Original Article

Prognostic clinical variables in childhood tuberculous meningitis: An experience from Mumbai, India

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Background: In India, tuberculous meningitis (TBM) is still a major cause of neurological disabilities and death. **Aim:** To identify the clinical variables which predict the outcome in childhood TBM. **Setting:** Tertiary teaching hospital. **Design:** Prospective observational study. **Materials and Methods:** Thirty-six clinical variables were analyzed in 123 consecutive children with TBM admitted between May 2000 and August 2003. The outcome was assessed in terms of survival or death. Survival meant that the patient was discharged from hospital having made a complete recovery, or with disability. **Results:** Twenty-five (20%) children recovered completely, 70 (57%) survived with disability, and 28 (23%) died. Employing univariate analysis nine variables correlated with survival with disability outcome: presence of tonic motor posturing, cranial nerve palsy, focal neurological deficit, hypertonia, moderate to severe hydrocephalus, cerebral infarction on cranial CT, and requiring shunt surgery, and absence of extracranial tuberculosis and no antituberculous-related hepatotoxicity; two variables correlated with fatal outcome: presence of deep coma (Glasgow coma scale score < 6), and absence of extrapyramidal movements. When logistic regression was applied only the presence of hypertonia (P = 0.012, d.f. = 1, OR 0.12, 95% CI 0.02–0.62) correlated with survival with disability outcome, and presence of deep coma (P = 0.030, d.f. = 1, OR 0.35, 95% CI 0.14–0.90) with fatal outcome. **Conclusion:** In children with TBM, the presence of hypertonia at admission is an independent predictor of neurological sequelae in survivors, and deep coma is an independent predictor of mortality.

Key Words: Hydrocephalus, meningeal tuberculosis, multivariate analysis, prognosis, computed tomography

The incidence of tuberculosis (TB) is on the increase worldwide.[1] Between 1 and 2% of children with untreated extracranial TB develop tuberculous meningitis (TBM).[2] Several retrospective [3]–[6] and prospective [7]–[9] studies have been conducted to predict the outcome of TBM in childhood. However, most of the data were in the pre computed tomography (CT) scan era,[3],[4] and also the treatment protocols were not uniform or were inadequate as per current recommendations.[3]–[5] These studies by univariate analysis identified 14 clinical variables significantly associated with a poor outcome: (i) young age,[3],[4],[8],[9] (ii) male sex,[9] (iii) prolonged duration of symptoms,[3] (iv) seizures,[5] (v) advanced stage of the disease,[3],[4],[6]–[9] (vi) coma,[9] (vii) tonic motor posturing,[9] (viii) papilloedema,[9] (ix) cranial nerve palsy,[9] (x) focal neurological deficit,[9] (xi) hydrocephalus,[7] (xii) associated miliary TB,[3] (xiii) absence of extra-cranial TB,[5] and (xiv) requiring shunt surgery.[5] Only three studies in childhood TBM[4],[5],[9] have employed multivariate analysis to identify significant prognostic variables, and only one [9] was conducted prospectively. Multivariate analysis has identified seven '*independent clinical variables*' which adversely affect the outcome, viz. (i) young age,[4],[9] (ii) seizures,[5] (iii) advanced stage of disease,[4],[9] (iv) tonic motor posturing,[9] (v) papilloedema,[9] (vi) focal neurological deficit,[9] and (vii) absence of extracranial TB.[5]

The aim of the present study was to identify the clinical variables, which predict the outcome of TBM in children.

Materials and Methods

Patient enrolment

Children with TBM, aged between 1 month and 12 years admitted to our hospital were enrolled prospectively. The study was conducted over a period of 40 months, from May 2000 to August 2003. The patient sample was by necessity a convenience sample, and all patients who met the study criteria were included in the study. All patients had an informed consent form signed by their parents.

The diagnosis of TBM was based on the clinical case definition [Table 1] devised by Doerr *et al*.[10] All children had comprehensive physical and neurologic examination at the time of admission. Cerebrospinal fluid (CSF) examination and cranial CT scan were done soon after admission in every child. A standardized data entry form was used to document demographic data, clinical symptoms and signs, laboratory findings, Mantoux test result, chest radiograph and ultrasound of the abdomen findings, CSF, and cranial CT scan find-

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ings of each patient at presentation. Each patient was screened for human immunodeficiency virus (HIV) infection using the enzyme-linked immunosorbent assay (ELISA) test. Pre and post-test counseling for HIV infection was offered to the parents. The ELISA kits met the minimum standards (sensitivity > 99%, specificity > 95%) as recommended by the World Health Organization (WHO).[11] The diagnosis of HIV infection was confirmed as per the WHO strategy II: when two ELISA tests based on different antigen preparations and/or different principles were positive.[12] Family members were screened for tuberculous infection.

