



ORIGINAL ARTICLE

Childhood tuberculosis in southern Taiwan, with emphasis on central nervous system complications



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Background/Purpose: Childhood tuberculosis (TB) continues to be a major public health problem in Taiwan. Taiwan remains a highly endemic area despite neonatal Bacillus Calmette–Guérin (BCG) vaccination and the availability of anti-TB therapy. The presentation is highly variable and it is often difficult to make an accurate diagnosis. This study was designed to evaluate the demographic, clinical, and laboratory findings and outcomes of TB in children with emphasis on central nervous system (CNS) complications.

Methods: The medical records of 80 children diagnosed with TB at a medical center in southern Taiwan over the past 24 years (1988–2012) were reviewed.

Results: Among them, 48.8% (39/80) had pulmonary TB, 27.5% (22/80) had isolated extrapulmonary TB, and 23.7% (19/80) had disseminated TB. Most infected cases were aged either < 4 years or > 12 years. TB contact history was found in 42.5% (34/80) cases. Fourteen (17.5%) of the cases had CNS involvement. The most common presentations were fever (85.7%), signs of increased intracranial pressure (71.4%), drowsiness (64.3%), and focal neurological signs (57.1%). The major radiological findings were tuberculoma (50%), basilar enhancement (41.6%), infarction (41.6%), hydrocephalus (16.6%), and transverse myelitis (16.6%). The case fatality of CNS TB was 14.3% and 21.4% had neurologic sequelae.

Conclusion: Findings suggest that positive exposure history and suspicious clinical presentations are important clues for further confirmatory laboratory and image studies in childhood

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TB. CNS TB usually presented as part of disseminated TB in children. Early diagnosis and treatment may lead to favorable outcomes in CNS TB.

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Introduction

According to the World Health Organization, at least half a million children become ill with tuberculosis (TB) each year. It is estimated up to 70,000 children die of TB every year.¹ Pulmonary diseases constitute 70–80% of childhood TB infection. Disease patterns are different between children and adults. Infants and young children are at increased risk of severe disseminated disease associated with high mortality, such as miliary TB or central nervous system (CNS) TB. Adolescents are at particular risk of developing adult-type disease.¹ Due to nonspecific symptoms and difficulties in diagnosis, the diagnosis of TB in children is still a challenge. Taiwan remains a high endemic area despite universal neonatal *Bacillus Calmette–Guérin* (BCG) vaccination and active surveillance with anti-TB therapy. Data from Taiwan's National Tuberculosis Registry show that there were 57.2 TB cases/100,000 population in 2010, and the incidence of TB in persons aged < 18 years was 9.61/100,000 person-years.² Childhood TB is an important public health issue because acquisition of TB infection during childhood contributes to the future reservoir of cases.³ CNS TB may cause permanent neurologic complications or death in spite of specific anti-TB therapy. The incidence of CNS TB is low, ranging from 2% to 5% of all childhood TB cases.^{2,3} The mortality rate is estimated to range from 15% to 32% and varies according to clinical stage.^{4,5} Advanced stage TB meningitis and hydrocephalus on admission are associated with poor prognosis.⁶ Early diagnosis may prevent neurologic complications or devastating outcomes. Only a few reports on childhood TB and CNS TB are available in Taiwan.^{2,7–9} Further, severe childhood TB diseases and the mortality of CNS TB remain high even under effective anti-TB treatment. The objective of this study was to investigate the characteristics of childhood TB with emphasis on CNS complications at a medical center in southern Taiwan during a period of 24 years.

Materials and methods

Patient enrollment

Patients aged < 18 years diagnosed with TB diseases at National Cheng Kung University Hospital from January 1988 to June 2012 were enrolled. Demographic characteristics, clinical features, diagnostic methods, underlying diseases, laboratory findings, treatment regimens, and outcomes were retrieved from chart review. The diagnosis of TB diseases was based on positive results of acid-fast stain (AFS) smears, mycobacterium cultures, polymerase chain reactions (PCR), or histopathological findings or clinical

manifestations with contact history of the index case or favorable response to anti-TB therapy.

