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Retrospective review of paediatric pulmonary tuberculosis from two local hospitals in Hong Kong

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Abstract

Objectives: This study aimed to (1) review demographic and clinical data of children and adolescents with pulmonary TB managed in two local hospitals, and (2) evaluate the use of computed tomography (CT) thorax in its diagnosis. ***Methods:*** We retrospectively reviewed medical records of paediatric patients (age on admission </=18 years old) with the discharge diagnosis of "Respiratory tuberculosis" or "Pulmonary tuberculosis" and were admitted to Tuen Mun Hospital and Prince of Wales Hospital between 1 January 2003 and 31 December 2012. Data on demography, clinical presentation, investigations and imaging results were captured. Further subgroup analysis was performed between younger children (age </=12 years old) and adolescents (age >12 years old). ***Results:*** One hundred and thirty-four patients (mean age (SD)=14.3 (3.5) years old, 71 males) with pulmonary TB were identified. Eighty-six of them (64.2%) were born in Hong Kong. The two commonest presentations were cough (80.6%, mean 4.1 weeks) and fever (61.9%, mean 11.6 days). Twenty-eight patients (20.9%) presented with pleural effusion. Thirty-nine patients (29.1%) had positive contact history with an individual diagnosed to have TB. One hundred and six subjects (79.1%) had positive Mantoux test (induration >/=10 mm). Respiratory samples (sputum, gastric aspirate or broncho-alveolar lavage) were obtained in 130 patients. Positive TB smear was found in 38 patients (29.2%) and mycobacterium tuberculosis was isolated in 94 patients (72.3%). Older age (age>12 years old, 89.5% vs. 26.1%, p=0.05), prolonged cough (>/=2 weeks, 73.7% vs. 40.2%, p=0.001), night sweating (34.2% vs. 15.2%, p=0.03) and higher ESR (63.9 mm/hr. vs. 48.3 mm/hr., p=0.016) were found in significantly higher proportion of patients with positive smear result. One hundred thirty-two patients (98.5%) had abnormal chest X-ray (CXR); upper zones involvement was more likely to be present in smear positive group (71% vs. 46.7%, p=0.013). Computed tomography (CT) of thorax was performed in 50 patients (38.8%) and it was more likely to be performed in patients with negative TB smear (45.7% vs. 21.1%, p=0.01) and younger age (58.6% vs. 33.3%, p=0.018). Anti-TB treatment was started in 17 patients (13.1%) with negative TB smear basing on the CT thorax findings. In subgroup analysis comparing younger aged children with adolescents, latter were more likely to present with shorter duration of fever (10.1 days vs. 17.2 days, p=0.044), haemoptysis (33.3% vs. 10.3%, p=0.019) and malaise (13.3% vs. 0%, p=0.04). Adolescents with pulmonary TB were also more likely to have upper zones involvement on CXR (60% vs. 24.1%, p=0.001). Greater proportion of adolescents had positive TB smear and culture compared to subjects of a younger age (33.3% vs. 14.3%, p=0.05; 79.4% vs. 46.4%, p=0.001). Furthermore, adolescents were more likely to have tiny nodules, tree-in-bud appearance and cavitation present in their CT imaging (46.2% vs. 11.5%, p=0.034; 32.7% vs. 5.8%, p=0.035; 21.2% vs. 1.9%, p=0.044 respectively), resembling adult-type TB disease. ***Conclusion:*** We documented age difference in clinical presentation and imaging findings, with pulmonary TB in adolescents behaving like an adult disease. In cases of diagnosis dilemma, CT thorax might be helpful in guiding management.

Keywords: Childhood, Hong Kong, Paediatric, Pulmonary tuberculosis

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Introduction

Hong Kong is regarded as a high tuberculosis (TB) burden, low HIV (Human Immunodeficiency Virus) burden region. Prevalence of tuberculosis in Hong Kong was 100 in 100,000 population, and paediatric tuberculosis (age <15 years old) accounted for <1% of all reported cases in 2011. This figure probably underestimated the true burden of tuberculosis in Hong Kong, as TB in adolescence was not included in the paediatric group calculation.[1] There is limited local data on paediatric tuberculosis. This can be partly explained by diagnostic difficulty of the paucibacillary nature of disease and therefore, negative TB smear and culture. Another reason is that childhood TB may not be considered as a public health threat to general population when compared with adults. However, undiagnosed tuberculosis may carry mortality and morbidity as well as serving as a reservoir for adult forms of disease.

