TREATMENT OF TUBERCULOUS MENINGITIS WITH 6-MONTH COURSE OF CHEMOTHERAPY

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Abstract. The results of a 6-month course of chemotherapy for treatment of 29 patients with tuberculous meningitis were analyzed. There were 7 patients in stage 1, 12 patients in stage 2 and 10 patients in stage 3. The result was recovery of 20 patients, death of 4 patients, while 4 patients were lost to the study and 1 patient dropped out from serious side effects. Three patients had residual neurological deficits.

INTRODUCTION

Tuberculous meningitis is a common infectious disease of the central nervous system in developing countries. The unsatisfactory results of treatment depend on the delay in diagnosis, severity of disease, management of the complications and on the nature of the chemotherapy. Over the last few years treatment of this disease with antituberculous drugs has advanced (Phuapradit and Vejjajiva, 1987; Visudhiphan and Chiemchanya, 1989; Alarcon *et al,* 1990). However, optimal duration of treatment has not been agreed upon.

The purpose of this report is to review the results of short-course chemotherapy in adult patients with tuberculous meningitis.

MATERIALS AND METHODS

From January 1988 to June 1990, 29 patients with a diagnosis of tuberculous meningitis were admitted to the Department of Medicine, Srinagarind Hospital, Khon Kaen, Thailand. All cases were diagnosed according to the characteristic clinical features and typical cerebrospinal fluid findings (lymphocytic meningitis with low glucose level and elevation of protein content).

The severity of the disease was classified according to the system of Gordon and Parsons (1972). In stage 1 the patients were conscious and rational with meningism but no focal neurological signs or signs of hydrocephalus. In stage 2 the patients were confused or had focal neurological signs such as squint, hemiparesis or signs of hydrocephalus. In stage 3 the patients's mental state could not be assessed because of stupor or delirium, complete hemiplegia or paraplegia.

Each patient was treated with oral isoniazid 300 mg, rifampicin 600 mg (450 mg for those who weighed less than 45 kg), pyrazinamide 1500 mg and intramuscular streptomycin 750 mg per day as single dose for the first two months, followed by isoniazid and rifampicin in the same dose for four months. In patients who could not take streptomycin, ethambutol 800 mg was used as a replacement. During treatment serum transminase level and bilirubin levels were measured in patients who developed symptoms and signs of hepatitis or jaundice.

Prednisolone 45-60 mg per day was given in some patients with mental change, high CSF protein content and spinal arachnoiditis. The dose was gradually tapered off over 2-4 weeks.

Patients with a high CSF pressure (more than 200 mm H_2O) were relieved by repeated lumbar puncture, while ventriculo-peritoneal shunt was indicated in a case who had a persistent high CSF pressure after 3 to 4 weeks of daily lumbar puncture. In the case of patients who had severe mental change with hydrocephalus, ventriculostomy was done immediately.

RESULTS

Of the 29 patients, 7 were admitted in the first stage, 12 in stage 2 and 10 in stage 3. Age incidence ranged from 16-61 years with a mean of 35 years. The main presenting symptoms were subacute

headache (86%) and fever (89%). The neurological complications are summarized in Table 1. Abnormal chest x-ray was observed in 10 patients. Three cases had other foci of tuberculosis (peritonitis, osteomyelitis and laryngitis). Mean CSF cell count was 315 cells/mm^3 and protein content was 493 mg%. Cultures of CSF for *Mycobacterium tuberculosis* were positive in 6 patients. Twenty-six patients were received streptomycin in the first two months of treatment and prednisolone was administered in 9 patients. Ventriculo-peritoneal shunt was inserted in 8 patients.

The results of treatment are summarized in Table 2. Twenty patients had complete treatment. Immediate CSF studies were done after complete treatment in 15 patients. Nine cases were within normal limits. Of the 6 remaining cases, 5 had mild elevation of protein content (55-137 mg%, mean 93.6 mg%) and 1 had mild pleocytosis (8 cells/mm^3). Only one case had severe hepatitis due to isoniazid and treatment was continued with rifampicin and ethambutol for 18 months with full recovery. Of 4 dead cases, 3 died from underlying disease and hospital-acquired infection. In the remaining case, symptoms of meningitis were improved but the patient died from an infected shunt.

Table 1

Neurological complications in the 29 patients.

Complication	No. affected
Increased intracranial pressure	22/29
Communicating hydrocephalus	7/18*
Cranial nerve palsy	3/29
Impaired vision	1/29
Spinal arachnoiditis	3/29
Tuberculoma	4/18*
Hemiplegia	1/29

* CT scans were not done in 11 patients.

Follow-up

The 20 patients were observed for 4 to 33 months (mean 16.3 months) after completion of treatment. No evidence of recurrence of meningitis was observed. Three patients had residual neurological deficits, consisting of visual impairment, spastic hemiplegia with mental impairment and mild lateral rectus muscle palsy. Interestingly, 4 cases who were lost to the study (received antituberculous drugs for about 2, 2, 3 and 4 months respectively), had good recovery, with a mean duration of 16.5 months after treatment, as indicated by letters.

DISCUSSION

The result of treatment of patients with tuberculous meningitis depends on many factors, including the severity of the disease, early diagnosis and treatment, the effectiveness of antituberculous drugs, the management of neurological complications and appropriate supportive treatment. Active management of patients with increased intracranial pressure and hydrocephalus is of great importance (Newman *et al,* 1980; Bullock and Van Dellan, 1982; Peacock and Denny, 1984). Repeated lumbar punctures are useful to relieve the raised intracranial pressure.

Antituberculous medication is one of the most important factors contributing to successful treatment. However the optimal regimen and duration of chemotherapy in tuberculous meningitis has not been agreed upon. Phuapradit and Vejjajiva (1987) reported good results from a nine-month course of an antituberculous regimen consisting of isoniazid, rifampicin, streptomycin and pyrazinamide daily during the first two months, fol-

Table 2

Results of treatment.

Stage	No. of patients	No. of patients lost to study	No. of patients with recovery	No. of patients who died	No. of patients with drug intolerance
1	7	2	5	-	-
2	12	1	9	1	1
3	10	1	6	3	-

lowed by isoniazid and rifampicin daily for seven months. Recently Alarcon *et al* (1990) demonstrated that a 6-month therapeutic regimen, consisting of isoniazid, rifampicin and pyrazinamide for the first two months, followed by isoniazid and rifampicin, was also effective. The side effects from these regimens were minimal.

The present study also demonstrated that a 6-month regimen of antituberculous drugs was effective, with good results and minimal toxic effects. It is suggested that this short-term regimen is a good therapeutic option for treatment of tuberculous meningitis because of its efficacy, few side effects and good compliance.

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