Tuberculosis in South and Central Africa

Understanding epidemiology - Improving diagnosis and management

Bélard, S.M.

Citation for published version (APA):
Chapter 4

Sonographic Findings of Abdominal Tuberculosis in Children with Pulmonary Tuberculosis

The Pediatric Infectious Disease Journal 2017 Dec 36(12):1224-1226
ABSTRACT

Ultrasound reports of 102 children with microbiologically confirmed or clinically diagnosed pulmonary tuberculosis (TB) showed that 23 of 37 (64%) and 23 of 65 (36%) had TB suggestive abdominal lymphadenopathy, and 16 of 37 (44%) and 8 of 65 (13%) had splenic microabscesses, respectively. Splenic microabscesses were associated with HIV infection (P = 0.041). These data suggest that pulmonary TB is often complicated by abdominal TB in children.
INTRODUCTION

Childhood tuberculosis (TB) accounts for a considerable burden of pediatric morbidity and mortality worldwide [1]. Because of nonspecific signs and symptoms, paucibacillary disease and difficulty in obtaining adequate specimens for microbiologic investigation diagnosing pulmonary TB in children remains challenging, and development of novel-diagnostic tools is a research priority. Children are at particular risk of progression to disseminated and severe forms of TB [1].

Ultrasonography findings suggestive of abdominal TB have been reported to occur in a substantial proportion of both pediatric and adult patients for whom chest radiography (CXR) does not indicate TB [2,3]. Abdominal lymphadenopathy and splenic microabscesses are considered diagnostic of TB in particular clinical and epidemiologic settings [4]. A point-of-care ultrasound protocol for focused assessment with sonography for HIV-associated TB has been developed for adults and has successfully been implemented in emergency settings in South Africa [5,6].

Abdominal ultrasound data in children with pulmonary TB are limited. Focused assessment with sonography for HIV-associated TB has not been systematically studied in children but may be a valuable tool to support diagnosis and assess the extent of disease. This study was performed to investigate the prevalence of ultrasound findings suggestive of abdominal TB in children with pulmonary TB and the association of HIV infection with these.

MATERIALS AND METHODS

This secondary analysis reviewed ultrasound reports available for children hospitalized at Red Cross War Memorial Children’s Hospital in Cape Town, South Africa, who participated in a TB diagnostic study [7] in 2008–2013 and who had an abdominal ultrasound. Children up to 13 years of age were enrolled if they met the following inclusion criteria: cough plus one or more of the following criteria: (1) failure to thrive or loss of weight in the last 3 months; (2) a positive tuberculin skin test (>10 mm in HIV uninfected and >5 mm in HIV infected); (3) CXR suggestive of active TB and (4) household or close TB contact. Exclusion criteria were TB treatment or prophylaxis for more than 72 hours. Diagnostic TB workup comprised history taking, physical examination, CXR, tuberculin skin test and repeated induced sputum for smear microscopy, liquid culture and GeneXpert (Cepheid, CA). Children were categorized as “definite TB” (culture or GeneXpert positive), “TB negative” (culture or GeneXpert negative and documented resolution of symptoms and signs after 3 months in the absence of TB treatment) or “clinical TB” (microbiologically negative
but clinically diagnosed and treated for TB). CXRs were interpreted by 2 independent readers blinded to clinical data including ultrasound findings; in case of discrepant readings, a third reader was added and diagnosis was based on majority opinion. HIV testing was done in all children unless their HIV status was known. The study was approved by the Research Ethics Committee of the Faculty of Health Sciences, University of Cape Town, and written informed consent was obtained from a parent or legal guardian.

Children with definite or clinical pulmonary TB who underwent a formal abdominal ultrasound examination at the hospital’s pediatric radiology department were included. The indication for the abdominal ultrasound examination was determined by the individual child’s attending physician. The ultrasound equipment consisted of a Philips iU22 (Philips, Amsterdam, The Netherlands) and Toshiba Aplio 400 machine (Minato, Tokio, Japan). A curvilinear probe 5–8 MHz was used for infants; and a curvilinear probe 2.5–6.2 MHz, for children older than 6 months. For the evaluation of splenic microabscesses, a linear probe 5–12.6 MHz was employed. The standard abdominal imaging protocol included evaluation of the liver, portal vein, hepatic veins, hepatic artery, common bile duct, gallbladder, aorta, inferior vena cava, pancreas, spleen, right and left kidney, bladder and pelvis. Lymphadenopathy was evaluated in the peri-pancreatic region, porta hepatis, splenic hilar region and mesenterium and defined as lymph nodes larger than 10 mm in short axis. Splenic

Figures 1. Splenic microabscesses (*) in a 12-year-old HIV-infected boy.
microabscesses are defined as multiple focal hypoechoic lesions throughout the spleen parenchyma usually measuring 0.5–1 cm and best visualized with a linear high-frequency transducer. Copies of images were obtained selectively. Ultrasound examinations were performed by consultant radiologists, radiology registrars under supervision, qualified sonographers and student sonographers under supervision. Ultrasound data that were extracted from radiology reports comprised presence or absence of abdominal lymphadenopathy and splenic microabscesses (Fig., Supplemental Digital Content 1 and 2, http://links.lww.com/INF/C700). Data were analyzed using SPSS (Macintosh) version 22.0 (IBM Corp., Armonk, NY); \( \chi^2 \) test was used 2-sided at \( \alpha = 0.05 \).

