CASE REPORT

Delayed diagnosis of pulmonary tuberculosis in a 13-year-old Malawian boy

Niall Johnston, Nichola Sandys

Paediatric Department, Nkhoma Mission Hospital, Nkhoma, Malawi

Correspondence to
Dr Niall Johnston,
nijohnst@gmail.com

Accepted 23 March 2017

SUMMARY

Childhood tuberculosis (TB) is a significant global health burden. There are more than 1 million new cases of childhood TB annually. Despite this, many national TB control programs largely focus on identification and treatment of smear positive adults. Early case detection is essential if childhood TB is to be controlled and eradicated.

Delayed diagnosis of TB is associated with more advanced disease and worse treatment outcomes. Younger children who go undiagnosed for long periods are at risk of developing severe pulmonary and extrapulmonary disease, such as meningitis. Additionally, advanced childhood TB is a common respiratory cause of death in TB-endemic areas. Undoubtedly, delayed diagnosis contributes significantly to TB-related morbidity and mortality.

Diagnostic delay may be divided into patient delay, the duration between development of symptoms and presentation to healthcare provider, and healthcare provider delay, the duration between presentation and initiation of appropriate treatment.

CASE PRESENTATION

An 13-year-old boy presented to a rural mission hospital in Malawi with 12 months history of nocturnal cough with wheeze, chest discomfort and exertional dyspnoea. He had five previous presentations to a local rural health clinic, where a clinical diagnosis of severe asthma was made. He was treated with antibiotics, inhaled salbutamol and low-dose inhaled corticosteroids. These treatments provided partial symptomatic relief. He also attended a traditional healer, who provided herbal remedies over the preceding year. There was no history of tuberculosis (TB) contacts and his HIV status was negative. He lived with his mother and father and six siblings in a small rural village. His parents had no primary school education.

On examination, he was thin, diaphoretic and unwell. His height was on the 50th centile and weight was on the 3rd centile for age and gender. He displayed conjunctival pallor, prominent cervical lymphadenopathy and hepatosplenomegaly. His respiratory examination revealed tachypnoea, chest indrawings and marked expiratory wheeze. There was reduced air entry at the left base. He had no finger clubbing.

Blood investigations showed an elevated white cell count ($18.1 \times 10^9/L$) with lymphocytosis ($11.4 \times 10^9/L$, 63% total). Red blood cell indices revealed a normocytic anaemia; haemoglobin 5.4 g/

dL (normal range 12–15 g/dL) and mean corpuscular volume 63 fL (normal range 80–100). The erythrocyte sedimentation rate was elevated at 121 mm/hour (normal 0–5). Chest radiograph revealed hilar lymphadenopathy and left-sided pleural effusion (figure 1). Tuberculin skin testing was unavailable. Rapid PCR-based testing (Gene Xpert) of both induced sputum and pleural fluid was positive for *Mycobacterium tuberculosis*, confirming the diagnosis 12 months after the onset of symptoms. In this time, he had developed severe symptoms, marked lung damage and faltering growth.

GLOBAL HEALTH PROBLEM LIST

1. Childhood TB is not viewed as a key global health priority.
2. Delayed diagnosis of TB (figure 2) leads to more severe disease and increased mortality.
3. Delayed diagnosis is closely linked to poor parental knowledge of TB, fear of stigmatisation and rural residence.
4. Use of non-formal healthcare providers such as traditional healers also contributes to diagnostic delay.
5. In children, pulmonary TB may mimic other respiratory illnesses, such as asthma that can lead to missed or delayed diagnosis.
6. Establishing a timely diagnosis is problematic because diagnostic tests may be unreliable, difficult to interpret and often not available.