Case definition

TB disease was categorized according to the site of involvement as pulmonary TB, isolated extrapulmonary TB (EPTB), and disseminated TB. The definition of pulmonary TB was disease confined to lung, pleura, and intrathoracic lymph nodes. Isolated EPTB was disease confined to one extrapulmonary organ. Disseminated TB was defined as: (1) positive AFS bacilli or TB culture or TB-PCR from blood, bone marrow, liver, or specimens from more than two noncontiguous organs; (2) positive AFS bacilli or TB culture or TB-PCR from one organ and typical histopathological findings in another noncontiguous organ; or (3) positive AFS bacilli or TB culture or TB-PCR from one organ and radiographic findings of miliary lung or CNS lesions.⁷ CNS TB cases were defined as microbiologic or clinical cases. The microbiological case definition was: (1) positive AFS bacilli or TB culture or TB-PCR from cerebrospinal fluid (CSF); or (2) abnormal neurologic signs and symptoms, CSF or brain image consistent with CNS TB, and positive AFS bacilli or TB culture or TB-PCR from any site. The clinical case definition presented two or more of the following: (1) close TB contact history; (2) CSF abnormalities without evidence of other infectious cause; (3) brain computed tomography or magnetic resonance imaging findings consistent with CNS TB and response to anti-TB therapy.⁵

Clinical staging of TB meningitis

Clinical staging of TB meningitis was classified by the Medical Research Council staging.¹⁰ In Stage I, patients were fully conscious and did not have focal neurological signs; in Stage II, patients were inattentive, confused, and showed signs of clouding consciousness or had focal neurological signs; in Stage III, patients were stuporous or comatose or had multiple cranial nerve palsies or complete hemiplegia or paraplegia.

Treatment outcomes

According to World Health Organization guidelines,¹¹ treatment outcomes of TB patients were categorized as cured, died, or treatment failure. Cured patients were defined as being sputum-smear negative in the last month of treatment. Died patients referred to those who died for any reason during the course of treatment. Treatment failure was defined as sputum-smear positive at 5 months or later after starting treatment.

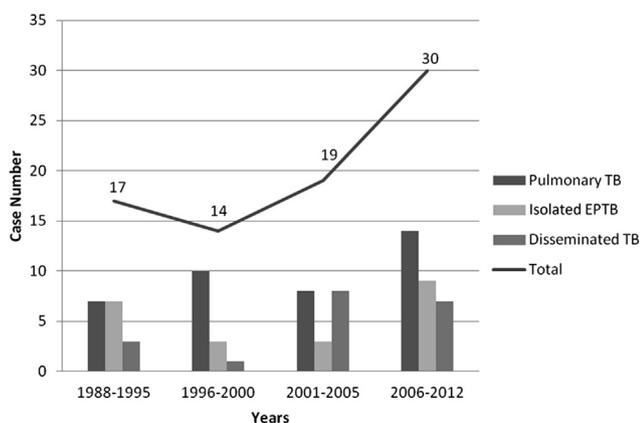


Figure 1. Case numbers of childhood tuberculosis (TB) during a period of 24 years in a single medical center.

Statistical analysis

Statistical analysis was done using SPSS software (Statistical Package for Social Sciences, version 12.0; SPSS Inc., Chicago, IL, USA). Categorical variables were analyzed using the Mann–Whitney *U* test, Chi-squared test, and ANOVA. A *p*-value < 0.05 was considered statistically significant.