Pulmonary tuberculosis in adolescence tends to be symptomatic and thence have more positive bacteriological results than younger children. Their clinical and radiological findings behave more like "adult-type" tuberculosis.[2-4] However, diagnosing pulmonary TB in the paediatric population is not straightforward. In cases of diagnosis dilemma, further investigations include molecular tests and computed tomography (CT) of thorax will be performed. Although CT thorax is not incorporated into the diagnostic algorithms of pulmonary TB,[5-7] CT scan can provide additional diagnostic information in many of the cases.

This study aimed to review demographic and clinical data of paediatric pulmonary tuberculosis in two local hospitals (Tuen Mun Hospital and Prince of Wales Hospital, New Territories). Clinical presentations and laboratory results between younger children and adolescents were evaluated. The use of CT thorax in the diagnosis of pulmonary tuberculosis was also reviewed.

Methods

This was a retrospective review of paediatric patients admitted to Tuen Mun Hospital and Prince of Wales Hospital within a 10-year period. These two hospitals are two of the major regional hospitals in New Territories, Hong Kong. A study period of ten years was chosen because medical records before this period were mostly incomplete. Eligible patients from these two hospitals were identified from the Clinical Data Analysis and Reporting System (CDARS). Patients were regarded as eligible if (1) they were admitted between 1 January 2003 and 31 December 2012; (2) age less than or equal to 18 years old at the time of admission; (3) discharge diagnosis of "Respiratory tuberculosis" or "Pulmonary tuberculosis" was made. Hospital numbers were retrieved and relevant clinical data and investigation results were evaluated. Hospital Ethnic Committee approval was obtained for this study.

Children were defined as age less than or equal to 12 years while those with age greater than 12 years were classified as adolescents. Confirmed disease was defined as isolation of mycobacteria tuberculosis in specimen with compatible clinical, radiological, and/or histopathological features. Probably disease was defined as negative bacteriological growth of mycobacteria tuberculosis but have compatible tuberculin skin test (induration >/=10 mm), clinical presentation, radiological findings and/or histopathological diagnosis. In Hong Kong, tuberculin skin test (TST) was performed by intradermal injection of 2 tuberculin units of PPD-RT23 (0.1 ml) and results were evaluated 48-72 hours after the injection. A positive TST was defined as induration >/=10 mm.

SPSS version 20.0 was used for data analysis. Differences between groups were compared with Chi-square test for categorical variables; when appropriate, Fisher exact test was used. ANOVA test was used for comparison of means. Statistical significance was defined as $p<0.05$.

Results

Demographics

There were 135 paediatric patients identified from the study period (Table 1). One patient presented with isolated TB cervical lymphadenopathy without any respiratory involvement was excluded. The remaining 134 patients were diagnosed with pulmonary TB (including microbiological confirmed cases and probable tuberculosis) with standard anti-tuberculosis treatment given and were followed up by either hospital outpatient clinics or Chest clinics. The mean (standard deviation, SD) age of our study population was 14.3 (3.5) years old (Range: 11 months to 18 years old) with male to female ratio=1.1. More than 60% of them were born in Hong Kong; 12.7% was born in Mainland China and 3% was born in other Asian countries like Indonesia, Nepal, Pakistan and Philippines. There were 11 patients

with comorbidities that required long term follow up. There were four patients with asthma, one patient with Bechet disease, one patient with Juvenile idiopathic arthritis, two patients with leukemia, two patients with nephrotic syndrome/lupus nephritis and one patient with psoriasis. Some of them had history of long-term systemic steroid use.

Clinical presentation

Among the classical presenting symptoms of pulmonary tuberculosis, the commonest symptom was cough (80.6%) with a mean duration of 4.1 weeks; followed by fever (61.2%) with a mean duration of 11.6 days (Table 2). Other symptoms included haemoptysis (28.4%), subjective weight loss (28.4%), night sweating (21.6%), malaise (10.4%) and shortness of breath (9.7%). Twenty-eight patients (20.9%) presented with pleural effusion. There were 15 patients with extrapulmonary involvement (11.2%) in addition to pulmonary tuberculosis. Twenty-eight patients (20.9%) travelled to mainland within 6 months before admission while 39 patients (29.1%) had contact history with individuals diagnosed to have tuberculosis (37 out of 39 patients had contacted family members with TB). Ninety-one patients had positive physical signs on admission (mainly reduced air entry and crepitation). Only one patient required oxygen supplement upon admission. Forty-seven patients (35.1%) received antibiotics prior to hospital admission.

