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Research paper

Potentially preventable tuberculosis cases in children exposed to a contaminant case

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ABSTRACT

Early screening is recommended in children exposed to a contagious case of tuberculosis (TB), to prevent rapid progression to active TB. The aim of this study was to evaluate the percentage of potentially preventable cases of pediatric TB stemming from inadequate screening. The data gathered on children aged 0 to 10 years, who were evaluated by the Paris Center for TB Control (CLAT75) between January 2009 and December 2013, were extracted and retrospectively analyzed. French National Guidelines for screening were used as reference. During the study period, 1232 children 0–10 years were screened, because of a known exposure to an index case, including 124 (10%) with criteria for latent tuberculosis infection (LTBI) and 26 (2%) with active TB. Twelve additional cases of TB were reported, diagnosed based on symptoms or systematic exams. As a whole, 68% of pediatric TB cases were diagnosed at screening around an adult index case, highlighting the quality of the screening network. Among the 38 TB cases, 19 (50%) had a missed opportunity for potential prevention, due to the absence of screening despite a known contaminant ($n = 2$) or to screening not in compliance with current recommendations ($n = 17$). Delayed first evaluation was the most frequent error of the screening procedures. In conclusion, despite the quality of the screening network set up in Paris, half of the pediatric TB cases in this study did not undergo the recommended screening procedures. A significant reduction in the number of pediatric TB cases can be expected through the optimization of screening networks.

1. Introduction

The incidence of pediatric cases of tuberculosis (TB)-related infections or diseases is a good marker of the level of performance of public health actions. Indeed, a case of TB in a child indicates a probable recent transmission from a contagious adult. Following exposure, infection occurrence in children is evidenced by a positive immune test, either a tuberculin skin test (TST) or an interferon-gamma-releasing assay (IGRA). In most vulnerable children, including children younger than 5 years of age and immunocompromised children, rapid progression to disease may be observed in absence of chemoprophylaxis. International guidelines have been established for screening children exposed to an active TB case and rapidly identifying those requiring chemoprophylaxis [1,2]. These recommendations are usually adapted in each country, to take into account national particularities of healthcare policies. The French guidelines were established in 2006 and updated in 2013 [3]. Inadequate screening may be missed opportunities to prevent active TB pediatric cases [4]. This may include extended delays in testing children, incomplete assessment of these children, or failure to comply with prophylaxis indications. The aim of this study was to evaluate the percentage of potentially preventable cases of pediatric TB, because of screening that was not in accordance with current recommendations.

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2. Methods

2.1. Organization of TB management in France

In France, screening of individuals exposed to a case of TB is provided free of charge by dedicated Centers for TB Control, called *Centres de Lutte Anti-Tuberculeuse* (CLAT). According to national recommendations, all children, up to 15 years of age, sharing the same home and/or having close and repeated contact with a case of pulmonary TB should be screened. If the index case has a negative microscopic examination, screening must be initiated without waiting for culture results. The first visit should take place within 2 weeks of the diagnosis of the index case. During this first visit (V1), a clinical examination, a chest x-ray (frontal view), and an immune test are performed in the exposed children. IGRAs are not recommended for children under 5 years of age. In the absence of initial criteria for a latent TB infection (LTBI), a second evaluation (V2) must be carried out, within 8–12 weeks after the last contact. Immune test and chest x-ray are repeated during this visit. During the interval between V1 and V2, prophylaxis with isoniazid and rifampicin is recommended in all children under 2 years of age and immunocompromised patients. In 2013, these recommendations were simplified in children over 5 years of age. It is now proposed to carry out only one immune test (TST or IGRA), 8–12 weeks after the last contact. All children with LTBI should receive treatment with isoniazid and rifampicin for 3 months. In exposed children, LTBI is defined by a positive immune test, in the absence of clinical and radiological signs. The thresholds for TST are 10 mm in children not vaccinated with BCG, and 15 mm in those vaccinated with BCG. For IGRA tests, the thresholds considered are those provided by the manufacturers. If clinical and/or radiological signs are present, the diagnosis of TB disease is considered. Children for whom anti-TB treatment is initiated are classified as confirmed TB or unconfirmed TB, according to microbiological results [5]. All cases of TB disease are reported to the CLAT.