Results

Demographic characteristics and diagnostic methods

Eighty patients with TB diseases were reviewed during a period of 24 years in a single medical center. More cases were diagnosed during 2001–2012 (61.3%, 49/80) than the previous 12 years (38.7%, 31/80; Fig. 1). Overall, 39/80 (48.8%) had pulmonary TB, 22/80 (27.5%) had isolated EPTB, and 19/80 (23.7%) had disseminated TB (Table 1). The mean age was 9.9 ± 6.6 years (range, 1 month to 18 years) with male-to-female ratio of 1.1 (42/38). A bimodal age distribution was noted in TB disease, which peaked at 0–4 years and 12–18 years (Fig. 2). The age of pulmonary TB was older than isolated EPTB and disseminated TB

($p < 0.05$). Eleven patients (13.8%) had underlying disease, including human immunodeficiency virus (HIV) infection, malignancy, connective tissue disease, prematurity, immunodeficiency disease, renal disease, and epilepsy. Higher rates of TB contact history and positive culture results were more frequently found in children with pulmonary and disseminated TB than those with isolated EPTB ($p < 0.05$). Tuberculin skin test was positive in 69.2% (36/52). The AFS smear, TB culture, and TB PCR positive rates were 42.7% (32/75), 57.6% (39/66), and 76.2% (32/42), respectively (Table 2).

Anatomical distribution, laboratory data, and outcomes

The most common sites of isolated EPTB infections were lymph nodes (7/22, 31.8%), CNS (6/22, 27.3%), and skeletal system (6/22, 27.3%). However, lung (18/19, 94.7%), CNS (8/19, 42.1%), and gastrointestinal system (8/19, 42.1%) were predominantly involved in disseminated TB (Table 1). Patients with disseminated TB had significantly higher platelet counts, lower hemoglobin, and higher C-reactive protein levels. Isolated EPTB had significantly lower C-reactive protein levels than the other two groups ($p < 0.05$; Table 3). The majority of these patients responded well to anti-TB therapy, except for three with relapses (3.8%), five with treatment failures (6.3%), and three fatal cases (3.8%). Factors of treatment failures may include poor drug compliance before directly observed treatment short-course policy, anti-TB drug resistance, and HIV infection. The causes of deaths included pneumothorax, lung cavitations with intractable hemoptysis, and deep coma with brain swelling.

Characteristics of CNS TB cases

In this series, 14 patients fulfilled the criteria for CNS TB (Table 4). Half of the patients had concomitant pulmonary TB and four presented with miliary pattern. Eight of them presented with disseminated TB. A bimodal age distribution was noted with a two-peak range, at age < 4 years (50%) and > 10 years (43%). Half of the patients had household TB contact history. The most common clinical manifestations

Table 1 Anatomical distribution of 80 children with tuberculosis

Type	Organ involvement	<i>n</i> (%)
Pulmonary tuberculosis (<i>n</i> = 39)	Lung	39 (100)
Isolated extrapulmonary tuberculosis (<i>n</i> = 22)	Lymph node	7 (31.8)
	CNS	6 (27.3)
	Skeletal system	6 (27.3)
	Soft tissue	3 (13.6)
	Disseminated tuberculosis (<i>n</i> = 19)	CNS and lung
	GI and lung and/or lymph node	6 (31.6)
	Skeletal and lung and/or bone marrow	3 (15.8)
	CNS and GI and skeletal and/or lung/urogenital/ bone marrow	2 (10.5)
	Soft tissue and lung and/or lymph node	2 (10.5)

CNS = central nervous system; GI = gastrointestinal.

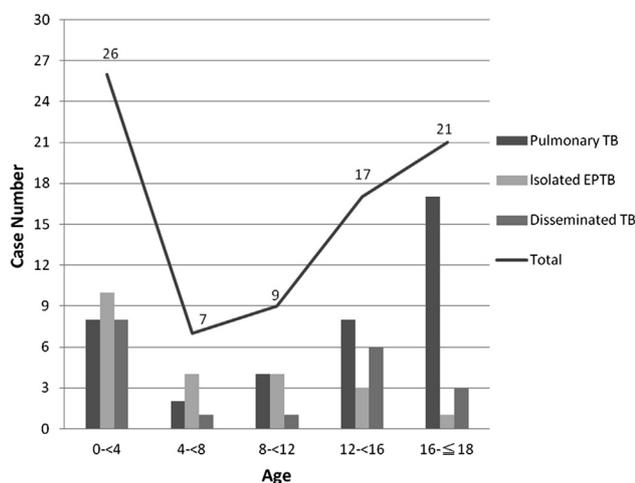


Figure 2. Age distribution of 80 children with tuberculosis (TB).

were fever (85.7%), symptoms of increased intracranial pressure (headache/nausea/vomiting; 71.4%), drowsiness (64.2%), and other focal neurological signs (facial palsy/limb weakness; 57.1%). Ten (71.4%) patients had hyponatremia (serum sodium level < 130 meq/L). The tuberculin skin test was positive in only two patients who were tested (2/11, 18.2%). Microscopic examination of CSF failed to identify any AFS bacilli. Microbiological evidence of TB infection was obtained in 11 (78.5%) of these patients from either CSF, gastric aspirates, or other tissues. The radiological findings in 12 cases included tuberculoma (50%; Fig. 3), basilar enhancement (41.6%; Fig. 3), infarction (41.6%; Fig. 4), hydrocephalus (16.6%), and transverse myelitis (16.6%). According to the stage of TB meningitis, one patient was in Stage I (7%), seven in Stage II (50%), and six in Stage III (43%). Five of the patients in Stage II received concurrent steroid treatment with anti-TB therapy and only one case had sequelae of mental retardation. The outcomes of patients in Stage III were generally poor, including two deaths (respiratory failure and brain swelling) and

significant neurological sequelae in three cases (i.e., hydrocephalus with shunt surgery, paraplegia, urinary retention). Paradoxical responses during anti-TB therapy were found in five of the patients.

Discussion

The global burden of childhood TB is underestimated due to the difficulty in confirming the diagnosis and lower reporting of cases. The current study demonstrated that childhood TB continues to be an important issue in Taiwan. More cases were diagnosed during 2001–2012 than in the previous 12 years. The risk of disseminated or CNS TB following primary infection is greatest in children aged < 4 years, around 10–20% in those aged < 1 year, and 2–5% when aged 1–2 years.¹² The disease incidence decreased to a nadir at age 5–10 years and increased rapidly in adolescence.¹³ The result of our study is in line with this tendency. Age-related differences in disease patterns probably reflect differences in immunological status.

Diagnosis of disseminated TB in children is difficult because the clinical manifestations may be nonspecific, including poor appetite, failure to thrive, and prolonged fever. The risk factors for disseminated TB include HIV infection, medication with immunosuppressive drugs, immunodeficiencies such as chronic granulomatous disease, and Mendelian susceptibility to mycobacterial diseases.^{7,11} In our series, 26.3% (5/19) disseminated TB had underlying diseases. Wang et al reported that the most common organs involved in disseminated TB in adults were the lung (87.2%), the musculoskeletal system (19.5%), and the urogenital system (17.1%).⁷ In our study, the major involved organs were the lung (94.7%), the CNS (42.1%), and the gastrointestinal system (42.1%). Only two of our patients underwent bone marrow examination. Both specimens showed positive culture results and the typical caseating granuloma. Bone marrow examination should be considered in patients with clinically suspected disseminated TB.

Superficial lymphadenitis ranges from 46% to 67%.^{9,14} In our study, only 31.8% of patients with isolated EPTB had

Table 2 Comparison of demographic characteristics and diagnostic methods of children with tuberculosis (TB) by disease category