Table 1. Demographics of the study population

		Percentage (%)
Age		
Mean (years)	14.3 (range: 11 months to 18 years old)	
Median	16.0	
</=12 years old	29	21.6
>12 years old	105	78.4
Gender		
Male	71	53
Female	63	47
Place of Birth		
Hong Kong	86	64.2
Mainland China	17	12.7
Others	4	3.0
n/a	27	20.1
Comorbidities (*)	11	8.2
Respirology	4	
Rheumatological	2	
Haematological	2	
Renal	2	
Dermatological	1	

Note (*)

Respirology – 3 cases of asthma with ventolin use as required and 1 case with regular inhaled corticosteroid.

Rheumatology – 1 case of Bechet disease without use of steroid/immunosuppressant and 1 case of Juvenile idiopathic arthritis required steroid/immunosuppressant

Haematology – 2 cases of leukaemia with history of high dose systemic steroid

Renal – 2 cases of nephrotic syndrome/lupus nephritis

Dermatology – 1 case of psoriasis

Biochemistry, microbiological and imaging results

Mantoux test was performed in all cases. Positive mantoux test was defined by induration >/=10 mm in this study. One hundred and six patients (79.1%) had positive mantoux test and the mean induration was 14.9 mm (SD=9.1 mm). The mean erythrocyte sedimentation rate (ESR) was 53.5 mm/hr. (SD=33.4), mean C-reactive protein (CRP) was 41.7 mg/L (SD=48.1) and mean white cell count (WCC) was $9.7x10^9$/L (SD=4.3). There were altogether 130 patients with respiratory samples obtained. Respiratory samples included sputum, gastric aspirate or broncho-alveolar lavage (BAL). If a patient had both sputum and gastric lavage samples taken, it would be counted as one respiratory sample. Any positive result in any one of the sample types would be regarded as positive respiratory sample. There were 38 patients (29.2%) with positive TB smear and 94 patients (72.3%) with positive TB culture from the respiratory samples.

Among the AFB smear positive group, they were significantly found in patients with older age (89.5% vs. 26.1%, p=0.05), prolonged cough >/=2 weeks (73.7% vs. 40.2%, p=0.001), night sweating (34.2% vs. 15.2%, p=0.03), positive physical signs (81.6% vs. 62%, p=0.039) and higher ESR (63.9 mm/hr. vs. 48.3 mm/hr., p=0.016). Fewer cases of effusion were found in smear positive group (5.3% vs. 25%, p=0.013).

Early morning urine (EMU) on three consecutive days was obtained in 85 patients (63%). All were smear negative and positive culture was found in 6 cases (7.1%). All had positive respiratory culture for the diagnosis of tuberculosis. Among the 6 cases: two patients had isolated pulmonary TB, one patient had miliary TB and three patients had extrapulmonary involvement (TB meningitis, TB larynx and TB abdomen with liver and spleen involvement).

One hundred and thirty-two patients (98.5%) had abnormal chest radiographs (CXR). (Descriptions include non-specific infiltration, hilar lymphadenopathy, effusion, collapse and fibrotic changes). Upper zones

Table 2. Summary of clinical presentation and microbiological characteristics

	Frequency	Percentage (%)
Fever	83	61.9
Mean (days)	11.6 (among fever +ve cases)	
>1 week	38	28.4
Cough	108	80.6
Mean (weeks)	4.1 (among cough +ve cases)	
>/=2 weeks	68	50.7
>/=3 weeks	50	37.3
Night sweat	29	21.6
Haemoptysis	38	28.4
Weight loss (subjective)	38	28.4
Malaise	14	10.4
Shortness of breath	13	9.7
Cervical lymph nodes	5	0.9
Effusion	28	20.9
Miliary TB	1	0.7
TB meningitis	1	0.7
Other extrapulmonary# involvement other than cervical lymphadenopathy	8	6.0
Travel history	28	20.9
Contact history	39	29.1
Physical sign	91	67.9
Antibiotic before	47	35.1
Biochemistry		
MT2 – mean	14.9 (SD=9.1)	
MT2 >/=10 mm	106	79.1
ESR (mm/hr) – mean	53.5 (SD=33.4)	
CRP (mg/L) – mean	41.7 (SD=48.1)	
WCC (10^9/L) – mean	9.7 (SD=4.3)	
Microbiology		
Resp smear done*	Total=130	
Positive	38	29.2
Negative	92	70.8
Resp culture done	Total=130	
Positive	94	72.3
Negative	36	27.7
Imaging		
Abnormal CXR	132	98.5
CT thorax done	50	37.3

SD = standard deviation

(#) 5 cases of bowel or peritoneal involvement, 1 case of larynx and renal involvement, 1 case of constrictive pericarditis, 1 case with subcutaneous abdominal mass.

(*) Resp smear/culture = smear/culture obtained from respiratory tract by sputum, gastric lavage or bronchoalveolar lavage.