Nutritional status of the child was assessed by the Wellcome classification.[13] The severity of the disease at admission was classified as per the Medical Research Council (MRC) guidelines:[14] Stage I (early) = conscious, nonspecific symptoms, and no neurological signs; Stage II (intermediate) = signs of meningeal irritation with slight or no clouding of sensorium, with or without minor neurological deficit (cranial nerve palsy or limb paresis); Stage III (advanced) = severe clouding of sensorium, convulsions, focal neurological deficit, and/or involuntary movements. The child's level of consciousness was assessed by Glasgow coma scale (GCS).[15] The degree and significance of hydrocephalus on the cranial CT scan was calculated by ventricular size index (VSI), a ratio of bifrontal diameter over the frontal horn diameter.[16] A VSI of 30–38% indicates mild hydrocephalus, 39–45% moderate hydrocephalus, and >45% severe hydrocephalus.[16]

Management of cases

All children received standard antituberculous therapy (ATT) as recommended by the Indian Academy of Pediatrics:[17] isoniazid (5 mg/kg/day), rifampicin (10 mg/kg/day), pyrazinamide (25 mg/kg/day), and ethambutol (20 mg/kg/day); other supportive measures (steroids, anticonvulsants, and mannitol) within 24–48 h of admission. Pyrazinamide and ethambutol were discontinued after 2 months, and isoniazid and rifampicin continued for another 4 months. Corticosteroids were administered during the first month, intravenous dexamethasone (0.6–1.2 mg/kg/day in three divided doses) for the first 7 days, followed by oral prednisolone (2 mg/kg/day in three divided doses) and then gradually tapered over a week. Children with mild to moderate hydrocephalus received acetazolamide (20 mg/kg/day orally in three divided doses).

All the children who had neurological deterioration during the course of the hospital stay had repeated cranial CT. Children with moderate to severe hydrocephalus and neurologic deterioration received ventriculoperitoneal (VP) shunt.[18] When the CSF protein was more than 1 g/l, the child received initial external ventricular drainage using a chamber and later it was converted to VP shunt with the decrease in CSF protein. Liver function tests were done initially at a weekly interval to monitor ATT-related hepatotoxicity.

Table 1: Clinical case definition of tuberculous meningitis devised by Doerr *et al*.[10]

Abnormal neurological signs and/or symptoms, and 2 or more of the following
1. Discovery of adult source patient with contagious tuberculosis who had significant contact with child
2. Presence of Mantoux (5 Tuberculin units) skin test reaction ≥ 10 mm of induration, or ≥ 5 mm of induration if child had close contact with infected adult
3. Cerebrospinal fluid abnormalities without evidence of other infectious cause
4. Abnormalities on cranial computed tomography consistent with central nervous system tuberculosis

Outcome assessment

Survival or *death* was the outcome measure. Survival was further categorized into: (i) discharge with '*complete recovery*' (no neurologic deficit), (ii) discharge with *'disability' (neurologic deficit).*

Data analysis

The data were analyzed using the Statistical Package for Social Sciences, Version 11 for Windows (SPSS, Chicago, IL, USA). A univariate analysis was initially performed by the chi-square test to assess the relationship between the 36 variables and the three outcomes, viz. complete recovery, survival with disability, and death. Applying logistic regression to significant variables obtained in the univariate analysis, multivariate analysis was performed. Wherever appropriate the odds ratio (OR) was calculated and 95% confidence intervals (CI) were estimated around the OR. Statistical significance was considered as P value < 0.05. The power of analysis for the present study was 80%.

Results

One hundred and twenty-three children were studied [Table 2]. The mean age was 3.1 years (range 3 months–12 years; ±SD 2.7 years). Almost one-third of the children were malnourished: 34 had marasmus, 3 had kwashiorkor, and 1 had marasmic–kwashiorkor. Three-fourth of the children had extracranial TB: with pulmonary involvement in 87 (71%), lymphadenopathy in 35 (28%), and abdominal involvement in 34 (28%). Forty-one (33%) children had cranial nerve palsy: 34 had facial palsy, 20 had abducens palsy, and four had oculomotor palsy. At admission, 5 (4%) children had Stage I disease, 12 (10%) had Stage II disease, and 106 (86%) had Stage III disease.