Characteristics and methods	Pulmonary TB, n (%)	Isolated EPTB, n (%)	Disseminated TB, n (%)	<i>p</i>
No. (%)	39 (48.8)	22 (27.5)	19 (23.7)	
Female	21 (53.8)	8 (36.4)	9 (47.4)	0.386
Age (y, mean ± SD)	12.4 ± 6.2 ^{a,b}	6.4 ± 5.1	8.9 ± 7.0	0.002
Underlying disease	5 (12.8)	1 (4.5)	5 (26.3)	0.127
Contact history	19 (48.7) ^a	4 (18.2) ^c	11 (57.9)	0.02
TST test	16/19 (84.2)	12/20 (60)	8/13 (61.5)	0.206
Acid fast stain	17/36 (47.2)	6/20 (30.0)	10/19 (52.6)	0.340
TB culture	22/30 (73.3) ^a	2/18 (11.1) ^c	14/18 (77.8)	<0.001
TB PCR	14/18 (77.8)	10/14 (71.4)	8/10 (80)	0.91
Histology	—	14/22 (63.6)	8/19 (42.1)	0.168

^a Pulmonary TB vs. isolated EPTB, *p* < 0.05.

^b Pulmonary TB vs. disseminated TB, *p* < 0.05.

^c Isolated EPTB vs. disseminated TB, *p* < 0.05.

EPTB = extrapulmonary TB; PCR = polymerase chain reaction; SD = standard deviation; TST = tuberculin skin test.

Table 3 Comparison of laboratory findings of children with tuberculosis (TB) by disease category

	Pulmonary TB	Isolated EPTB	Disseminated TB	<i>p</i>
WBC ($\times 10^9/L$)	11.1 \pm 5.5	12.2 \pm 6.3	11.6 \pm 4.7	0.772
Segment (%)	59.8 \pm 19.1	56.2 \pm 19.9	62.3 \pm 15.1	0.595
Band (%)	8.9 \pm 8.3	4.5 \pm 5.9	9.3 \pm 9.4	0.212
Lymphocyte (%)	24.9 \pm 19.4	27.7 \pm 16.4	19.5 \pm 13.2	0.344
Hb (g/L)	125 \pm 18 ^b	123 \pm 17 ^c	104 \pm 21	0.001
Platelet ($\times 10^{12}/L$)	344 \pm 136 ^{a,b}	452 \pm 102	473 \pm 166	0.003
CRP (mg/L)	59.1 \pm 62.9 ^a	24.1 \pm 33.7 ^c	120.9 \pm 227.5	0.095
AST (U/L)	36.1 \pm 24.3	34.9 \pm 13.7	42.4 \pm 40.3	0.441
ALT (U/L)	29.6 \pm 24.5	27.3 \pm 12.7	32.8 \pm 30.9	0.79
ESR (mm/h)	49.8 \pm 38.8	37.5 \pm 32.6	65.4 \pm 45.8	0.26

^a Pulmonary TB vs. isolated EPTB, *p* < 0.05.

^b Pulmonary TB vs. disseminated TB, *p* < 0.05.

^c Isolated EPTB vs. disseminated TB, *p* < 0.05.

ALT = alanine aminotransferase; AST = aspartate aminotransferase; CRP = C-reactive protein; EPTB = extrapulmonary TB; ESR = erythrocyte sedimentation rate; Hb = hemoglobin; WBC = white blood cell count.

lymphadenitis, which is less than the previous report.⁹ Most of the TB lymphadenitis was diagnosed by histopathologic findings, tuberculin skin tests, and contact histories. Lack of mycobacterium culture results or molecular evidence may make it difficult to differentiate from non-TB mycobacterium lymphadenitis. Clinicians should be alert to the diagnosis of cervical TB lymphadenitis and look for microbiological or molecular evidence of *M. tuberculosis* infection. Bone is also a frequently involved organ in EPTB. The proportion of skeletal TB in our study was 27.3%, which was compatible with the previous report (27–35%).⁹

CNS TB is the most severe, life-threatening form of TB in young children and accounts for approximately 5% of patients.² Up to 79% of children with CNS TB are aged < 5 years,^{15,16} which is higher than our series (8/14, 57%). The most common presentations of CNS TB in this study were fever, symptoms of increased intracranial pressure, altered consciousness, and focal neurological deficits. Seizure was observed in three patients (3/14, 21.4%), which is less frequent than other childhood study (50%).¹⁷ Cranial nerve deficits were found in 30–50% of cases, which most commonly involved sixth and seventh cranial nerves.¹⁷ However, only two cases (14.3%) had seventh cranial nerve involvement in our series. Young age and late-stage presentation are usually associated with poor outcomes.¹⁸ Therefore, in young children with meningitis and household TB contact history, CNS TB should be listed as a differential diagnosis.

The tuberculin skin test in CNS TB was positive in only 18.2% (2/11) of our patients, which was much lower than other TB disease (69.2%). The positive rate was similar with previous study, which ranged from 10–30% in children with CNS TB.^{5,19,20} A negative tuberculin skin test did not exclude the possibility of TB diseases because disseminated TB, including meningitis and miliary, may induce an anergic reaction to the skin test.

About 10–18% of patients with CNS TB have been reported to have a so-called paradoxical response.^{2,21} These phenomena generally occur within 3 months after treatment and do not represent treatment failure.^{21–23} The paradoxical response in CSF (lymphocyte predominant shift

to segment predominant) during anti-TB therapy was observed in 35.7% (5/14) of our patients and two of them had clinical deterioration.

In this study, no AFS bacilli could be found in CSF and *M. tuberculosis* cultures were positive in only 21.4%. The identification rate of AFS bacilli in CSF was 80% in adult, but only 10–20% in children, whereas the positive culture rate ranged from 30% to 74%.^{5,11} It had been postulated that a higher volume of CSF (> 6 mL) and taking more samples increases bacteriological yield rate.^{3,24} Thwaites et al reported that > 6 mL fluid tapping was safe for infants and children.²⁴ We suggest that repeated lumbar punctures and a higher CSF volume may increase the bacteriological detection rate in CSF. The molecular method of TB-PCR has been used in the diagnosis of CNS TB.²⁵ In our study, eight patients (8/11, 73%) had positive TB-PCR results in CSF. Mycobacterial DNA remained identifiable within the CSF even after 1 month of anti-TB treatment,²⁰ which may provide more chance for mycobacterium detection. Many new modalities, such as interferon- γ assay, urine lip-oarabinomannan, and Xpert MTB/RIF test, have been applied to the diagnosis of TB infection.^{26–28}

Kumar et al reported basilar enhancement, hydrocephalus, tuberculoma, and infarctions as typical findings of CNS TB.²⁹ The reported incidence was 75–92% for basilar enhancement, 68–100% for hydrocephalus, and 10–27% for tuberculoma. Andronikou et al found that hyperdensity in the basal cisterns before contrast is the most characteristic image finding on computed tomography.³⁰ The incidence of hydrocephalus correlated with the duration of disease. Only two patients (14.3%) had complication of hydrocephalus in our cases, which may be due to earlier diagnosis and treatment. Tuberculoma (50%) is more common in our series. Tuberculoma may develop before or during the course of treatment.³¹

Despite anti-TB treatment for tuberculous meningitis, mortality remains high. The current treatment recommendation consists initially of 2 months of isoniazid, rifampicin, pyrazinamide, levofloxacin or moxifloxacin, and aminoglycoside or prothionamide, followed by 10 months of isoniazid and rifampicin.^{32,33} Isoniazid, pyrazinamide, and

Table 4 Descriptions of 14 children with central nervous system (CNS) tuberculosis (TB)

