

TUBERCULOUS MENINGITIS IN CHILDREN—CLINICAL PROFILE, MORTALITY AND MORBIDITY OF BACTERIOLOGICALLY CONFIRMED CASES

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ABSTRACT

One hundred and seven cases of tuberculous meningitis were registered as a part of a case—control study during the period 1990-1992. The CSF of nil cases was positive for, culture and/or smear for acid fast bacilli. Children were examined at the time of admission and at the time of discharge and they were contacted at the end of 1 year. Clinical picture, mortality and morbidity were analyzed. Mortality of children during the first month of illness was 22%. Some of the cases presented as acute neurological illness. We also came across CSF picture with minimal cytological and biochemical changes but with positive culture results.

Key words: *Tuberculous meningitis, Clinical profile, Cerebrospinal fluid, Mortality, Morbidity.*

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Received for publication: June 19, 1994;

Accepted: November 21, 1994

Tuberculosis in children is a major health problem especially in developing countries. Among the various forms of tuberculous infection, tuberculous meningitis (TBM) is the most dangerous one resulting in a high degree of mortality and morbidity, despite availability of effective chemotherapy. TBM occurs in 7-12% of tuberculous patients in developing countries(1). Neurological sequelae occur in 20-25% of patients with TBM(2). Poor outcome is directly associated with delay in diagnosis. Hence, early diagnosis is of vital importance in the management of this condition. Therefore, 107 cases of bacteriologically proved TBM were analyzed to find out the signs and symptoms. It was also attempted to find out the association between clinical picture and outcome of the disease. Cerebrospinal fluid (CSF) profile in these cases were analyzed to find out whether this could be used as a prognostic factor.

Subjects and Methods

A case-control study to assess the efficacy of BCG vaccine in protecting children from tuberculous meningitis was carried out at the Institute of Child Health and Hospital for Children, Egmore, Madras. In this study, from August 1990 to August 1992, 406 clinically suspected cases of TBM were registered. Out of this, in 107 cases, the CSF became bacteriologically positive for AFB. Information regarding the clinical picture, mortality and morbidity of these 107 patients were gathered prospectively and analyzed separately to get an insight into the prognostic factors. These results are being presented here.

AH children below the age of 12

years admitted to the hospital with symptoms suggestive of TBM were considered for selection. The following inclusion and exclusion criteria were applied:

Inclusion Criteria

Two or more of the following features, with or without fever, should be present to suggest a clinical diagnosis of TBM—altered sensorium varying from drowsiness to coma, headache, vomiting, history of convulsions (focal or generalized), meningeal signs, bulging fontanel, papilledema, cranial nerve palsy and motor weakness of the limbs.

Exclusion Criteria

Old cases of TBM treated outside the hospital before referral, children suffering from chronic illness or malignancy and children on immunosuppressive drugs were not included in the study.

After registration, detailed history was elicited. Vaccination history and history of contact with a known patient suffering from pulmonary tuberculosis in the house or in the neighborhood was elicited.

A complete clinical examination was carried out and findings regarding neurological status were recorded. The nutritional status was assessed and classified according to the classification recommended by the Nutrition Subcommittee of the Indian Academy of Pediatrics(3).

For all registered cases, a lumbar puncture (LP) was carried out within 24 hours after admission. The CSF was examined for cells within 10 minutes after LP. Neubauer chamber was used to

count the cells after staining the CSF with methylene blue. The cells were counted in all the nine large squares. The number of cells in any one large square was added to this number to get the total value(4).

The CSF was sent for biochemical estimation of protein levels. A sample of CSF was sent for isolation of acid-fast bacilli (AFB) by smear and culture. To identify AFB in smear, fluorescent microscopy method using auramine phenol, (the standard procedure followed at the Tuberculosis Research Centre, Madras), was used. For AFB culture, the following 4 media were used: Lowenstein-Jensen Medium, Lowenstein—Jensen Medium with 0.5% sodium pyruvate, 7H11 Middlebrook Medium and Kirschner's Medium.

One loopful of CSF was inoculated into the above three solid media and 0.2 ml was added to the Kirschner's medium, using a sterile pipette. The bacteriological examinations were carried out at the Tuberculosis Research Centre Madras(5).

Chest radiograph and mantoux skin test were carried out for all patients. The parents of the children were also screened for pulmonary tuberculosis by examination of sputum and chest radiograph.

No alterations were made in the treatment given to the child while at hospital. The standard regimen followed at our hospital for treatment of TBM is streptomycin (20 mg/kg), isoniazid (10 mg/kg), rifampicin (10 mg/kg) and pyrizinamide (30 mg/kg) for 2 months followed by isoniazid and rifampicin for the next 10 months. Ste-

roids are given for the first 4-6 weeks. All these patients were reviewed at the time of discharge and advised to continue anti-tuberculous treatment at the TB clinic in our hospital.

The mortality and morbidity of all cases, were assessed at the end of one month irrespective of bacteriological confirmation of CSF, because, generally the CSF culture results were available only after 6-8 weeks. Subsequently culture positive cases were grouped and the mortality and morbidity rates were estimated. Attempts were made to contact the survivors at the end of one year to reassess their neurological status.

Results

Among 107 cases of TBM, 32 (30%) were less than 2 years of age and 42 (40%) were between 2 and 5 years of age. The rest, 33 (30%) were above 5 years of age. The youngest, child we came across was 6 months old. Of these children, 63 (59%) were males and 44 (41%) were females. The mothers of 70% of the children were illiterate. A large proportion of parents of the children (73%) belonged to the lower-socioeconomic strata of the society. Further, 70% were malnourished out of which 10% were severely malnourished.

History of contact with a family member suffering from pulmonary tuberculosis was present in 35 (33%) cases while 6 (6%) gave history of contact with a neighbor suffering from pulmonary tuberculosis.

The average duration of symptoms prior to admission for these cases was 23 days. Twenty three (21%) children

had symptoms lasting for 5 days or less, 32 (30%) for 5-10 days and 52 (49%) for more than 10 days. Only one patient had symptoms lasting for 120 days.

Twenty four patients died in hospital. The hospital stay for these patients ranged from 2-40 days with a mean (\pm SD) of 11 (\pm 9) days. Eighty three children (80%) were discharged from hospital. For these patients, stay in hospital ranged from 3-120 days with a mean (\pm SD) of 21 (\pm 26) days.

The presenting signs and symptoms of the study population are shown in *Table I*. Cranial nerve palsy alone was seen in 17 (16%), motor deficit alone in 22 (21%) and combination of the two in 16 (15%) cases. At the time of admission 22 (20%) were in Stage I defined as conscious children with nonspecific symptoms, with or without meningeal symptoms but with no neurological deficit. Sixty three (60%) subjects were in Stage II defined as mentally confused child with or without neurological deficit. Twenty two (20%) cases were in Stage III defined as deeply comatose child with neurological deficit (*Table IF*). Clinical staging was based on state of consciousness and the presence of focal neurological signs as described by Gordon and Parson(6).

Mantoux skin reaction was positive (>10 mm) in only 14 (13%) patients. BCG scar was present in 35 (33%) cases. Chest X-ray was normal in 69 (65%) of our patients while 18 (17%) had pneumonitis, 5 (5%) had bronchopneumonia and 5 (5%) had miliary TB. Changes like hilar adenitis and thickened pleura were seen in 9 (8%) cases. On screening of parents of the children,

TABLE I—Presenting Signs and Symptoms (n=107)

| Symptoms | No. | % | Signs | No. | % |
|---------------------------------|-----|----|---------------------|-----|----|
| Fever | 102 | 95 | Cranial nerve palsy | | |
| Altered sensorium | 86 | 80 | VII nerve | 24 | 22 |
| Convulsions | 85 | 79 | VI nerve | 5 | 5 |
| Vomiting | 81 | 76 | III nerve | 1 | 1 |
| Meningeal irritation | 60 | 65 | Bulbar palsy | 2 | 2 |
| Headache as a prominent symptom | 36 | 34 | Papilledema | 13 | 12 |
| Headache & vomiting | 5 | 5 | Hemiplegia | 21 | 20 |
| | | | Quadriplegia | 16 | 15 |

The total numbers will not add up to 107 because signs and symptoms were present in various combinations.

TABLE II—Association Between Age and Outcome of the Disease at One Month

| Outcome | Age (years) | | | | | |
|-----------------------|-------------|----|------------|----|-----------|----|
| | <2 (n=32) | | 2-5 (n=42) | | >5 (n=33) | |
| | No. | % | No. | % | No. | % |
| Alive without deficit | 12 | 38 | 14 | 33 | 18 | 55 |
| Alive with deficit | 11 | 34 | 18 | 43 | 10 | 30 |
| Dead | 9 | 28 | 10 | 24 | 5 | 15 |

8 (either mother or father) had evidence of active pulmonary tuberculosis.

CSF Findings

Pleocytosis (more than 5 cells/cu mm) was seen in 93 (85%) cases. It was lymphocytic in 50 (54%) and mixed in the rest. The remaining 14 (15%) did not show any pleocytosis.

Ten (9%) of our cases had normal CSF protein values (<40 mg/dl). Elevated protein levels (>40 mg/dl) were

present in 97 (91%) patients. In 62 (58%) the protein level was more than 100 mg/dl.

In 93 cases, CSF culture alone was positive for AFB. In 8 cases, smear alone was positive for AFB. In 6 cases both culture and smear were positive.

Outcome

At the end of one month, out of the 107 cases, 24 (22%) had died while 83 (78%) survived. Of the survivors, 39

(47%) children had neurological deficit and 44 (53%) survived without deficit.

Among the 39 survivors with deficit, 14 (36%) had motor deficit (either hemiparesis or quadriparesis), 8 (20%) had cranial nerve palsy, 3 (8%) had optic atrophy, 1 (3%) had convulsions and 13 (33%) had more than one of the deficits mentioned above in various combination.

In our study, we found that the younger the child, the greater was the mortality and morbidity (*Table II*). We also observed that the more advanced the stage of the disease, the greater was the mortality and morbidity (*Table III*).

The study results showed that mor-

tality was higher in children with higher CSF protein values (*Table IV*). Clinical staging correlated positively with CSF protein values. Out of 22 children in Stage III, 17 (77%) had CSF protein levels greater than 100 mg/dl whereas in Stage I, out of 22 children only 11 (50%) had such high values (*Table IV*). Hydrocephalus, diagnosed by ultrasound or CT scan was present in 23 out of 25 patients for whom these investigations were done. Among the 23 children with hydrocephalus, 19 had CSF protein values above 100 mg/dl.

At the end of one year, among the 83 survivors we were able to contact 51 children. Out of these 23 had persistent neurological deficit while the remaining children (28) were normal.

TABLE III—Association between Clinical Stage and Outcome of the Disease at One Month

| Outcome | Clinical stage | | | | | |
|-----------------------|----------------|----|--------------|----|---------------|----|
| | I (n=22) | | II (n=63) | | III (n=22) | |
| | No. | % | No. | % | No. | % |
| Alive without deficit | 12 | 55 | 27 | 43 | 5 | 23 |
| Alive with deficit | 8 | 36 | 24 | 38 | 7 | 31 |
| Dead | 2 | 9 | 12 | 19 | 10 | 46 |

TABLE IV—Association between CSF Protein Levels and Outcome

| Clinical stage | CSF protein <100 mg/dl (n=45) | | | | CSF protein >100 mg/dl (n=62) | | | |
|----------------|----------------------------------|----|--------|----|----------------------------------|----|--------|----|
| | Survivors | | Deaths | | Survivors | | Deaths | |
| | No. | % | No. | % | No. | % | No. | % |
| I (n=22) | 11 | 24 | 0 | 0 | 9 | 15 | 2 | 3 |
| II (n=63) | 24 | 53 | 5 | 11 | 27 | 14 | 7 | 11 |
| III (n=22) | 4 | 9 | 1 | 2 | 8 | 13 | 9 | 15 |

Acknowledgements

We acknowledge the International Clinical Epidemiology Network (INCLEN) for providing the pharmaco-epidemiology seed grant to carry out this project.

We thank the Tuberculosis Research Centre, Madras for their valuable help in carrying out bacteriological investigations on CSF samples.

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