

## Severe airflow obstruction in vertically acquired HIV infection

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### Abstract

It is becoming increasingly clear that human immunodeficiency virus (HIV) infection, either independently or in concert with opportunistic infections like pulmonary tuberculosis, is a risk factor for the development of chronic airflow limitation. In the majority of patients the etiology of this obstructive ventilatory defect is multifactorial. Post-infectious obliterative bronchiolitis, post-tuberculous lung damage (including bronchiectasis), immune reconstitution and the direct effects of HIV viral infection may all play a role. With increases in life expectancy and decreases in infectious complications in patients taking antiretroviral medications, the importance of HIV-associated chronic lung disease as a cause of pulmonary disability is likely to increase. This is particularly relevant in regions like sub-Saharan Africa, where both HIV infection and tuberculosis are highly prevalent. Here, to illustrate the complexity of this interaction, we present the case of a 15-year-old girl with vertically acquired HIV infection, multiple episodes of pulmonary infection, and severe airflow obstruction.

### Introduction

Human immunodeficiency virus (HIV) infection is a major contributor to the burden of respiratory disease in sub-Saharan Africa. Mortality from HIV infection in this region is still dominated by infectious complications like tuberculosis (TB), bacterial pneumonia, and *Pneumocystis* pneumonia [1]. However, with increasing access to antiretroviral therapy (ART) and widespread antimicrobial prophylaxis, a constellation of noninfectious conditions associated with treated HIV infection is emerging [2]. In particular, an association between HIV infection and chronic airflow obstruction is increasingly recognized [3]. In order to illus-

trate this clinical presentation, we report here a case of a 15-year-old girl with vertically acquired HIV infection and repeated pulmonary infections with severe irreversible chronic airflow limitation.

### Case

A 15-year-old girl presented to our pulmonology outpatient department with a long history of chronic productive cough (clear sputum) and shortness of breath on exertion. She was able to comfortably perform activities of daily living, but complained of being unable to participate in school sports because of cough and dyspnea. Her background medical history included vertically acquired HIV infection for which she had been treated with ART since age 3 years. She had two previous episodes of fully treated, culture-confirmed, drug-sensitive pulmonary tuberculosis, both before the age of 5 years. There had also been three documented admissions for severe pneumonia in childhood. She had been switched to second-line ART two years previously for virological and immunological failure

This case report is an illustration of an invited review available in *Respirology*: <http://dx.doi.org/10.1111/resp.12385>. Calligaro GL, Gray DL. Lung function abnormalities in HIV-infected adults and children. *Respirology*, 2014, doi: 10.1111/resp.12385.

secondary to nonadherence, coinciding with a time when her HIV-infected mother was also ill and unable to supervise her treatment.

Physical examination revealed digital clubbing, hyperinflation and reduced breath sounds with mild wheeze globally, and crackles in the lower zones. There was no clinical or electrocardiographic evidence of pulmonary hypertension. Her growth chart showed decreased growth velocity; both height-for-age and weight-for-age were on the third centile. Spirometry showed marked airflow limitation (forced expiratory volume in one second (FEV<sub>1</sub>) 33%



**Figure 1.** A chest radiograph showing hyperlucency of the left lung with multiple cystic shadows in the lower zones bilaterally.

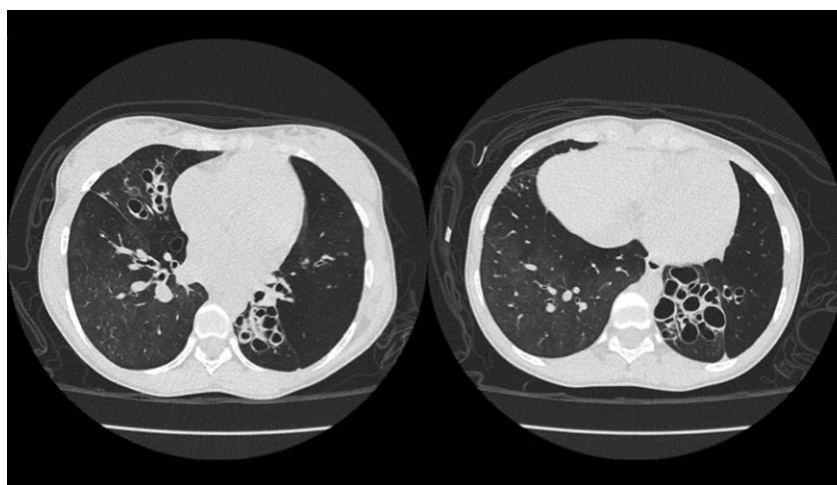
predicted) with nonsignificant bronchodilator reversibility, and a moderate-to-severe impairment in diffusing capacity (53% predicted).