N	Age, sex	Stage	Sites of infection	Contact history	Presenting symptoms and signs	Imaging findings	CSF findings WBC ($\times 10^6/L$) Lactate (mM)	Diagnostic methods	Treatment regimens	Steroid	Outcome
1	10 y, F	I	CNS Lung	Y	Fever 4 wk, cough, headache, vomiting	1. Infarction over pos, right MCA 2. Right Sylvian tuberculoma with encasement of MCA	WBC: 13 Lactate: 3.1	CSF and gastric lavage culture: Pos	INH (13 mo) RIF (13 mo) PZA (3 mo) EMB (3 mo) SM (2 wk)	N	Survival
2	13 y, F	II	CNS Lung	Y	Fever, headache, nausea, slurred speech, drowsiness, photophobia	1. Infarct at bilateral basal ganglia, left frontal area, temporal lobes 2. Lep-tomenigeal enhancement over pons and midbrain 3. Tuberculoma at bilateral frontal, left occipital lobes, CNS	WBC: 360 Lactate: 5.1	CSF and gastric lavage culture: Pos CSF and gastric lavage PCR: Pos	INH (12 mo) RIF (12 mo) PZA (3 mo) EMB (3 mo) AMK (2 mo) TBN (4 mo) LEV (4 mo)	Y	Survival
3	2 mo, M	II	CNS	Y	Fever, vomiting, drowsiness, irritable	No focal lesion in CNS	WBC: 360 Lactate: 1.4	CSF PCR: Pos	Lost to follow-up	N	Lost to follow-up
4	6 mo, M	II	CNS Skeletal GI	Y	Left lower limb weakness for 1 mo, diarrhea	Tuberculoma over bilateral frontal, left occipital, right pons and T11-12 spine	WBC: 7 Lactate: 1.4	Gastric lavage culture: Pos Retroperitoneal abscess PCR: Pos	INH (12 mo), RIF (12 mo), PZA (3 mo), EMB (2 mo), SM (1 mo)	Y	Survival
5	12 y, M	II	CNS	N	Fever, headache ataxia, slurred speech, vomiting, drowsiness	No focal lesion in CNS	WBC: 216 Lactate: 3.2	CSF PCR: Pos	Lost to follow-up	Y	Lost to follow-up
6	13 y, F	II	CNS	N	Fever 2 wk, headache, neck stiffness, vomiting, drowsiness	No image	WBC: 84l Lactate: 3.5	CSF PCR: Pos	INH (12 mo), RIF (12 mo), PZA (3 mo), EMB (2 mo)	Y	Survival

9	6 mo, M	III	CNS Lung	Y	Fever 2 d, vomiting, seizure, limb weakness, failure to thrive, bulging fontanel	1. Infarction at pons and basal ganglion 2. Tuberculoma over pons, right sylvian fissure	WBC: 231 Lactate: 2.4	Gastric lavage culture: Pos	Lost to follow-up	Y	Lost to follow-up
10	4 y, M	III	CNS Lung	Y	Bilateral lower limb paralysis and anesthesia for 7 d, urine and stool retention	T3–T9 transverse myelitis	WBC: 1 Lactate: 1.9	CSF and Gastric lavage PCR: Pos	INH (12 mo) RIF (12 mo) PZA (2 mo) EMB (2 mo)	Y	Survival Paraplegia
11	2 y, M	III	CNS	N	Fever 4 wk, seizure, aphasia, ataxia	Hydrocephalus with basilar enhancement	WBC: 121 Lactate: 2.4	CSF PCR: Pos	INH (12 mo) RIF (12 mo) PZA (2 mo) SM (1 mo)	Y	Survival Shunt surgery, Mental retardation
12	17 y, M	III	CNS	N	Fever 17 d, headache, vomiting, drowsiness, urine retention and bilateral leg weakness	T7-8 myelitis	WBC: 470 Lactate: 2.4	Image and clinical response	INH (9 mo) RIF (9 mo) PZA (2 mo) EMB (9 mo) SM (1 mo)	Y	Survival Voiding dysfunction
13	6 y, F	III	CNS	N	Fever 2 wk, vomiting, lethargy, seizure	No image	WBC: 100 Lactate: 2.1	CSF PCR: Pos	INH (12 mo) RIF (12 mo) PZA (2 mo) EMB (2 mo)	N	Survival
14	5 mo, F	III	CNS Lung Skeletal GI Renal	N	Fever 4 wk, cough, poor appetite, failure to thrive, hemiplegia	1. Lep- tomeningeal enhancement at basal and prepontine cistern 2. Infarcts at bilateral ACA, MCA and right PCA territories 3. Tuberculoma at right cerebellum	WBC: 18 Lactate: 3.4	CSF, gastric lavage, urine culture: Pos CSF and gastric lavage PCR: Pos	INH (7 wk) RIF (7 wk) PZA (7 wk) PTN (3 wk)	Y	Expired, Respiratory failure with tension pneumothorax