GLOBAL HEALTH PROBLEM ANALYSIS

Childhood TB is not viewed as a serious health priority

At present, childhood TB is a neglected global health issue.¹ While high-resource countries have enjoyed significant reductions in childhood TB over the last number of decades, this has not occurred in low-resource countries. Because of their minimal risk of infection transmission, young children are not felt to contribute significantly to perpetuating the TB epidemic.² As a result, TB management strategies in low-resource countries, such as Malawi, focus mainly on the treatment of sputum-positive adults. However, the burden of disease and death caused by childhood TB is enormous. There is approximately one million children with TB worldwide, which represents 5%–10% of total TB cases.³ In fact, this figure is likely to be a gross underestimate due to difficulties with accurate diagnosis of TB in children and lack of notification data.² As a consequence, childhood TB has not received adequate

CrossMark

To cite: Johnston N, Sandys N. *BMJ Case Rep* Published Online First: [please include Day Month Year]. doi:10.1136/bcr-2016-218953

Figure 1 Chest radiograph showing bilateral hilar adenopathy and large left-sided pleural effusion.

attention from child health programs, paediatricians, research, industry and policy-makers. Recently, the Roadmap for Childhood TB has identified 10 key steps, which attempts to bring the disease into the global health spotlight.³

Delayed diagnosis leads to more severe disease and increased mortality

In high-resource settings, many cases of childhood TB are diagnosed early in the disease course and have excellent outcomes. In contrast, low-resource countries like Malawi, where there is no active case finding, children present with advanced disease and complications such as pleural effusion, bronchial obstruction or miliary disease.⁴ Those at greatest risk of such complications and death are children under 5 years of age and children with malnutrition, HIV infection or immune suppression.⁵ A large study of Zambian children who died from respiratory disease showed that TB was the second most common cause for death identified at autopsy (second only to acute pyogenic pneumonia) and was present in 26% of cases.⁶

Delayed diagnosis is closely linked to poor parental knowledge of tuberculosis and stigmatisation of the disease

Children with TB often come from families that are poor, have low educational attainment and lack even basic knowledge about TB.³ Many parents are not aware of the symptoms of childhood TB. A study from Peru⁷ showed that some parents were not even aware that children could acquire TB infection. In countries like Malawi, where there is strong association between HIV and TB, fear of stigmatisation of the disease may be even more marked⁸

and acts as a further barrier to seeking healthcare. Promotion of TB education and awareness within such communities is vital to dispel common myths about the disease, reduce stigmatisation by reinforcing that it is a treatable condition and to improve recognition of symptoms.

Use of non-formal healthcare providers such as traditional healers also contributes to diagnostic delay

Instead of attending hospitals or health clinics, parents may seek care for their children from alternative practitioners, which include street drug sellers, pharmacies, religious authorities, herbalists or traditional healers. Reasons for using non-formal healthcare providers include the perception that they may be less time consuming and less expensive.⁷ The role of the traditional healer is of particular importance in Malawian society and may be consulted by up to one-third of patients with TB before they ever reach a formal healthcare provider.⁹ They administer treatments of unproven efficacy and potential harm such as roots, bark or herbal drinks, and may see patients for several weeks, leading to harmful diagnostic delay. The solution to this problem is for TB services to engage with traditional healers, who have great influence over patients' health beliefs and care-seeking behaviour, so that they may be educated regarding the symptoms of TB and be encouraged to refer to centres with diagnostic facilities and clinical expertise.⁸ In addition, families could be encouraged to use formal healthcare providers if such services were more accessible, cheaper and more time efficient.

In children, pulmonary tuberculosis may mimic other respiratory illnesses such as asthma, potentially delaying diagnosis

Unlike adults, young children with pulmonary TB may not present with classical features of cough, night sweats and weight loss. Instead, atypical symptoms such as wheeze may occur. Paediatric asthma shares many of the symptoms of TB infection¹⁰ making differentiating between the two conditions challenging, especially for inexperienced clinicians. A key priority, therefore, in tackling childhood TB is to develop training and reference material for all healthcare workers so that they may be equipped with the skills to recognise and manage the condition.¹

Establishing a timely diagnosis is problematic because diagnostic tests may be unreliable, difficult to interpret and often not available in primary health centres

Sputum microscopy is often the only diagnostic tool used in primary care to diagnose TB. Unfortunately, children have low bacillary counts in sputum and therefore are 'smear-positive' in

Diagnostic delay in childhood TB

Figure 2 Factors that lead to delayed diagnosis of childhood tuberculosis (TB).

less than 10%–15% of cases.¹¹ Furthermore, obtaining sputum samples in younger children is difficult due to poor expectoration.¹² Gastric or bronchiolar lavage sampling is technically difficult and not practical outside the hospital setting. Other diagnostic tools such as tuberculin skin tests, rapid PCR-based tests (Gene Xpert) and chest radiography are often unavailable in primary care centres and hospitals in low-income countries. Therefore, the diagnosis of childhood TB is heavily reliant on clinical signs and symptoms, which may be non-specific.² Clearly, there is urgent need for a test that could quickly and correctly diagnose TB. Such a test should also be point-of-care, low cost and child-friendly. Increased access to good-quality chest radiography and laboratory services for all children is also critical to achieving a prompt diagnosis.

