

TUBERCULOUS ENCEPHALOPATHY IN SABAH CHILDREN

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SUMMARY

A series of 18 cases of tuberculous encephalopathy (TBE) in children studied between June 1983 and October 1984 at Queen Elizabeth Hospital, Kota Kinabalu is presented. The data suggest that: the incidence is not as rare as previously thought; the occurrence of TBE is related to the absence of BCG vaccination; the presentation is often late; laboratory data, although helpful is not often confirmatory; early treatment is the key to better outcome; the clinical picture should outweigh laboratory diagnosis in the initial assessment and management.

INTRODUCTION

Tuberculosis, like other infectious diseases, is still a major problem in Sabah although the Ministry of Health had established a control programme since 1960.¹ This health problem is further compounded by the large continuous movement of displaced persons and illegal immigrants from the Southern Philippines, poor communication within the state, a high prevalence of community (*kampung*) births, a high default rate amongst TB patients and an inefficient

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contact tracing system. It is often said that the prevalence of TBE reflects the general quality of any TB control programme.² This study is based on the author's personal observations in Queen Elizabeth Hospital, the referral centre for the west coast of Sabah.

MATERIALS AND METHODS

All children, aged between one month – 12 years, admitted with encephalopathy with lymphocytic meningitis between June 1983 and October 1984, were personally assessed by the author or a medical officer specially instructed by the author. Those considered on clinical and initial laboratory data to have TBE were included in the study. Full personal data concerning vaccination status, history and contacts were obtained. A thorough clinical assessment was also performed together with laboratory investigations including detailed microbiology.

Cerebro-spinal fluid (CSF) specimens were taken for cell count, protein, chloride and glucose estimations. Zeil Neilsen, Gram and Indian ink stains were performed on all CSF specimens as well as routine and Lowenstein Jensen cultures. All patients had chest radiographs which were subsequently sent for reporting by a radiologist elsewhere. Routine full blood counts and serum electrolytes were also performed as well as blood glucose estimations at the time of lumbar puncture. Tuberculin testing was performed using the Mantoux technique with 1 TU.

The patients were commenced on anti-tuberculous treatment with a combination of three or four drugs (isoniazid rifampicin, pyrazinamide and/or streptomycin) as soon as the clinical diagnosis was made (within one to four days). All were continued for two months and were subsequently put on intermittent regimes for a further nine months in consultation with the TB physician. Attempts were made to contact defaulters including those who discharged their children against medical advice as well as the patient who absconded. If found, they and those who attended follow up were assessed regularly.

RESULTS

Personal Biodata

Six (33%) children fell in the less-than-one year age group, seven (38%) in the one-to-three year age group and five (27%) being older than three years. Filipinos comprised five (27%), Kadazans four (22%), whilst Bisaya three (16%), Dusun and Bajau two (11%) each and the Rungus and Murut one each (5%). There were 13 females (72%) and five males (28%). The majority of children (14 = 77%) had not been vaccinated with BCG; those vaccinated ($n = 4$) had scars of 4 mm or less. Tuberculin tests read between 1 and 18 mm.

Symptoms

Table I shows the main symptoms as obtained in the history from the parent or referring doctor. It also shows the duration of symptoms before presentation. In all (100%) patients, loss of interest, drowsiness as well as fever were common features. Two children (11%) had some history of headache. Convulsions were a presenting feature in 13 (72%) children. Paralysis occurred in three (17%). Vomiting was a complaint in seven (39%). The contact history, obtained by thorough questioning by the paediatric team as well as the TB control staff (when available) yielded a positive history of contact of five (28%). Duration of one or more of the above symptoms varied from three days to one-and-half months.

Laboratory Findings

The total cells in the CSF ranged from 0 – 1400/ml; percentage of mononuclear cells being 0 – 100%; polymorphonuclear neutrophils 0 – 59%. The protein content ranged from 40 – 610mg%; glucose content between 8 – 68mg%. The blood glucose to CSF glucose ratio (when the former was available) ranged from 2.2 – 8.4. CSF chloride ranged from 409 – 1053mg%. Zeil Nielsen stains on CSF did not yield any positive results whereas culture on Lowenstein Jensen media only yielded one positive result. Serum sodium (when available, $n = 14$) varied between 119 – 140 mmol/l on admission. All the above samples were also negative for conventional culture as well as for fungal infection.

Outcome

When the patients were assessed in December 1984, six patients (33%) had died and 12 (67%) had survived. Among the survivors, two had fully recovered with no neurological sequelae; four had mild impairment of higher and / or motor function, six had severe neurological sequelae.

Chest Radiographs

All chest films obtained were reported independently without clinical data. None had evidence of pulmonary TB disease.

DISCUSSION

Since the proper description of tuberculous encephalopathy in the 1800s,³ authors have always encountered two main problems: delay in presentation and delay in diagnosis. The former is due to non-specific signs of presentation. The natural course is also long drawn which gives a false impression of a chronic benign disease. Delay in diagnosis is due to a low index of suspicion, the clinician very often considering a differential diagnosis of viral meningitis and awaiting for natural recovery to take place.

Another reason for delay is the very low incidence of positive CSF smears. It is not

TABLE I
SYMPTOMOLOGY WITH DURATION OF SYMPTOMS, DELAY BEFORE INITIATION OF TREATMENT AND
TUBERCULIN (1 TU) TEST READINGS

Patient	Drowsiness + ——— +++	Fever	Headache	Fits	Paralysis	Vomiting	Loss of interest	Contact History	Duration of symptoms	Duration of symptoms before treatment	Mantoux (mm)
1	+++	+	+	-	-	+	+	+	1½m	1½m	4
2	+++	+	-	-	-	+	+	-	2w	3w	3
3	++	+	-	+	-	-	+	-	1w	2w	X
4	+++	+	-	+	-	-	+	-	5w	1w	7
5	+++	+	-	-	-	-	+	-	1w	10d	0
6	++	+	-	+	+	+	+	-	3w	3w	18
7	++	+	+	-	+	-	+	-	1w	2w	-
8	+++	+	-	+	+	-	+	+	2w	2w	17
9	++	+	-	-	-	-	+	-	1w	1w	3
10	+++	+	-	+	-	-	+	-	1w	10w	5
11	+	+	-	+	-	-	+	-	2w	10d	3
12	++	+	-	+	-	+	+	+	1m	2w	4
13	++	+	-	+	-	-	NA	-	3d	NT*	-
14	++	+	-	+	-	+	+	+	8d	10d	4
15	++	+	-	+	-	-	+	-	1m	1m	-**
16	++	+	-	+	-	-	+	+	10d	14w	5
17	+	+	-	+	-	+	+	-	1w	1w	-
18	++	+	-	+	-	+	+	-	2w	2w	-

* Patient 13 also had optic atrophy and microcephaly at presentation.

 Patient 3 was discharged against medical advice before reading.

** Patient 15 died before reading.

NA-not applicable.

NT-not treated.

uncommon for a laboratory technician in developing countries on call to be responsible for all the subdisciplines of laboratory services. Thus, the limited time taken for screening a suspected TB meningitis CSF may vary from 5 – 10 mins. It is generally accepted that mycobacteria in the CSF is difficult to demonstrate.⁴ Also unless

there is a rupture from a small TB focus into the CSF this is unlikely to be present.⁵

Once TBE is suspected, treatment should be initiated and that bacteriological confirmation is only of academic importance.⁶ However due to the abovementioned reasons, there is never a

100% positive yield in the CSF cultures. In the above study, there was only one case of positive culture and none of positive smears. Two series from Nigeria and Thailand reported a 15 – 20% in culture yield.^{7,8}

The majority of patients belonged to the 0–3-year-age group and all but four had not been vaccinated, strongly suggesting that BCG vaccination protects against TBE. Those vaccinated had very small and non significant scars (6mm being the accepted size for good immunity). BCG does not necessarily protect children from TB especially those under two years of age.⁹ All the children in this series were either Filipinos or indigenous natives of Sabah. The incidence of TB meningitis in the southern Philippines, some islands of which are just next to Sabah, is also high (personal communication, WHO Chronic Diseases Unit, Manila). Female predominance is seen in this series, the reason not being known.

Classical TBE often has a long drawn course of presentation with headache, fever, vomiting and non-specific symptoms.¹⁰ In this series, however the most common symptoms were fever and altered consciousness. Headaches were present in only two children who were aged 10 and 11 years. This contrasts with adults when headache is a common symptom. Convulsions were present in a good proportion of the patients and this is considered a pathologically late sign with arteritis and/or tuberculoma with or without acute hydrocephalus.¹¹ Vomiting was present only in 40%. The actual duration of symptoms is often very vague and in this series it ranged from three days to one-and-a-half months, in agreement with Paul's¹² observations.

TBE is a sequel of a primary focus elsewhere.¹¹ Most common is pulmonary TB. In this series, none of the children showed evidence of pulmonary infection and similarly retrospective investigations of sputum and gastric washing samples taken earlier did not reveal any growth of mycobacteria. This contrasts with other series^{10,12} where 31 – 75% of associated pulmonary disease was noticed. It may be concluded that evidence of associated pulmonary

TB may favour the diagnosis of TBE but its absence does not rule it out.

The CSF cell counts may be typically classical or totally unhelpful. However, the mononuclear cell count is almost always consistently elevated in established disease. Cell counts often vary with the course of the disease with normal count or polymorphonuclear cell predominance and later changing to a mononuclear cell dominated picture.

A low glucose value in the CSF is a sign par excellence of bacterial, fungal or TB meningitis in the presence of an appropriate level of blood glucose. However, the existence of a normal CSF glucose in TBE is possible. When available all the blood glucose to CSF glucose ratios were in excess of 2.0.

A "classical" value range for CSF protein is often quoted for TBE but it must be emphasised that pockets of loculated CSF may contain high protein levels and that spinal block, a possible consequence of TBE, may result in low spinal fluid pressures and high protein levels.¹¹ Thus, the protein value is helpful but not diagnostic.

Included in the differential diagnosis of all these patients were bacterial meningitis and fungal meningitis. The other two conditions were meticulously excluded by staining with Indian ink and gram stain as well as CSF cultures. The high incidence of CSF Zeil-Nielsen negatives (100%) only suggest that improved methodology and repeated collection of CSF is probably the only solution in the local situation. Similarly, efficient transport and more specific culture media, for example, Selective Kirshner, may improve the yield as also with fluorescent microscopy of smears using auromine staining.¹² However, it is interesting that most workers from tropical regions report a very low bacteriological verification rate (15 – 20% in the best of hands),⁴ as compared with higher rates by Western workers (45%).⁸ It must be pointed out that repeated CSF examinations, even after the initiation of chemotherapy, progressively improves the yields.¹³

It was noted in a British series that a high proportion of adult patients on admission had hyponatraemia, due to syndrome of inappropriate anti-diuretic hormone (SIADH).¹⁴ In this series, seven out of 14 patients had hyponatraemia which could be due to SIADH although measurements of serum and urine osmolalities were not available.

Recently Sada *et. al.*,¹⁵ reported a very promising technique in identifying cell wall antigens of myobacteria spp. using an ELISA technique on CSF of patients with TBE. This was shown to be effective in confirming the diagnosis early and other studies to verify this method and that using agglutination with anti-body coated latex particles are under way.

The outcome of TBE in this series is depressing and it demonstrates that prevention is probably the main line of attack. Despite a high index of suspicion and early intervention by our unit, only six patients recovered sufficiently satisfactorily. The main problem of delay in seeking treatment will continue and education of the layman may play a part in earlier presentation.

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