : ELISA and hemagglutination test. *Am J Trop Med Hyg* 1986; 35 : 965-73.

Leopold GW, Ungethum W, Groll E, *et al.* Clinical pharmacology in normal volunteers of praziquantel. A new drug against schistosomes and cestodes : an example of a complex study covering both tolerance and pharmacokinetics. *Eur J Pharmacol* 1978; 14 : 281.

McCormic GF, Zee C-S, Heiden J. Cysticercosis cerebri : review of 127 cases. *Arch Neurol* 1982; 39 : 534-9.

Rim HJ, Won CHR, Chu JW. Studies on human cysticercosis and its therapeutical trial with praziquantel (Embay 8440). *Korea Univ Med J* 1980; 17 : 459.

Shanley JD, Jordan MC. Clinical aspects of CNS cysticercosis. *Arch Intern Med* 1980; 140 : 1309-13.

Sotelo J, Eseobedo F, Rodriquez-Carbajal J. Therapy of parenchymal brain cysticercosis with praziquantel. *N Engl J Med* 1984; 310 : 1001-7.

Vanijanonta S, Bunnag D. Treatment of cysticercosis with praziquantel at the Bangkok Hospital for Tropical Diseases. *Southeast Asian J Trop Med Public Health* 1985; 16 : 435-40.

Xu ZB, Chen WK, Zhong HL, Feng ML, Cao WJ. Praziquantel in treatment of cysticercosis cellulosae. Report of 200 cases. *Chin Med J* 1985; 98 : 489-94.