



ORIGINAL ARTICLE

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



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Tuberculosis

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.

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