What is the main cause of childhood non-cystic fibrosis bronchiectasis in the developing world – should pulmonary tuberculosis be the number one accused?

Non-cystic fibrosis (CF) bronchiectasis remains a common condition in many paediatric pulmonology clinics in low- to middle-income country (LMIC) settings. Most of these children only present to a hospital when they have severe disease, usually because of an acute exacerbation. Given the severity of the disease at this stage, it is difficult, and often nearly impossible, to identify its cause and timeline.

In children living with HIV (CLWH), it is easier to understand the pathogenesis, as these children are prone to recurrent infections, have a slow response to antibiotic treatment and have reduced immunity, and certain decisive diseases, such as lymphoid interstitial pneumonia, are well known to cause bronchiectasis.[1]

In the developing world, respiratory tract infections and tuberculosis (TB) have always been speculated to cause bronchiectasis, but this remains mostly unproven. In very few affected children, the original infection is known, or they had a previous normal chest radiograph (CXR) to base this assumption on.

TB has long been identified and made a scapegoat as the cause of bronchiectasis. In adolescent children, this may be the case, as they can present with cavities and structural parenchymal lung disease similar to adults, especially if bilateral. In younger children, this is not clear, as most young children with TB have lymph node disease and not severe destructive disease. Goussard *et al.*[2] have reported a small percentage (2.4%) of children with bronchiectasis in a cohort of 250 children with severe airway obstruction. The children who did develop bronchiectasis were either HIV positive or had a broncho-oesophageal fistula to the left main bronchus, leading to chronic aspiration. Children with expansile pneumonia may be considered high-risk candidates for bronchiectasis, but even among these, very few will develop bronchiectasis. Expansile pneumonia mostly affects the upper lobes with better drainage and heals with fibrosis.[3] So which TB children are then at high risk for bronchiectasis? Juggernath *et al.*[4] reported that 86% of children were presumed to have a post-infectious cause of bronchiectasis, which was based on a previous history of a severe lower respiratory tract infection. Other causes included inborn errors of immunity (4%), secondary immune deficiencies (4%) or primary ciliary dyskinesia (PCD) (6%). They reported that 67 children (74%) had previously been treated for pulmonary TB (PTB), with only 5 (7%) of these having confirmed PTB. In this study, 42% of the children were CLWH, which highlights the difficulty in diagnosing TB in children, but also suggests that not all chronic lung diseases are due to TB.

In a high-incidence area for TB and HIV, TB is underdiagnosed but also overdiagnosed, which makes it extremely difficult to find the correct cause of bronchiectasis. Except for CF, PCD, HIV and immunodeficiency, the rest of the causes of bronchiectasis are very difficult to identify, and bronchiectasis is typically blamed on infectious diseases. Post-adenovirus bronchiolitis obliterans is a disease with a high incidence in LMICs. It can only be diagnosed on a chest computed tomography (CT) scan. Depending on the severity of the insult, there may be mosaic diffusion and areas of bronchiectasis visible on the CT scan.[5] This cause of bronchiectasis is relatively easy to diagnose based on the history of severe adenovirus infection and the CT scan changes. The same applies to hydatid disease, which very infrequently is reported as a cause of bronchiectasis, especially in children with complicated, ruptured and infected cysts.[6]

Children from LMICs live in a different environment to those in the developed world; they have higher biofuel and cigarette smoke exposure, are more prone to recurrent infections, and receive fewer vaccinations. So, the simple question is, is it the chicken or the egg situation? Van der Zalm *et al.*[7] have recently reported on adolescents with and without TB; evaluating their lung function, they found a significant number who had not had TB having abnormal lung function.

Prospective long-term cohort studies are necessary to determine the long-term growth, lung function and structural outcome of these children with more sophisticated biomarkers, looking at the underlying reason why children in LMICs develop bronchiectasis without a clear cause.

Treatment of bronchiectasis in children remains mostly conservative, such as infection prevention, vaccination and physiotherapy. Physiotherapy services are lacking in South Africa (SA), and the number of patients who can be treated remains limited. Parents must be trained, as physiotherapy devices are far too expensive. Azithromycin is used in most of these children with bronchiectasis, but evidence as to its value remains lacking.[8]

Surgery remains an option if children fulfil the criteria of lobar, non-bilateral disease, but except for HIV-positive children, the numbers of children having a lobectomy performed for bronchiectasis have significantly decreased. In the Tygerberg Hospital system, there has been a significant decline in recent years, which could be due to the more conservative, supportive treatment these children now receive.

So, before we blame TB as an important cause of bronchiectasis, more information is needed. Without microbiological confirmation, TB remains unproven and cannot be blamed as the cause of the child's bronchiectasis owing to many overlapping radiological presentations of other conditions. It is also important to make clear notes on what appeared on the CXR that suggested TB, as this will be useful when the child is seen in a later stage. SA lacks a universal picture archiving and communication system for the whole country, leading to the loss of some of these children's original CXRs.

Currently, the jury is still out on whether TB can be blamed as the cause of many children's bronchiectasis, and more research is needed before TB can be given a life sentence. What is clear from the Juggernath et al.[4] study is that preventing HIV will reduce the incidence of bronchiectasis in the developing world.

Pierre Goussard, FC Paed (SA), PhD
Head of Clinical Unit: Paediatric Pulmonology and Paediatric Intensive Care, Department of Paediatrics and Child Health, Faculty of Medicine and Health Sciences, Stellenbosch University and Tygerberg Hospital, Cape Town, South Africa
pgouss@sun.ac.za

Ernst Eber, MD, ATSF, FERS
Head of Division of Paediatric Pulmonology and Allergology and Chair of Department of Paediatrics and Adolescent Medicine, Medical University of Graz, Austria

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