**RESULTS**

A total of 102 South African children (median age: 37 months; interquartile range: 17–73) were included. Thirty-four (33%) children were HIV infected with a median CD4 percentage of 17% (interquartile range: 8–26); and 24 (71%) were receiving antiretroviral treatment. Thirty-seven (36%) children had definite pulmonary TB and 65
(64%) had clinical pulmonary TB. All but 1 isolate belonged to the Mycobacterium tuberculosis complex, and all but 2 isolates were susceptible to rifampicin and isoniazid. Thirteen of 92 (14%) children had received previous treatment for latent TB infection. HIV status and median age did not differ significantly between children with definite and clinical TB.

Abdominal lymphadenopathy was present in 46 of 100 (46%) children. Splenic microabscesses were reported in 24 of 97 (25%) children (Table 1). Abdominal lymphadenopathy was located in the epigastrium in 25 (56%), in the paraaortal or paracaval regions in 16 (36%), in the splenic hilum in 7 (16%) and in the lower abdomen in 5 (11%) of the children.

Abdominal lymphadenopathy or splenic microabscesses were significantly more common in children with definite pulmonary TB than in children with clinical pulmonary TB ($P < 0.007$; Table 1). Splenic microabscesses were associated with the presence of concurrent abdominal lymphadenopathy ($P < 0.001$); 19 of 46 (41%) children with abdominal lymphadenopathy also had splenic microabscesses. Both abdominal lymphadenopathy and splenic microabscesses were associated with clinical signs of abdominal distention ($P < 0.001$ and $P = 0.04$, respectively). While splenic microabscesses were associated with HIV infection ($P = 0.041$), abdominal lymphadenopathy was not. Median CD4 cell counts did not differ between HIV-infected children with and without splenic microabscesses. Neither age, nor sex, nor previous treatment for latent TB infection was associated with abdominal ultrasound findings.

| Table 1 Abdominal ultrasound findings in children by TB category and by HIV status |
|-----------------------------------|----------|-----------------|-----------------|-----------------|-------------------|------------------------|--------------------------|
|                                  | Definite TB | Clinical TB | Total | HIV-infected | HIV-uninfected | p value |
|                                  | n = 37 (36%) | n = 65 (64%) | n = 102 (100%) | n = 34 (33%) | n = 67 (66%) | p value |
| Abdominal lymphadenopathy, n (%) | 23 (64) | 23 (36) | 46 (46) | 15 (44) | 31 (48) | n.s. |
| Splenic micro-abscesses, n (%)  | 16 (44) | 8 (13) | 24 (25) | 12 (38) | 12 (19) | 0.041 |

NS indicates not significant.

CXR reports were available for 98 of 102 children; of those, 56 (57%) were interpreted as suggestive of TB and 15 (15%) as not suggestive of TB; in 27 (28%), CXR interpretation was inconclusive. Of 32 children with clinical TB and with a CXR not suggestive or inconclusive for TB, 13 (40%) had either abdominal lymphadenopathy or splenic microabscesses.
Duration of treatment was lengthened in 30% of children for whom these data were available; neither in HIV-uninfected nor in HIV-infected children, duration of treatment was associated with abdominal ultrasound findings.

DISCUSSION

To our knowledge, this is the largest evaluation of abdominal ultrasound findings of TB in a well-defined cohort of children with pulmonary TB. Our data support the observation that concurrent pulmonary TB and abdominal TB are common in children [3] and thereby highlight the risk of extrapulmonary TB (EPTB) or disseminated TB in children with pulmonary disease.

Consistent with reports on abdominal TB in adults and children [3,8], abdominal lymphadenopathy was the most common finding. Splenic microabscesses were also a common feature, especially in children with abdominal lymphadenopathy. Children with definite TB were more likely to have concurrent abdominal lymphadenopathy or splenic microabscesses compared with children without microbiologic confirmation. This may indicate poor host control (uncontrolled disease) [9], suggesting that clinicians should consider possible extrathoracic spread in children with confirmed pulmonary TB.

A considerable proportion (40%) of children without microbiologic confirmation and who had a CXR which was not interpreted as suggestive of TB had either abdominal lymphadenopathy or splenic microabscesses supporting that abdominal ultrasound may play an adjunctive role in the investigation of children with suspected pulmonary TB particularly in high-risk populations such as HIV-infected children [3].

While HIV is a risk factor for EPTB including abdominal lymphadenopathy in adults [10], abdominal lymphadenopathy was not associated with HIV infection in children in a smaller retrospective study [3]. Our data confirm this. In contrast, a novel finding was the significant association of splenic microabscesses with HIV infection in our study.

Our data are limited by the selective referral of children for abdominal ultrasound precluding any calculation of the true prevalence of concurrent abdominal TB in children presenting with pulmonary TB. Furthermore, we did not have ultrasound data from a control group of children with non-TB respiratory disease. Abdominal features suggestive of EPTB were not confirmed by microbiology; precluding definite knowledge on their etiology. Abdominal lymphadenopathy is a common finding in children [11–13]; however, the high TB prevalence in this setting, stringent inclusion criteria, strict case definitions as well as microbiologic confirmation of pulmonary TB in half of the patients with abdominal lymphadenopathy and concurrence with
splenic microabscesses as a further sonographic feature of EPTB in 41% of patients suggest that enlarged lymph nodes in this cohort most likely reflect tuberculous lymphadenitis.

This study suggests that detection of features of abdominal TB by ultrasound may be a useful investigation for defining the extent of TB in children with pulmonary TB, particularly in HIV infected children, and with implications for treatment as extensive or severe TB should be treated with a 4-drug regimen in South Africa. As portable point-of-care ultrasound devices become more affordable, ultrasound is an imaging modality that may be increasingly useful in resource-limited areas, where radiography may not be widely available. A prospective larger evaluation of the usefulness of abdominal ultrasound in a cohort of HIV-infected and HIV uninfected children is warranted.
REFERENCES