The chest radiograph showed hyperlucency of the left lung with multiple cystic shadows in the lower zones bilaterally (Fig. 1). The high-resolution computed tomography of the chest confirmed bilateral cylindrical and saccular bronchiectasis, with mosaic attenuation and gas trapping on expiratory views (Fig. 2). She had a recent CD4 count of 406 cells/milliliter and a suppressed HIV viral load. Sputum cultured a sensitive *H. influenzae*; Xpert® (Cepheid Inc., Sunnyvale, CA, USA) MTB/RIF and culture for *M. tuberculosis* were negative.

She was prescribed inhaled corticosteroids and long-acting beta-agonists and azithromycin three times a week (on alternate days) on a continuous basis. She was given the polysaccharide pneumococcal and influenza vaccines. In the subsequent visits in the 12 months of follow-up so far, her shortness of breath has subjectively improved, but there has been no appreciable improvement in her lung function. She has had no further infective exacerbations.

## Discussion

Several studies have documented impairments in spirometry in HIV-infected adults and children, with chronic respiratory symptoms and reductions in exercise tolerance [3–5]. However, the etiology of airflow obstruction in HIV infection is largely unknown, and the putative causative factors are likely to be multifactorial and additive. The effects of repeated pulmonary infection (in particular, TB) are likely to be important, with the HIV-infected patients shown to have increased systemic and pulmonary inflammation, and



**Figure 2.** High-resolution computed tomography of the chest showing bilateral cylindrical and saccular bronchiectasis with mosaic attenuation. The areas of low attenuation showed little change in cross-sectional area during expiration, and also did not show the normal increase in attenuation, confirming gas trapping (expiratory sequence not shown here).

antioxidant pathways that are chronically down regulated. Obliterative bronchiolitis and bronchiectasis are important causes of chronic airflow obstruction after pulmonary infection in childhood. Uncontrolled HIV viral replication is also associated with accelerated lung function decline, but whether this is directly related to viral factors, or is simply a surrogate for poor HIV treatment outcomes, is unclear. Evidence suggests that HIV-infected individuals are more susceptible to the deleterious effects of cigarette smoke, developing abnormal lung function at lower cumulative pack years exposure. Lastly, immune reconstitution and chronic inflammation in response to persistent pulmonary microbial or viral antigens after the commencement of ART may play a role.

Although important preventive interventions such as early and widespread access to ART, childhood immunization against common respiratory pathogens, antibiotic prophylaxis and prompt treatment of opportunistic infections are likely to alleviate the burden of acute and chronic respiratory disease in HIV-infected children and adults, much work is still required in this area. Although several studies have examined airflow obstruction in adults living with HIV [3, 4], children in developing countries who acquire HIV via vertical transmission are a population substantially underrepresented in the literature. Correlations between structure and function have yet to be described. Furthermore, whether the pharmacological management of airflow obstruction is the same in HIV-infected versus HIV-uninfected patients is unknown. For example, inhaled corticosteroids may have negative drug interactions with ART medications and there are theoretical concerns that corticosteroids may increase risk of pneumonia and TB in HIV infected patients.

The association between HIV infection and airflow obstruction has major public health implications. With increased length of time living with HIV infection because of ART, and together with projected increases in tobacco use, biomass fuel exposures, and the high rates of childhood infections in sub-Saharan Africa, conditions for a “perfect

storm” of chronic pulmonary disability threaten to develop. This is particularly relevant to South Africa, which has the world’s largest number of patients living with HIV and the world’s largest antiretroviral program, and one of the highest rates of TB infection globally. Clinicians working with HIV-infected individuals should therefore have a high index of suspicion in patients with chronic respiratory symptoms, and consider screening patients with spirometry.

## Disclosure Statements

No conflict of interest declared.

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

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