Chest computerized tomography scan findings in 74 children with tuberculous meningitis in southeastern Turkey

Ahmet Yaramış[1], Yaşar Bükte[2], Selahattin Katar[1], M. Nuri Özbek[1]

Departments of [1]Pediatrics, and [2]Radiology, Dicle University Faculty of Medicine, Diyarbakır, Turkey

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This prospective study was done over seven years from 1996 to 2003 to investigate the chest computed tomography scan findings along with other radiologic examinations that included chest roentgenography and cranial computed tomography in children with tuberculous meningitis (TBM). Chest roentgenography demonstrated abnormal findings in 32 cases (43%) (hilar adenopathy, 32%; miliary pattern, 18%; bronchopneumonic infiltrate, 24%), while chest computerized tomography was abnormal in 65 cases (88%; p<0.005): mediastinal and hilar lymphadenopathy were present in 46% (p<0.005); miliary pattern, in 23% (p<0.05); and bronchopneumonic infiltrate, in 23% (p<0.05). Cranial computerized tomography was abnormal in 68 cases (92%). Chest computerized tomography scan helps establish the diagnosis of TBM when chest radiography is normal or inconclusive, and it is useful in assessing children with suspected TBM.

Key words: computed tomography, chest, children, tuberculous meningitis.

Rates of tuberculosis (TB) are increasing in many areas of the world, including Turkey, where the incidence is 36 per 100,000 population[1,2]. Despite the availability of many antituberculous agents, tuberculous meningitis (TBM) still carries significant morbidity in children, and its mortality is between 15% to 32%[3-6].

The diagnosis of TBM remains difficult in children, particularly in those younger than five years, because many patients initially have vague, non-specific signs and symptoms[7]. Childhood TBM arises as a complication of primary pulmonary infection, usually within six months of onset. Accurate diagnosis may be delayed because chest radiographs can be normal in 28-43% of children with intracranial tuberculosis[4,8]. Hilar adenopathy occurs in most cases of pediatric primary TB but may be difficult to detect in chest radiographs[9]. Thus, the use of other imaging methods such as computed tomography (CT) scan of the chest may be needed to improve the precision of the diagnosis. Our aim was to examine in a prospective study whether chest CT brings additional information for the diagnosis of pediatric TBM.

Material and Methods

From January 1996 to February 2003, a total of 74 children were admitted with TBM to Dicle University Hospital, Unit of Pediatric Infectious Diseases. Doerr et al.'s[10] criteria were used for diagnosis of TBM (Table I). Demographic and clinical data, history of exposure to adults with TB, and radiographic and microbiologic findings were recorded. Informed consent was obtained from the parents and the study protocol was reviewed and approved by the Institutional Review Board (IRB) of the Department of Pediatrics.

Patients were classified into three stages at admission: briefly, stage I: conscious, non-specific symptoms and no neurological signs; stage II: some degree of mental confusion and neurological signs; and stage III: unconscious, with paralyses and signs of intracranial hypertension[3]. The tuberculin skin test (Mantoux test) was performed by intradermal injection with 5 TU PPD solution into the most superficial layer of the skin of the forearm and induration (in mm) (not erythema) was measured after 72 hours in all patients. A response of ≥10 mm was considered positive

Table I. Case Definition of CNS TB by Microbiologic or Clinical Criteria

Microbiologic case definition. One of the following:
1. Isolation of *Mycobacterium tuberculosis* from CSF.
2. Abnormal neurologic signs and symptoms, CSF, or cranial CT or MRI consistent with CNS TB, and isolation of *Mycobacterium tuberculosis* from any site.

Clinical case definition. Abnormal neurologic signs and/or symptoms, and more than two of the following:
1. Discovery of adult source case with contagious TB who had significant contact with child.
2. Presence of Mantoux (5 TU) skin test reaction ≥10 mm of induration, or ≥5 mm of induration if child had close contact with infected adult*.
3. CSF abnormalities without evidence of other infectious cause.
4. Abnormalities on cranial CT or MRI consistent with CNS TB.