- 115 sputum samples obtained, 80 cases with TB culture +ve
- 48 gastric aspirates performed, 24 cases with TB culture +ve
- 15 BALs obtained, 6 cases with TB culture +ve

involvement was commonly found in smear positive group (71% vs. 46.7%, p=0.013). Computed tomography (CT) of thorax was performed in 52 patients (38.8%) and significantly more CT thorax was performed in patients with negative TB smear (45.7% vs. 21.1%, p=0.01).

Pleural effusion

Pleural effusion was found in 28 cases (Table 3). TB smear and culture of pleural fluid was collected in 24 cases. In the remaining 4 cases, no fluid sample was obtained due to small amount of pleural effusion. Only 2 patients had positive TB smear (7.1%) and 11 patients had positive TB culture of pleural fluid (39.3%). Among the 28 patients, pleural biopsy was performed in 19 patients and it was positive in 17 cases (89.5%). Positive pleural biopsy for TB was defined as positive TB smear or culture, presence of granuloma, or granulomatous inflammation.

Subgroup analysis according to age groups

There were 29 children with mean age of 9 years old and 105 adolescents with mean age of 15.8 years old in our study population (Table 4). There was no significant difference in terms of gender and race distribution. As for the clinical presentation, adolescents presented with shorter duration of fever than children (10.1 days vs. 17.2 days, p=0.044), more haemoptysis (33.3% vs. 10.3%, p=0.019) and malaise (13.3% vs. 0%, p=0.04). There was no significant difference in terms of travel history, contact history, antibiotics use before admission, physical signs, mantoux test and biochemical results including ESR, CRP and WCC.

More adolescents had disease involving the upper zones on CXRs (60% vs. 24.1%, p=0.001) while significantly more children had abnormalities over the lower zones (62% vs. 38.1%, p=0.033). More CT thorax was performed in children (58.6% vs. 33.3%, p=0.018). CT findings of tiny nodules, tree-in-bud appearance and cavitation were more likely to be present in adolescents (46.2% vs. 11.5%, p=0.034; 32.7% vs. 5.8%, p=0.035; 21.2% vs. 1.9%, p=0.044 respectively). One hundred and thirty respiratory samples were obtained for TB smear and culture. More positive TB smear and positive TB culture were found in the adolescent group (33.3% vs. 14.3%, p=0.05; 79.4% vs. 46.4%, p=0.001).

Table 3. investigation results from pleural fluid or biopsy

Pleural effusion (n=28)	Frequency	Percentage (%)
Smear		
Smear +ve	2	7.1
Smear -ve	22	78.6
Not done #	4	14.2
Culture		
Culture +ve	11	39.3
Culture -ve	13	46.4
Not done	4	14.3
Pleural biopsy (n=19)		
Positive *	17	60.7
Non-specific	2	7.1
Not done	9	32.1

Note: (#) Not done due to small amount of effusion only. (*) Include positive TB smear or culture or presence of granulomatous inflammation.

CT thorax findings and microbiology results

CT thorax in paediatric patients was not uncommonly performed. There were 50 patients with CT thorax performed (50/130=38.5%) and most of them were done during admission or shortly after discharge. Retrospectively analysis of the CT thorax findings and the respiratory samples results were performed (Table 5, Figure 1). There were 94 patients with positive TB culture and among them, 29 CT thorax (30.9%) were done. On the other hand, there were 36 patients with both negative TB smear and culture; and 21 CT thoraxes were performed (58.3%, p=0.05). Common CT thorax findings included: centrilobular tiny nodules, tree-in-bud appearance, perihilar lymphadenopathy, cavitation, consolidation, collapse, pleural effusion, pleural thickening, fibrosis, granuloma, bronchiectasis, interlobular septal thickening, bronchial thickening and military nodules. There was no statistical significant difference in most CT findings between TB culture positive and negative groups. CT finding of cavitation was the only statistical significant difference between culture positive and negative groups (37.9% vs. 4.8%, p=0.008).