ACA = anterior cerebral artery; AMK = amikacin; CN = cranial nerve; CNS = central nervous system; EMB = ethambutol; F = female; GI = gastrointestinal; INH = isoniazid; LEV = levofloxacin; M = male; MCA = middle cerebral artery; N = no; PCA = posterior cerebral artery; PCR = polymerase chain reaction; Pos = positive; PTN = prothionamide; PZA = pyrazinamide; RMP = rifampicin; SM = streptomycin; WBC = white blood cell count; Y = yes.



Figure 3. Magnetic resonance image of a 13-year-old girl showing enhanced nodules and plaques along basal, pre-pontine, and ambient cisterns.

fluoroquinolone show good cerebrospinal fluid penetration, but rifampicin does not. However, rifampicin is crucial in the treatment of TB meningitis because of the high mortality in patients with rifampicin-resistant disease. Recent data show that treatment containing a higher dose of rifampicin and moxifloxacin is associated with a survival benefit in patients with tuberculous meningitis.³³ However, most of the data regarding the therapy of TB meningitis with fluoroquinolone were from adults. Fluoroquinolone treatment in childhood TB meningitis needs further clinical investigations.

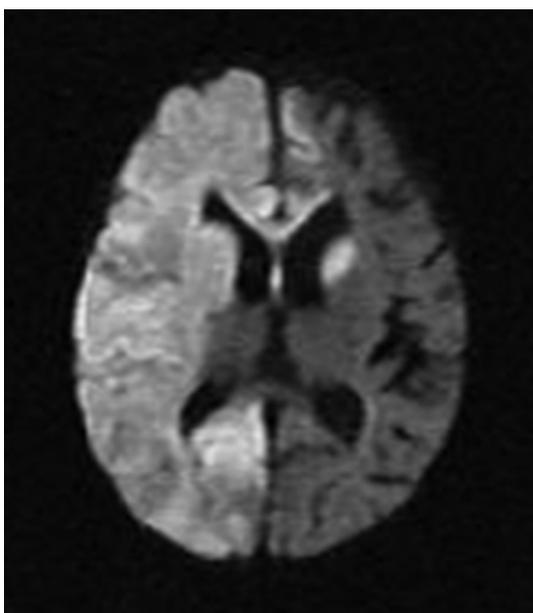


Figure 4. Magnetic resonance image of a 5-month-old girl showing vasculitis-related infarcts at bilateral anterior cerebral artery, bilateral middle cerebral artery, and right posterior cerebral artery territories.

Corticosteroid also improved survival and neurological outcomes in children with Stage II and Stage III TB meningitis.³⁴ In our experience, 10 (76.9%) of 13 patients in Stage II and Stage III received adjuvant steroid therapy and the outcome was generally good except for three (23.1%) in Stage III with sequelae of mental retardation, paraplegia, and voiding dysfunction; two of these patients died.

In conclusion, cases of childhood TB have increased in the past decade. This is probably due to higher clinical alertness and improved diagnostic modalities. A bimodal age distribution was noted in pulmonary and disseminated TB. Children with pulmonary and disseminated TB are more likely to have positive contact histories and culture results. An aggressive diagnostic approach and effective treatment are crucial for the prognosis of CNS TB because delayed diagnosis and treatment are associated with poor outcomes. CNS TB usually presents as part of disseminated or miliary TB in children. Therefore clinical manifestations, household contact history, CSF analysis, molecular microbiological method, image studies, and a search for other organ involvements are important for prompt diagnosis and treatment of CNS TB. Early diagnosis and treatment may lead to favorable outcomes in CNS TB.

Conflicts of interest

All contributing authors declare no conflicts of interest.

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