2.2. Population of the study

This study was carried out with the CLAT in charge of the city of Paris (CLAT75). Data for all children aged 0–10 years, and evaluated by CLAT75 between January 2009 and December 2013, were extracted from the computerized database, and retrospectively analyzed. Thus, data from pediatric TB disease cases as well as data from all of the children screened during this period were available. To take into account age-specific screening guidelines, children were divided into three age subgroups: children less than 2 years of age, for whom chemoprophylaxis is systematically recommended; children 2–4 years of age; and children 5–10 years of age, considered as having a lower risk of progression to TB disease following infection [6]. CLAT systematically referred to pediatric hospital services for children under 2 years of age, and a large part of the 2 to 4 year-old age group. Situations leading to the diagnosis of active TB were divided into discovery at screening, discovery upon symptoms, or discovery on systematic exam. If TB was diagnosed at screening, the following parameters were analyzed: time to V1 after the diagnosis of the index case, time between V1 and V2, performance of immune test and/or chest x-ray, availability of the results for these exams, initiation of a preventive treatment, and dosage of prescribed drugs.

This study was approved by Institutional Review Board of the French Society for Respiratory Medicine: (*Société de Pneumologie de Langue Française*) (CEPRO 2017-010).

2.3. Data analysis

Potentially preventable cases of TB were defined as:

- children who had been screened following exposure to a known index case, but at least one screening procedure was noncompliant with national guidelines: time to first visit exceeding 14 days; incomplete evaluation at V1 (no immune test, no x-ray, no TST reading); time to second visit exceeding 3 months after the last contact with the index case; incomplete evaluation at V2 (no immune test, no x-ray, no TST reading); inadequate prophylaxis between V1 and V2 (no prophylaxis given to children less than 2 years of age, inadequate dosage);
- children with TB discovered on the occasion of suggestive symptoms or a routine exam, and for whom a contaminant was actually reported but no screening was initiated.

Continuous data were expressed as median and interquartile range. The difference between groups was tested with a chi^2 test with correction of the *P*-value (Fisher exact test) when the numbers compared were less than 5. A *P*-value lower than 0.05 was considered significant.

3. Results

3.1. Cases of active TB

Between January 2009 and December 2013, 38 cases of active TB in children 0–10 years were reported to the CLAT75 (Table 1). Of these, 26 (68%) were secondary cases, identified during screening around an adult index case; eight (21%) were diagnosed upon symptoms, and four (11%) on systematic exams. Twenty-nine cases (76%) were younger than 5 years of age, including 11 cases (29%) younger than 2 years of age. Nine patients (24%) had confirmed TB, including eight cases with positive culture, and one child less than 2 years of age with positive PCR on bronchoalveolar lavage. Two cases had disseminated disease: one 18-month-old child had severe meningoencephalitis, and a 4 year-old child had miliary disease and was co-infected with HIV. All intrathoracic TB cases showed chest x-ray abnormalities. There was no case with multidrug-resistant TB.

3.2. Population of screened children

Between January 2009 and December 2013, 1232 children 0–10 years were screened, because of known exposure to an index case (Table 2). Of those, 124 (10.1%) had criteria for a LTBI and 26 (2.1%) had active TB. The screening network made it possible to recognize 68% (26/38) of active TB pediatric cases. Among the 26 cases with active TB, 19 (73%) were diagnosed at V1 and seven (27%) at V2 (Table 1). Of the last seven cases, four were between 2 and 5 years of age, raising the question of the risk of rapid progression to active TB in this population for which prophylaxis is not recommended in France, but still recommended in other European countries. To assess this risk, we analyzed the number of active TB cases occurring between V1 and V2 among children considered to be uninfected at V1 (i.e., children screened, excluding LTBI and active TB cases diagnosed at V1). Children under 2 years of age, who were provided prophylaxis, had the same risk of progression as children between 5 and 10 years of age (Table 3). Children between the ages of 2 and 5 had a relative risk of 4, compared to children between 5 and 10 years of age, without reaching significance.

3.3. Inadequate screening in children with active TB

Among the 38 pediatric TB cases, 19 (50%) had a missed opportunity for potential prevention, two because of the absence of screening despite a known contaminant and 17 because of a screening not in compliance with current guidelines (Table 4).

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