Cerebrospinal fluid examination was abnormal in all the children. Cellular response was lymphocytic predominance in 98 (80%) children. The means (range) of CSF cell count, protein, and glucose were 254 (8–8200) cells/mm^3, 1.6 (0.2–8.4) g/l, and 0.43 (0.1–1.5) g/l, respectively. Admission cranial CT scan was abnormal in 121 (98%) children and the hydrocephalus was the common abnormal finding in 103 (84%) children, mild in 46 (37%), moderate in 45 (37%), and severe in 12 (10%). Sixty-nine (56%) children required shunt surgery. In three (2%) children, ATT-induced hepatitis necessitated modified drug regimens.

Of the 123 children studied, 25 (20%) made complete recovery (2 with Stage I disease, 4 with Stage II disease, and 19 with Stage III disease), 70 (57%) survived with disability (3 with Stage I, 5 with Stage II, and 62 with Stage III), and 28 (23%) died (none with Stage I, 3 in Stage II, and 25 with Stage III). The mean length of stay for children who survived to discharge was 19.8 (5–90, ±11.7) days; for those who died was 20.8 (3–45, ±17.6) days.

On univariate analysis, nine variables were found to be the

predictors of good outcome, 'complete recovery:' the *presence* of extracranial TB ($P = 0.010$, d.f. = 1) and ATT-induced hepatotoxicity ($P = 0.043$, d.f. = 1); the *absence* of tonic posturing ($P = 0.004$, d.f. = 1), cranial nerve palsy ($P = 0.039$, d.f. = 1), focal neurological deficit ($P < 0.001$, d.f. = 1), hypertonia ($P = 0.006$, d.f. = 1), moderate–severe hydrocephalus ($P = 0.004$, d.f. = 2), cerebral infarction ($P = 0.002$, d.f. = 1), and shunt surgery being required ($P = 0.023$, d.f. = 1). Nine variables were found to be associated with 'survival with disability' outcome [Table 2]: the *presence* of tonic posturing ($P = 0.004$, d.f. = 1), cranial nerve palsy ($P = 0.016$, d.f. = 1), focal neurological deficit ($P < 0.001$, d.f. = 1), hypertonia ($P = 0.003$, d.f. = 1), moderate–severe hydrocephalus ($P = 0.005$, d.f. = 2), cerebral infarction ($P = 0.001$, d.f. = 1), and shunt surgery being required ($P = 0.014$, d.f. = 1); absence of extracranial TB ($P = 0.020$, d.f. = 1) and ATT-induced hepatotoxicity ($P = 0.017$, d.f. = 1). Of the 19 (15%) children without extracranial TB who survived, 18 survived with disability and only one patient made a complete recovery. Of the 93 (76%) who survived without developing ATT-induced hepatotoxicity, 70 survived with disability and only 23 made a complete recovery [Table 2]. When multivariate analysis was done using logistic regression analysis [Table 3], no variable proved to be independently associated with good outcome 'complete recovery' and only the presence of hypertonia at presentation ($P = 0.012$, d.f. = 1, OR 0.12, 95% CI 0.02–0.62) was found to be independently associated with the outcome, 'survival with disability.'

Univariate analysis identified two variables to be associated with a fatal outcome: presence of deep coma ($P = 0.018$, d.f. = 1), and absence of extrapyramidal movements ($P = 0.031$, d.f. = 1) at presentation. Of the 109 (89%) children who did not have extrapyramidal movements at presentation, 28 died and 81 survived, of which, 23 made a complete recovery and 58 survived with disability [Table 2]. On multivariate analysis [Table 3], only the presence of deep coma ($P = 0.030$, d.f.