Discussion

Hong Kong is classified as a high TB burden region, and the prevalence is about 100 in 100,000 population. Childhood tuberculosis roughly accounted for <1% for total TB cases.[1] This number might be underestimated due to the paucibacillary nature of disease and non-specific presentation of childhood pulmonary TB. Furthermore, Hong Kong is one of the most densely populated places in the world[8] and the population is rapidly expanding. Hong Kong population will be approaching 7.5 million by year of 2020. In order to control the spread of tuberculosis and minimise the disease reservoir for adult form of disease, early diagnosis and treatment of paediatric tuberculosis is necessary. In general, a person with active but untreated TB will infect 10-15 people per year.[9] Since the Human

Table 4. Subgroup analysis according to age groups

Total (n=134)	Age </= 12 (n=29)	Age > 12 (n=105)	P value
Mean age	9.0	15.8	
Gender			0.401
Male	13 (44.8%)	58 (55.2%)	
Female	16 (55.2%)	47 (44.8%)	
Race			0.469
Hong Kong	22 (75.9%)	64 (61.0%)	
Mainland China	2 (6.9%)	15 (14.3%)	
Others	1 (3.4%)	3 (2.9%)	
Not available	4 (13.8%)	23 (21.9%)	
Clinical presentation			
Fever			
Mean (days)^	17.2	10.1	**0.044**
>1 week	8 (27.6%)	30 (28.6%)	0.917
Cough			
Mean (weeks)^	3.6	4.2	0.972
>/= 2 weeks	13 (44.8%)	53 (50.5%)	0.677
>/= 3 weeks	10 (34.5%)	40 (38.1%)	0.830
Night sweat	5 (17.2%)	24 (22.9%)	0.617
Haemoptysis	3 (10.3%)	35 (33.3%)	**0.019**
Weight loss (subjective)	4 (13.8%)	34 (32.4%)	0.063
Malaise	0 (0.0%)	14 (13.3%)	**0.040**
Shortness of breath	2 (6.9%)	11 (10.5%)	0.733
Lymph nodes	1 (3.4%)	4 (3.8%)	0.928
Effusion	7 (24.1%)	21 (20.0%)	0.614
Travel history	6 (20.7%)	22 (21.0%)	0.975
Contact history	7 (24.1%)	32 (30.5%)	0.656
Physical sign	18 (62.1%)	73 (69.5%)	0.503
Antibiotic before	11 (37.9%)	36 (34.3%)	0.826
Biochemistry			
MT2 – mean (mm)	15.7	14.7	0.609
MT2 >/=10 mm	22 (75.9%)	84 (80%)	
ESR (mm/hr) – mean	47.3	55.1	0.270
CRP (mg/L) – mean	47.7	40.0	0.442
WCC (10^9/L) – mean	9.7	9.7	0.965
Radiology			
CXR-upper lobe	7 (24.1%)	63 (60%)	**0.001**
CXR-lower lobe	18 (62%)	40 (38.1%)	**0.033**

(continued on page 10)

Table 4. Subgroup analysis according to age groups (cont'd)

Total (n=134)	Age </= 12 (n=29)	Age > 12 (n=105)	P value
CT performed (n=52)	17 (58.6%)	35 (33.3%)	**0.018**
Tiny nodules	6 (11.5%)	24 (46.2%)	**0.034**
Tree-in-bud	3 (5.8%)	17 (32.7%)	**0.035**
Hilar LNs	9 (17.3%)	23 (44.2%)	0.532
Cavitation	1 (1.9%)	11 (21.2%)	**0.044**
Consolidation	11 (21.2%)	20 (38.5%)	0.549
Collapse	5 (9.6%)	8 (15.4%)	0.731
Effusion	4 (7.7%)	8 (15.4%)	0.910
Pleural thickening	5 (9.6%)	3 (5.8%)	0.092
Fibrosis	1 (1.9%)	4 (7.7%)	1.000
Granuloma	3 (5.8%)	5 (9.6%)	0.699
Bronchiectasis	0 (0.0%)	6 (11.5%)	0.159
Interlobular septal thickening	1 (1.9%)	1 (1.9%)	0.542
Bronchial thickening	0 (0.0%)	2 (3.8%)	1.000
Miliary	0 (0.0%)	1 (1.9%)	1.000
Microbiology			
Resp smear done# (n=130)	28	102	**0.050**
Positive	4 (14.3%)	34 (33.3%)	
Negative	24 (85.7%)	68 (66.7%)	
Resp culture done (n=130)	28	102	**0.001**
Positive	13 (46.4%)	81 (79.4%)	
Negative	15 (54.6%)	21 (20.6%)	
Positive TB culture in other samples in those with negative smear and culture*	10	11	

Notes:

(^) Mean duration of cough among patients with cough; mean duration of fever among patients with fever

(#) Resp smear = smear samples obtained from respiratory tract by sputum, gastric lavage or bronchoalveolar lavage

(*) Other culture samples include lymph nodes biopsy, pleural fluid culture and pleural biopsy culture

Table 5. Summary of CT finding between positive and negative microbiological culture

	Resp culture POS	Resp culture NEG	P value
Total resp culture N=130	N=94	N=36	
CT performed N=50	29 (30.9%)	21 (58.3%)	**0.005**
Tiny nodules	19 (65.5%)	11 (52.4%)	0.393
Tree-in-bud	15 (51.7%)	5 (23.8%)	0.079
Hilar LNs	17 (58.6%)	15 (71.4%)	0.388
Cavitation	11 (37.9%)	1 (4.8%)	**0.008**
Consolidation	20 (69.0%)	11 (52.4%)	0.255
Collapse	8 (27.6%)	5 (23.8%)	1.000
Effusion	6 (20.7%)	6 (28.6%)	0.738
Pleural thickening	3 (10.3%)	5 (23.8%)	0.255
Fibrosis	4 (13.8%)	1 (4.8%)	0.738
Granuloma	4 (13.8%)	4 (19.0%)	0.706
Bronchiectasis	5 (17.2%)	1 (4.8%)	0.380
Interlobular septal thickening	1 (3.4%)	1 (4.8%)	1.000
Bronchial thickening	2 (6.9%)	0 (0.0%)	0.503
Miliary	1 (3.4%)	0 (0.0%)	1.000

Immunodeficiency Virus (HIV) burden of Hong Kong is relatively low[10] and hence the HIV testing is not routinely carried out in paediatric subjects with TB. All cases included in this study were presumed to be HIV negative.

There was 12.7% children born in mainland and more than 90% of the study population was now residing in Hong Kong. The caseload from the immigrants was not as high as the situation reported by many western countries.[11-13]

In many low TB prevalence countries, contact tracing or screening program identified people with TB.[11,12] In this study, contact history was identified in 29.1% of our study population and most of them had a first-degree relative with pulmonary TB. Two cases were identified by contact tracing and screening at Chest Clinic. Actually less than 1% of pulmonary TB was found by contact CXR screening as of year 2000.[13] There was no significant difference in history of TB contact among younger and older age groups. Indeed, the approach of passive case-finding (i.e. diagnosis was made in those presented with symptoms and came for medical attention) had been adopted in Hong Kong and was found to be more cost-effective.[13]

Respiratory smear was obtained from 130 patients. Sensitivity of mantoux test among the culture positive population was 77.7% and it was in concordance with other studies (ranges from 60-80%).[14-17] False positive results can happen if there is prior administration of Bacille Calmette-Guerin (BCG), infection by non-tuberculosis mycobacteria and misinterpretation; while false negativity can occur in several situations like improper injection technique, very young age, immunocompromised status or overwhelming TB infection.[7] An alternative available screening test is Interferon gamma release assays (IGRAs). It is an in vitro blood test of cell-mediated response to mycobacteria tuberculosis but it cannot distinguish between active TB versus latent infection.[18-20] It is not widely used in Hong Kong.

Thirty-eight cases (29.2%) were TB smear positive. TB culture was positive in all smear positive cases. Overall, mycobacterium tuberculosis was isolated in 94 cases (72.3%). The sensitivity of respiratory smear among respiratory culture positive cases was 40.4%. The detection rate of mycobacterium tuberculosis in sputum, gastric aspirate and BAL were 69%, 50% and 40% respectively. Although obtaining BAL was a relatively invasive procedure and only 15 smear-negative patients underwent this procedure, 6 patients were confirmed to have pulmonary TB by the BAL cultures alone. In addition to obtaining samples for culture, bronchoscopy is useful for detecting endobronchial TB and excluding other infections commonly found in immunosuppressed children.[21]