* ≥15 mm of induration was considered positive for children with BCG (BCG is in the routine immunization program of Turkey). CSF: Cerebrospinal fluid, CT: Computerized tomography, MRI: Magnetic resonance imaging, CNS: Central nervous system, TB: Tuberculosis, TU: tuberculin unit.

for children without Bacille Calmette-Guérin (BCG) immunization, and ≥15 mm if the patient had received BCG immunization. BCG vaccination status was determined by the observation of scar formation. An epidemiologic linked source case was defined as contact with an active TB contagious person within the previous 24 months. Human immunodeficiency virus (HIV) infection was suspected in seven patients and tested by ELISA method. Chest radiograph, chest CT, and cranial CT were performed in all patients within 10 days after the admission. CT scanning of the chest and cranium were performed with a conventional scanner (Toshiba-Xvision spiral CT scanner, Japan). The criterion of mediastinal tuberculous lymphadenitis on contrast enhanced CT scans was accepted as the characteristic appearance consisting of central areas of low attenuation associated with peripheral rim enhancement and obliteration of surrounding perinodal fat[11]. Cerebrospinal fluid (CSF) as well as gastric aspirate and sputum specimens were obtained for acid-fast bacilli (AFB) stain and culture, following standard methods for collection and processing of the samples. Early-morning gastric aspirates were obtained in patients who were unconscious or too young to expectorate. A nasogastric tube was placed before awakening on three consecutive mornings and gastric secretions were obtained by lavage with 10 to 20 ml of distilled water. Cultures and susceptibility testing were performed using Lowenstein-Jensen medium and the Bactec radiometric system. Specimens were stained by the Ziehl-Neelsen method. Complete blood cell count, serum alanine and aspartate transaminase, uric acid, creatinine, blood urea nitrogen, and bilirubin levels were determined at the time of diagnosis in all patients.

Statistical analysis was done by "significance test between two percentages for dependent groups". Probability of error was $\alpha = 0.05$.

Results

The age of the patients (n=74) ranged from 5 months to 15 years (mean 4.3 years); 51 (69%) were younger than five years and 34 (46%) younger than two years. Thirty-nine (53%) were boys. The majority of patients were admitted in stage II (38%) and III (51%) of the disease. Twenty patients (27%) had malnutrition; none had HIV infection. A family history of TB was encountered in 52 patients (70%). Only 18 patients (24%) had a positive tuberculin skin test result at admission. Only 8 patients (11%) had a history of single BCG vaccination, and all of these patients had single BCG scar. The vaccination times in these patients were longer than five years before admission time. Fever was reported in 65 (88%), nuchal rigidity in 58 (78%), altered consciousness in 47 (64%) and seizures in 37 (50%) patients (Table II). None had received antituberculosis treatment before.

Table II. Symptoms and Signs at Presentation

N=74	%
Fever	88
Vomiting	83
Nuchal rigidity	78
Altered consciousness	64
Headaches	53
Seizures	50
Loss of appetite	47
Changes in personality	46
Weight loss	41
Irritability	32
Cranial nerve paresis	29
Cough	23

Mycobacterium tuberculosis grew in 14 of the 74 (19%) CSF samples. Only 5/74 patients (7%) had a CSF smear positive for AFB. Serum sodium concentration of 132 mmol/L or less without evidence of hemodilution suggested inappropriate antidiuretic hormone secretion in 41 patients (55%). Lumbar puncture was performed in all patients: CSF results were compatible with TBM (i.e., predominance of lymphocytes with elevated protein and reduced glucose concentrations) in 64 (86%) cases.

Patients were treated with a 12-month regimen, initially with isoniazid, rifampin, pyrazinamide, and streptomycin, and with two drugs (isoniazid and rifampin) after two months. Prednisolone 2 mg/kg/day was given for one month and then gradually tapered. One patient with multiple tuberculomata responded to anti-TB medications, but the duration of treatment was extended to 26 months until complete regression of the lesions.

Imaging Results

Abnormal chest X-ray was noted in 32 (43%) cases, with a variety of findings including hilar adenopathy (32%), bronchopneumonic infiltrate (24%), miliary pattern (18%), and, in one case, cavitation. Miliary infiltrates tended to occur in very young children (median age 31 months; range: 7 months - 6 years) while consolidation tended to occur over all ages.

On the other hand, abnormal chest CT was noted in 65 (88%) cases, with a variety of abnormalities including mediastinal and hilar lymphadenopathy (46%), bronchopneumonic infiltrate (23%), and miliary pattern (23%). The right paratracheal, tracheobronchial, and subcarinal nodes were involved in 20 (27%) patients, left hilar nodes in 6 (8%) patients, and bilateral hilar nodes in 8 (11%) patients. Six (8%) patients with bronchopneumonic infiltrate had segmental (n: 2) or lobar (n: 4) consolidation. In 13 (18%) cases, lymphadenopathy was seen with concomitant parenchymal lesions. Bilateral pleural thickening with loculated effusion was seen in 1 patient. Lesions not observed on chest radiographs but detected on CT scans were mediastinal or hilar lymphadenopathy (n=10 cases), parenchymal lesions (n=5 cases), miliary infiltrates (n=4), and cavitation (n=1). In addition, calcifications or necrosis within the enlarged nodes was seen on the CT scan but not on X-rays of 5 cases (7%) ($p<0.05$) (Table III).