Table 2: Univariate analysis of clinical variables for prediction of outcomes

Variables	Number of patients (*n* = 123)	Complete recovery (*n* = 25)			Survival with disability (*n* = 70)			Death (*n* = 28)		
	n (%)	*n*	OR	95% CI	*n*	OR	95% CI	*n*	OR	95% CI
Demographic variables										
Age <3 years	72 (58.5)	14	0.88	0.36–2.13	45	0.71	0.28–1.79	13	1.89	0.81–4.43
Male sex	65 (52.8)	15	1.44	0.59–3.52	33	1.68	0.67–4.25	17	0.66	0.28–1.56
Symptoms										
Illness >2 weeks	55 (44.7)	14	1.77	0.73–4.29	30	1.70	0.68–4.26	11	1.33	0.57–3.15
Fever	109 (88.6)	21	0.60	0.17–2.09	62	0.68	0.19–2.48	26	0.53	0.11–2.53
Personality changes	74 (60.2)	12	0.54	0.22–1.30	48	0.42	0.17–1.08	14	1.71	0.73–4.01
Weakness	89 (72.4)	17	0.77	0.30–1.99	53	0.68	0.25–1.86	19	1.33	0.53–3.31
Seizures	78 (63.4)	16	1.03	0.41–2.58	42	1.19	0.46–3.05	20	0.63	0.25–1.57
Contact with adult TB	48 (39.0)	9	0.85	0.34–2.12	24	1.08	0.42–2.80	15	0.46	0.20–1.08
Measles in last 6 months	13 (10.6)	1	0.30	0.04–2.41	9	0.28	0.03–2.35	3	0.98	0.25–3.84
Signs										
BCG received	73 (59.3)	17	1.59	0.63–4.04	40	1.59	0.61–4.18	16	1.13	0.48–2.64
Malnutrition	38 (30.9)	5	0.49	0.17–1.43	22	0.55	0.18–1.64	11	0.61	0.26–1.48
Anemia (Hb < 8 g/dl)	19 (15.4)	3	0.70	0.19–2.61	13	0.60	0.16–2.30	3	1.69	0.45–6.27
Neurological stage III of disease †	106 (86.2)	19	–	–	62	–	–	25	–	–
Deep coma	28 (22.8)	4	0.59	0.18–1.88	13	0.84	0.25–2.85	11	0.34 *	0.13–0.85
Meningeal signs	55 (44.7)	10	0.79	0.32–1.92	32	0.79	0.31–2.00	13	0.91	0.39–2.13
Tonic posturing †	26 (21.1)	0	– *		19	– *	–	7	0.75	0.28–2.02
Papilloedema	4 (3.3)	1	1.32	0.13–13.25	2	1.42	0.12–16.34	1	0.88	0.09–8.81
Optic atrophy †	6 (4.9)	0	–	–	5	–	–	1	1.50	0.17–13.40
Cranial nerve palsy	41 (33.3)	4	0.31 *	0.10–0.99	30	0.25 *	0.08–0.82	7	1.67	0.65–4.34
Focal deficit	63 (51.2)	5	0.17 *	0.06–0.50	45	0.14 *	0.05–0.42	13	1.28	0.55–2.98
Hypertonia	49 (39.8)	4	0.22 *	0.07–0.70	35	0.19 *	0.06–0.61	10	1.25	0.52–3.01
Hypotonia	44 (35.8)	7	0.64	0.25–1.68	24	0.75	0.27–2.03	13	0.56	0.24–1.32
Ankle clonus	31 (25.2)	7	1.20	0.45–3.22	17	1.21	0.43–3.40	7	1.01	0.38–2.68
EP movements †	14 (11.4)	2	0.62	0.13–2.98	12	0.42	0.09–2.03	0	– *	–
CSF parameters										
Cells >100 mm^3	54 (43.9)	13	1.51	0.62–3.64	31	1.36	0.55–3.40	10	1.55	0.65–3.71
Proteins >1 g/l	74 (60.2)	13	0.66	0.27–1.59	41	0.77	0.31–1.92	20	0.53	0.21–1.32
CT brain parameters										
Moderate–severe HC †	57 (46.3)	6	– *	–	40	– *	–	11	–	–
Parenchymal enhancement	80 (65.0)	16	0.94	0.38–2.36	45	0.99	0.38–2.56	19	0.85	0.35–2.08
Basilar inflammation	94 (76.4)	17	0.58	0.22–1.53	55	0.58	0.21–1.60	22	0.85	0.31–2.36
Cerebral infarct ± edema	54 (43.9)	4	0.18 *	0.06–0.57	37	0.17 *	0.05–0.55	13	0.88	0.38–2.04
Tuberculoma	28 (22.8)	8	1.84	0.69–4.86	13	2.06	0.73–5.80	7	0.85	0.32–2.28
Mantoux test positive	20 (16.3)	2	0.39	0.08–1.79	12	0.42	0.09–2.03	6	0.63	0.22–1.84
Extracranial TB	94 (76.4)	24	9.60 *	1.24–74.41	52	8.31 *	1.05–65.90	18	2.22	0.88–5.59
Shunt surgery required	69 (56.1)	9	0.36 *	0.14–0.89	45	0.31 *	0.12–0.81	15	1.14	0.49–2.66
HIV infection	8 (6.5)	3	2.54	0.56–11.42	4	2.25	0.47–10.85	1	2.15	0.25–18.24
ATT hepatotoxicity †	3 (2.4)	2	8.44 *	0.73–97.08	0	– *	–	1	0.58	0.05–6.65

*χ^2 test; $P < 0.05$ significant; OR, odds ratio; CI, confidence interval; † OR cannot be computed. They are only computed for a 2 x 2 table without empty cells; ATTT, antituberculous therapy; BCG, bacilli Calmette–Guerin; CSF, cerebrospinal fluid; CT, computed tomography; EP, extrapyramidal; HC, hydrocephalus; HIV, human immunodeficiency virus; TB, tuberculosis.

= 1, OR 0.35, 95% CI 0.14–0.90) proved to be independently associated with fatal outcome.

Discussion

Ours is probably the first study where clinical variables that predict complete recovery, survival with disability, and fatal outcome have been identified separately. In other studies [3]–[9] both death and survival with moderate to severe disability were included in the poor outcome group. In the present study, 57% of the children survived with neurologic sequelae and 23% died. The reported incidence of neurologic disability in other studies [3]–[9] varied between 32 and 56%. The reported mortality ranged from 7 to 38%. When compared to the other prospective study of TBM in childhood,[9] our study had a higher number of patients (123 *vs* 50) and we analyzed more variables (36 *vs* 24).

Some of the variables found to be associated with 'survival with disability' on univariate analysis in our study, like hypertonia at the time of presentation, presence of cerebral infarction on CT, and no ATT-induced hepatotoxicity, have not been reported in the earlier studies on childhood TBM,[3]–[9] Cerebral infarction occurs in 14–38% of children with TBM, most commonly from the involvement of medial striate and thalamoperforating arteries.[19],[20] This probably explains the associated disability seen in survivors. We have no proper explanation for why the absence of ATT-induced hepatotoxicity was associated with an outcome, 'survival with disability' and also absence of extrapyramidal movement disorders was associated with a fatal outcome. These aspects need detailed studies.

The results of univariate analysis do not adjust for the effect of covariates and therefore have obvious limitations. In the present study, multivariate analysis demonstrated that hypertonia at admission was the only independent predictor of the outcome 'survival with disability' and deep coma with a fatal outcome. When the power of the study was rechecked for these two significant variables, it was 76.4% for hypertonia as a predictor of the outcome 'survival with disability' and 86.9% for deep coma as predictor of fatal outcome. These precise findings have not been reported in earlier studies.[4],[5],[9]

The strengths of the present study are that: (i) it was a prospective study including 123 children, (ii) patient population received uniform treatment protocols, and (iii) a large number of variables were analyzed for significance. However, the present study has its limitations. First, the diagnosis of TBM was based on clinical criteria and not on microbiological confirmation. Although definitive diagnosis of TBM depends

Table 3: Multivariate logistic regression of clinical variables for prediction of outcomes

Variables	Regression coefficient	SE	*P* value *	d.f.	OR	95% CI
Complete recovery						
Hypertonia	-1.41	0.75	0.061	1	0.24	0.06–1.07
Extracranial TB	1.75	1.14	0.124	1	5.76	0.62–53.59
Focal deficit	-1.04	0.71	0.143	1	0.36	0.09–1.42
Cerebral infarct ± edema	-0.98	0.71	0.171	1	0.38	0.09–1.52
Hydrocephalus	–	–	0.178	2	–	–
Mild	-1.93	1.04	0.063	1	0.15	0.02–1.11
Moderate–severe	-0.84	0.75	0.265	1	0.43	0.10–1.89
ATT hepatotoxicity	2.63	2.48	0.288	1	13.87	0.11–17.75E+2
Cranial nerve palsy	-0.31	0.81	0.700	1	0.73	0.15–3.57
Tonic posturing	-7.81	28.84	0.787	1	0.00	0.00–14.31E+20
Shunt surgery required	-0.13	0.77	0.867	1	0.88	0.20–3.96
Constant	18.02	57.95	0.756	1	66.93E+6	–
Survival with disability						
Hypertonia	-2.13	0.85	0.012	1	0.12	0.02–0.62
Focal deficit	-1.30	0.80	0.103	1	0.27	0.06–1.30
Hydrocephalus	–	–	0.152	2	–	–
Mild	0.45	1.00	0.654	1	1.56	0.22–11.02
Moderate–severe	1.86	1.11	0.095	1	6.42	0.72–57.02
Extracranial TB	1.72	1.26	0.172	1	5.56	0.48–64.98
Cerebral infarct ± edema	-0.91	0.73	0.213	1	0.40	0.10–1.69
Cranial nerve palsy	-0.64	0.91	0.482	1	0.53	0.09–3.15
Tonic posturing	-7.88	32.98	0.811	1	0.00	0.00–44.47E+23
Shunt surgery required	-0.18	0.83	0.826	1	0.83	0.17–4.21
ATT hepatotoxicity	9.77	112.05	0.931	1	17.52E+3	0.00–4.21E+99
Constant	2.87	233.62	0.990	1	17.55	–
Death						
Deep coma	-1.05	0.48	0.030	1	0.35	0.14–0.90
EP movements	8.06	26.29	0.759	1	31.49E+2	0.00–75.00E+24
Constant	-15.37	52.58	0.770	1	0.00	–