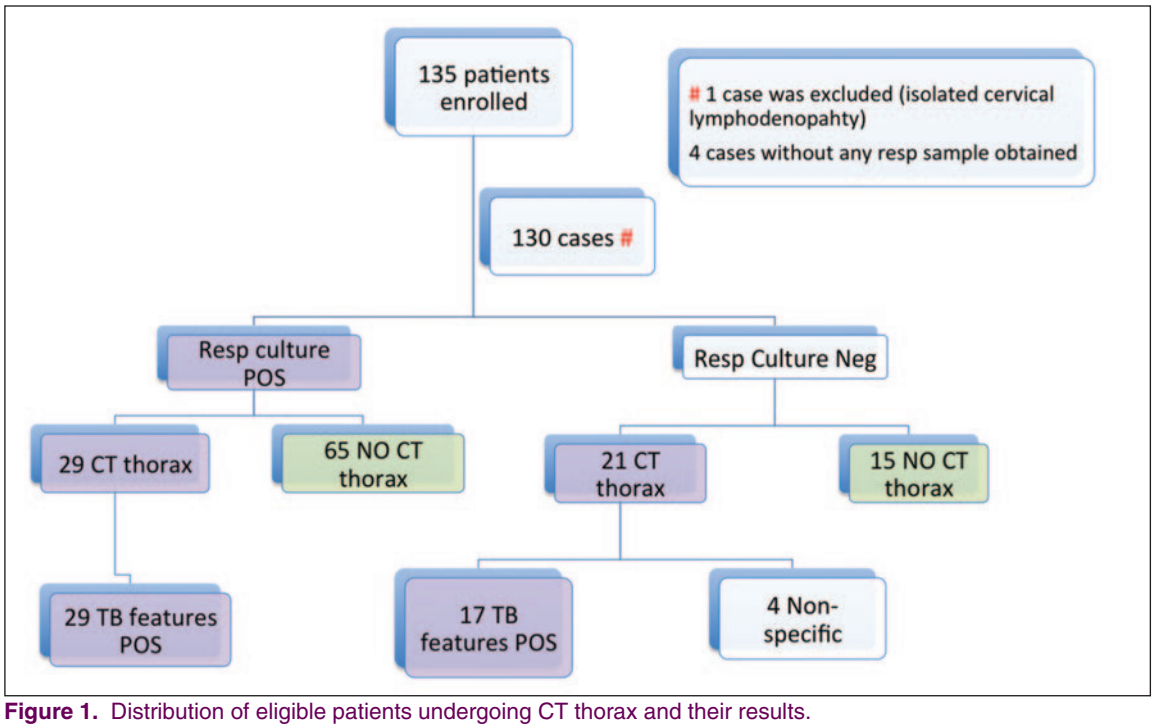

Figure 1. Distribution of eligible patients undergoing CT thorax and their results.

More than 60% (n=81) patients had EMU checked for mycobacteria tuberculosis in addition to the respiratory samples. All had negative TB smear and 6 of them had positive TB culture in the urine samples. Actually all of them were also culture positive in the respiratory samples. Two of them had isolated pulmonary TB and the other four had miliary or extrapulmonary involvement. These patients didn't have any urinary symptoms and all underwent imaging of urinary system and was normal. Based on this observation, this raises the question on whether it is necessary to save urine samples to diagnose pulmonary tuberculosis in patients without any urinary symptom. Further studies with larger population may be required to look into this.

It was postulated that children with TB was different from adolescents or even adults because of different physiological and immunological responses.[2,3,22-24] Their cell-mediated immunity is less effective than adult. Difference in clinical presentations, investigation findings and radiological involvements were found. Younger children presented with less systemic symptoms like haemoptysis and malaise than the older age group. Smear and culture positivity of respiratory samples were more commonly obtained in adolescents. This could be explained by the poor sputum expectoration effort and the paucibacillary nature of TB in younger children. Malaise is a subjective symptom and younger children might not be able to express their discomfort. The sensitivity of respiratory smear was 30% for younger children and 42% for adolescents among the positive respiratory culture. The sensitivity obtained from this study was slightly different from previous studies (less than 15% for younger children);[24-26] this may be due to difference in age group definition and different means of obtaining respiratory samples.

Upper zones involvement was likely due to post-primary TB (reactivation), an adult-type pattern. As for primary TB, lower zones were commonly involved; however, there was no consensus on the most common regions of involvements in primary TB.[27] In post-primary TB, the tendency of involvement of apicoposterior lung segments of upper lobes or the apical segments of lower lobes could be explained by the higher oxygen tension of that region and promote proliferation of mycobacteria.[28] There was age difference in CXR and CT thorax findings. Younger children had more lower zones involvement than adolescents while more adolescents had abnormal finding over upper zones of CXR. The typical CT findings of TB reactivation in adults (centrilobular nodules, branching linear and nodular opacities (tree-in-bud) and cavitation) were significantly noted in adolescence.[29] This echoed the findings of many previous studies, primary tuberculosis was usually diagnosed in young children, and adolescents behave more like the adult-type (reactivation).