Table III. Chest Radiography and CT Scan Findings in all Patients at Admission

	Chest radiography		Chest CT		
Findings	n=74	%	n=74	%	P value
Hilar-mediastinal lymphadenopathy	24	32	34	46	<.005
Miliary pattern	13	18	17	23	<.05
Bronchopneumonic infiltrate	18	24	23	31	<.05
Cavitation	1	1	2	3	>.05
Calcifications or necrosis within the enlarged nodes	0	0	5	7	<.05
Minimal pleural effusion with thickening	0	0	1	1	>.05

Cranial CT was abnormal in all cases: 68 (92%) had hydrocephalus, 27% basilar meningitis, 17% infarction, and 1 case, multiple tuberculomata of the brain.

Discussion

Diyarbakır, a province of southeastern Turkey, has consistently high TB and TBM rates among children. Our hospital is the main pediatric referral hospital for the region and admitted 332 children with TBM between August 1988 and July 2002[12-15]. As the current series illustrates, TBM presents with various nonspecific symptoms in children: coughing, weight loss, headache, and night sweats were common in patients above five years, while fever, irritability, loss of appetite, vomiting, changes in consciousness, seizures and cranial nerve paresis were frequent in those younger than five years. Accurate evaluation of pulmonary disease is important in such children because it may suggest the diagnosis of TBM in the absence of specific symptoms and signs, and affect clinical approach and management. Although the value of chest CT has been extensively investigated in adults with postprimary TB[16,17], to our knowledge,

it has not been discussed in children with central nervous system (CNS) tuberculosis. Chest CT scan detected paratracheal nodes in 70-88% of children with primary pulmonary TB[18,19]. It showed lymphadenopathy in up to 60% of children with pulmonary TB and normal radiographs[20]. Kim et al.[21] reported on 41 children with confirmed pulmonary TB in whom chest radiograms failed to reveal lymphadenopathy and parenchymal abnormality, which were detected by CT scan in 21% and 35%, respectively. In our previous study of 214 patients with TBM, we observed abnormal chest X-ray findings in 187 (87%), consisting of hilar adenopathy (33%), parenchymal infiltration (33%), miliary pattern (20%) and pleural effusions (1%)[12]. CT is more sensitive for the detection of enlarged lymph nodes and lung lesions such as endobronchial disease, early cavitation, and bronchiectasis following pulmonary TB when chest radiographs are normal or unhelpful. Our current study showed that up to 27% of cases with normal radiographs had abnormalities on chest CT, pointing to the value of this method in diagnosing TB. Miliary pattern and cavitation in the chest CT scan were noted in 17 (23%) and 2 (3%) cases, respectively. Miliary TB is one of the most severe manifestations of TB, commonly encountered in the young child[22,23]. Cavitation is rare in young children but more common in developing countries[24]. In chest CT scan images, hilar and mediastinal nodes present a central hypodense area corresponding to caseation necrosis and rim enhancement after contrast medium administration. This feature suggests the diagnosis but has also been described in lymphoma, metastasis and other infections[21,25,26]. The prevalence of lymphadenopathy in TB infection is highest in children less than three years of age: this is reflected in our patient group with a median age of 21.5 months[27,28].

Pathological changes in cranial TB are arteritis, infarction, hemorrhage, and hydrocephalus[29,30]. Communicating hydrocephalus in CNS TB usually is caused by blockage of the basilar cistern with thick tuberculous exudates in the acute stage and adhesive leptomeningitis in the chronic stage of disease[31]. In some cases, blockage and dilatation of the fourth ventricle can produce structural hydrocephalus. In this study, cranial CT was abnormal in all cases examined, with hydrocephalus being the most common finding. Waecker and Connor[32] described 30 children with TBM, all less than six years of age, in whom 100% had hydrocephalus at presentation. In another study in Turkey, hydrocephalus was present in 98% of 52 children with TBM[33]. While hydrocephalus or basilar meningitis suggests TBM especially in endemic areas, the demonstration of pulmonary involvement brings further contribution to this diagnosis.

Early diagnosis and treatment are essential to prevent morbidity and mortality in TBM. The use of chest CT scan may improve the precision of the diagnosis.

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