*$P < 0.05$ significant; SE, standard error; d.f., degree of freedom; OR, odds ratio; CI, confidence interval; ATT, antituberculous therapy; EP, extrapyramidal; TB, tuberculosis

on the detection of the tubercle bacilli in the CSF, either by smear examination or by bacterial culture; smears are usually positive in fewer than 10% of cases of TBM, while culture for *Mycobacterium tuberculosis* takes up to 8 weeks and also often negative.[18],[21] Most studies on outcome in childhood TBM have similarly diagnosed patients predominantly on clinical criteria.[3]–[7],[9] Second, the neurological outcome in children who survived was assessed purely on clinical examination at the time of discharge. We did not perform formal intelligence quotient or audiological evaluations. Third, since follow up after discharge from hospital is generally poor in our setting, we could not document the outcome after completion of ATT.

In conclusion, the present study documents that TBM continues to be a serious childhood illness with a high neurologic morbidity and mortality. We report that in children with TBM on admission to hospital the presence of hypertonia is an independent predictor of neurological sequelae in survivors, and the presence of deep coma is an independent predictor of mortality. Additional prospective studies employing multivariate analysis are required to determine the generalization of our findings.

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Invited Comments

In developing countries, childhood tuberculous meningitis (TBM) remains an important cause of neurological handicap and death. Current antituberculosis treatment is remarkably effective if administered timely; unfortunately, as in the present study, the diagnosis of childhood TBM is often delayed, resulting in severe neurological sequelae and even death.

Early diagnosis of TBM is notoriously difficult; the symptoms in stage 1 TBM are subtle, nonspecific, and relate more to the underlying primary infection (lung tuberculosis) than to the brain. Frequent diagnoses include gastroenteritis, otitis media, or upper respiratory infection. Poor weight gain, or loss of weight, reflected by crossing of weight centiles on the Road to Health Card, is an extremely valuable clue to early diagnosis.[1] In high prevalence tuberculosis areas, this should alert the clinician to the possibility of tuberculosis. A positive contact history, a chest radiograph and tuberculin skin testing are other most valuable simple procedures that may support an early tuberculosis diagnosis.[2]

Unfortunately, however, patients are often repeatedly seen without TBM being considered, resulting in disease progression to stages 2 and 3 TBM.[3] The majority of these patients will now have evidence of obstructive hydrocephalus on cranial computerized tomography (CT). Although noncommunicating hydrocephalus can result in serious neurological handicap and even sudden death due to cerebral herniation, if not recognized and managed appropriately, most

cases of childhood tuberculous hydrocephalus are communicating and respond well to medical treatment (antituberculosis drugs and diuretics). Progressive tuberculous periarteritis, however, almost invariably results in infarction of the basal ganglia, the clinical correlates of which are focal abnormalities of power, tone, and/or abnormal movements. Brainstem microinfarcts, although rarely demonstrated by CT, are a common autopsy finding in advanced TBM and present clinically with deep coma and decerebration.

The present study prospectively assessed an impressive array of clinical features in a large cohort of childhood TBM patients with regard to the clinical outcome. These features were separately evaluated for neurological handicap and death by both univariate and multivariate analyses. A significant number of variables correlated independently with these outcomes with regard to prognosis. However, on multivariate analysis only hypertonia featured as a prognostic indicator for neurological handicap and only deep coma for death. We agree with the authors that these findings most likely relate to vasculitis and infarction since most patients in this study had stage 3 TBM.

The results of this study re-emphasize the need for early diagnosis of this devastating disease.

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