Risk of TB progression is dependent on age and immunity. In view of the immaturity of immune system in young children, up to 50% of children less than 2 years old will progress to active disease within the 12 months of primary infection. The risk decreased with increased age until adolescence.[2] Primary TB acquired in adolescence was associated with higher risk (10-20%) of manifestation of adult-type disease.[2] In general, 50% of TB infection will progress early during the first 5 years after exposure and the remaining 50% will remain dormant and about 5-10% will have reactivation many years later.[4]

Since symptoms of pulmonary tuberculosis are non-specific most of the time. Screening by mantoux tests has limitations as discussed above. Inflammatory markers like ESR, CRP and WCC are non-specific as well and cannot differentiate from pulmonary TB from other pneumonia or lung pathologies. Yield of smear is notably low while yield of isolating mycobacteria tuberculosis (gold standard for diagnosis) from specimen is just slightly better. However, it takes at least 8-12 weeks for result. Therefore, the diagnostic clue of TB will rely on careful interpretation of CXRs. The finding of hilar or mediastinal lymph nodes is typical but not pathognomonic; and it is not easy to interpret. The sensitivity of CXR was about 40% and specificity was 70% in detecting TB related changes.[30,31] This is the reason why paediatric TB is a unique challenge for physicians in terms of making diagnosis and therapeutic choices. In cases of diagnosis dilemma, some cases will proceed for pleural fluid analysis, tissue diagnosis by pleural biopsy or lymph nodes biopsy if indicated. However, these are invasive procedures that can pose risks like sedation, trauma, infection and bleeding. In this case, CT thorax may play a role in diagnosis in those ambiguous cases before the availability of culture results.

In the last part of study, we retrospectively reviewed the CT findings among the positive and negative

respiratory culture groups to see if there is any significant difference. A total of 50 CT thoraxes were performed. From many literatures on CT thorax in pulmonary TB, the common findings include: centrilobular tiny nodules, tree-in-bud appearance, perihilar lymphadenopathy, cavitation, consolidation, collapse, pleural effusion, pleural thickening, fibrosis, granuloma, bronchiectasis, Interlobular septal thickening, bronchial thickening and military nodules.[9,29,32] We found that there was no statistical significant difference in most CT findings between TB culture positive and negative groups. The feature of cavitation was the only significant difference between them (37.9% vs. 4.8%, p=0.008). This difference could be accounted by the greater number of adolescents included in the positive culture group and actually more than 90% of CT evidence of cavitation was found within this group of patient. Cavitation is considered as the hallmark of TB reactivation and was present radiographically in 20-45% patients.[9,27,28] Although, there is no pathognomonic CT feature for diagnosing pulmonary tuberculosis, CT thorax may be useful in establishing the diagnosis of TB basing on this observation. In this study, 21 patients with negative respiratory smear (respiratory culture turned out to be negative as well) underwent CT thorax and 17 cases (13.1%) had the typical features mentioned above. Anti-tuberculosis medications were started based on the clinical presentation, CXR and CT findings. Good clinical responses were observed on follow-ups.

High-resolution CT (HRCT) carries a high sensitivity and negative predictive value as shown in previous study (Sensitivity 80-96%, specificity 50-76%, positive predictive value 67% and negative predictive value 93%).[20,33,34] It can help us to identify some significant or even subtle changes that were not detectable by plain radiographs. It may also help to delineate the extent of lung involvement and its complications, as well as differentiating primary or post-primary TB. It provides additional information in ambiguous cases like symptomatic patients with equivocal investigations or doubtful CXR.[33-36]

Radiation and possible cancer risks are of concern especially on young children.[37] Therefore, a wise selection of patients by treating physicians is required. With the development of low-dose CT and the emerging evidence of the usefulness of Magnetic Resonance Imaging (MRI) of thorax, we hope the risk of radiation will be further minimised.[30,38]

Limitations

Firstly, this is a retrospective study and information was retrieved by reviewing the admission notes and electronic medical records. There was missing data and possible data entry error. Secondly, the sample size in this study was not large but it was comparable with other cases series. Thirdly, control subjects (patients with other pulmonary pathology other than tuberculosis) were not included and we were unable to illustrate any significant clinical features or biochemical markers between patients with TB and other pulmonary diseases. Last but not the least, there might be interpersonal variation in interpretation of chest radiographs and CT thoraxes. CXR findings were based on the description in the case notes, as some old films were not available on the computer medical system. Features of pulmonary TB on CT were analysed according to the CT reports, which were written by different radiologists and from two different centers. It was possible that some radiological features of pulmonary TB were mentioned in more detail in some cases and less in others.

Conclusion

The burden of pulmonary TB is high in Hong Kong and paediatric tuberculosis contributed to a relative small proportion when compared with adults; however, this number cannot be ignored and diagnosis should not be delayed. A missing diagnosis will serve as a reservoir of adult disease and promote the spread of TB. The presenting symptoms are nonspecific and diagnosis are challenging. We are able to identify some difference in clinical presentation and investigations findings among the younger age group and adolescence. More efforts would be needed in order to diagnose pulmonary TB in young children. We found that there was no significant difference in CT thorax finding among the positive and negative culture groups. CT thorax was helpful in diagnosing 13.1% cases of pulmonary TB in the study population.

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