Learning points

- ▶ Tuberculosis (TB) services must engage with traditional healers and other non-formal health providers, so that they may be taught to recognise symptoms of TB and advised to refer patients to an appropriate health facility.
- ▶ TB health education within high-burden communities may help to improve parental symptom recognition and reduce delay in seeking healthcare.
- ▶ Delayed diagnosis is common and is associated with more advanced disease and poorer treatment outcomes. Early case detection is therefore essential if the epidemic is to be controlled.
- ▶ Childhood TB is global health crisis, which requires urgent attention.
- ▶ In low-resource settings, many clinicians have limited access to diagnostic tools. There is an urgent need for a new, accurate, point-of-care test to aid with microbiological confirmation.

Contributors NJ identified and managed the case. NJ and NS were both responsible for manuscript preparation, figure design, revision and final production.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

© BMJ Publishing Group Ltd (unless otherwise stated in the text of the article) 2017. All rights reserved. No commercial use is permitted unless otherwise expressly granted.

REFERENCES

- 1 Starke JR. Improving tuberculosis care for children in high-burden settings. *Pediatrics* 2014;134:655–7.
- 2 Dodd PJ, Gardiner E, Coghlan R, *et al.* Burden of childhood tuberculosis in 22 high-burden countries: a mathematical modelling study. *Lancet Glob Health* 2014;2:e453–e459.
- 3 World Health Organization. *Roadmap for childhood tuberculosis: towards zero deaths*. Geneva, Switzerland: WHO Document Production Services, 2013. http://apps.who.int/iris/bitstream/10665/89506/1/9789241506137_eng.pdf. (accessed Dec 2016).
- 4 van Rie A, Beyers N, Gie RP, *et al.* Childhood tuberculosis in an urban population in South Africa: burden and risk factor. *Arch Dis Child* 1999;80:433–7.
- 5 Swaminathan S, Rekha B. Pediatric tuberculosis: global overview and challenges. *Clin Infect Dis* 2010;50(Suppl 3):S184–94.
- 6 Chintu C, Mudenda V, Lucas S, *et al.* Lung diseases at necropsy in African children dying from respiratory illnesses: a descriptive necropsy study. *Lancet* 2002;360:985–90.
- 7 Paz-Soldan VA, Alban RE, Dimos Jones C, *et al.* Patient reported delays in seeking treatment for tuberculosis among adult and pediatric TB patients and TB patients co-infected with HIV in Lima, Peru: a qualitative study. *Front Public Health* 2014;2:281.
- 8 Makwakwa L, Sheu ML, Chiang CY, *et al.* Patient and health system delays in the diagnosis and treatment of new and retreatment pulmonary tuberculosis cases in Malawi. *BMC Infect Dis* 2014;14:132.
- 9 Brouwer JA, Boeree MJ, Kager P, *et al.* Traditional healers and pulmonary tuberculosis in Malawi. *Int J Tuberc Lung Dis* 1998;2:231–4.
- 10 Kurokawa La Scala CS, La Scala CR, Wandalsen GF, *et al.* Childhood tuberculosis diagnosed and managed as asthma: case report. *Allergol Immunopathol* 2006;34:276–9.
- 11 Zar HJ, Hanslo D, Apolles P, *et al.* Induced sputum versus gastric lavage for microbiological confirmation of pulmonary tuberculosis in infants and young children: a prospective study. *Lancet* 2005;365:130–4.
- 12 Piccini P, Chiappini E, Tortoli E, *et al.* Clinical peculiarities of tuberculosis. *BMC Infect Dis* 2014;14(Suppl 1):S4.

Copyright 2017 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow