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Review

The chest X-ray features of chronic respiratory disease in HIV-infected children – a review

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EDUCATIONAL AIMS

- The contributory factors
- The leading causes
- The common chest X-ray findings

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SUMMARY

Several features of human immunodeficiency virus (HIV) infection contribute to the development of chronic respiratory disease in children. These include the frequency and severity of acute chest infections, as well as the increased risk of pulmonary tuberculosis, aspiration, cardiovascular disease, lymphocytic interstitial pneumonitis or pulmonary neoplasia. The chest radiograph (CXR) remains the most accessible investigation for respiratory disease and plays an important role in the baseline assessment and follow-up. This review focuses on the CXR abnormalities of HIV-related chronic respiratory disease in children. The most commonly documented chronic CXR abnormalities are homogeneous opacification and pulmonary nodules, with pulmonary tuberculosis and lymphocytic interstitial pneumonitis the leading respective causes. Deficiencies in radiographic reporting methodology and relative paucity of radiographic data contribute to current limitations in knowledge and understanding of this field. The review highlights the need for standardised terminology and systematic reporting methodology in future studies. Prospective research on the natural history of lymphocytic interstitial pneumonitis, response to anti-tuberculous therapy, the impact of anti-retroviral therapy and HIV-associated bronchiectasis are needed.

INTRODUCTION

Several features of HIV-infection favour the development of chronic respiratory disease in young children who are not on anti-retroviral therapy(ART) [1–6].

Firstly, HIV–related acute chest infections are characterised by their frequency [7–9], severity [9–13], broad range of aetiological agents, [10,11,14–20] high rate of co-infections [21–24] and poor response to antimicrobial treatment [9–11,25]. These factors prolong acute chest infections, delay chest X-ray(CXR) resolution [18,21,26], predispose to persistent [10] and recurrent pneumonia [8,18,21,22,27,28] and the evolution of bronchiectasis [29–31]. This is especially true in sub-Saharan Africa, where there is a high incidence of childhood respiratory infections, a high prevalence of malnutrition and limited access to healthcare [32,33]. The early use of prophylaxis regimes, newer conjugate vaccines and/or highly active antiretroviral therapy (HAART) has reduced the incidence of acute respiratory morbidity and mortality, and has prolonged survival in young HIV-infected children [34,35]. However, longer survival may increase the prevalence of chronic respiratory disease [31,36,37].

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Secondly, HIV infection increases the risk of childhood tuberculosis (TB) [38–41], while TB accelerates the progression of HIV disease [42] and TB in HIV-infected children has a less favorable outcome [9,14,38,39,43–45].

Thirdly, HIV-related progressive encephalopathy(PE) [46], esophagitis and gastro-esophageal reflux predispose to oro-pharyngeal inco-ordination with micro-aspiration [6,46–48], which may lead to aspiration pneumonia or recurrent wheezing.

Fourthly, there is a high prevalence of anaemia and cardiovascular disease, particularly HIV-related cardiomyopathy, which may manifest with cardiomegaly and chronic pulmonary congestion [3,49–51] and ultimately pulmonary hypertension.

Fifthly, the association of paediatric HIV-infection with lymphocytic interstitial pneumonitis is well recognised [2,25,52–55]. In addition, HIV-related pulmonary neoplasms, particularly Kaposi's sarcoma, non-Hodgkin's lymphoma and bronchial smooth-muscle tumours [1,56–58] have been reported as rare causes of refractory CXR abnormalities, while pulmonary involvement in the immune reconstitution inflammatory syndrome (IRIS) is increasingly implicated in similar changes [4,59,60].

To our knowledge, there has been no comprehensive review of the published CXR features of chronic respiratory disease in young HIV-infected children, and there has been little documentation of the impact of ART on the radiological findings in these children. The two reviews of chronic respiratory disease in HIV-infected children published to date have focused on clinical rather than radiographic features [61,62].

The CXR remains the most accessible investigation for respiratory disease, and plays a pivotal role in the baseline assessment and follow-up of respiratory disease in HIV-infected children. A review of the current knowledge of the CXR features of chronic respiratory disease in HIV-infected children could assist in the clinical management of these children, while highlighting areas requiring additional research.

Soon after the onset of the HIV pandemic, guidelines for the systematic reporting of CXR abnormalities appeared in two landmark radiological publications. The first [63] proposed a revised reporting tool for systematic CXR analysis. Although intended for epidemiological studies of diffuse pulmonary disease in adults, the principles outlined can be applied to CXR abnormalities in general. The second article suggested a standard terminology for CXR reporting [64]. Used in conjunction, these two articles afford both a precise description of CXR features and a tool for defining the extent of disease.

The aim of this study is to review the reported CXR features of chronic respiratory disease in young HIV-infected children and to assess whether these have been systematically analysed utilising standard radiological terminology.

METHODS

Medline and Google Advanced Scholar searches were conducted for English language articles published from 1981 through 2013 with descriptions of the CXR features of HIV-related chronic respiratory disease in young children.

The initial search included the Keywords: "chronic or persistent" and "pulmonary or lung" and "disease or illness" and "infant or child or children or paediatric or pediatric" and "HIV" and "chest X-ray" or "chest radiograph". Similar search iterations were then conducted using known predisposing factors to chronic respiratory disease in HIV-infected children as additional key words; namely "persistent or chronic pneumonia"; "tuberculosis"; "aspiration pneumonia"; "bronchiectasis"; "lymphocytic interstitial pneumonitis"; "pulmonary congestion"; "pulmonary neoplasms" and "pulmonary IRIS". Finally; searches were conducted using "anti-retroviral therapy" or "combined anti-retroviral therapy" or "highly active anti-retroviral therapy" with "infant or child" and "chest X-ray".

The titles and abstracts of articles were reviewed and the full manuscripts of eligible articles were retrieved. Reference lists of the articles retrieved were examined for further eligible articles.

Research articles, case series or case reports which reported the CXR findings of conditions associated with chronic respiratory disease in children aged 0-14 years, with vertically-transmitted HIV-infection were included. Chronic respiratory disease was defined as any condition with the potential to cause respiratory symptoms for three months or longer [25,65]. Only reports including biopsy-proven LIP were considered. *Pneumocystis* pneumonia was analysed separately from other fungal pneumonias.

Eligible articles were collated according to the main predisposing conditions and tabulated by journal, country of origin, publication date, authorship and main CXR findings.

CXR findings were critically assessed with respect to the use of a systematic method of analysis of the patterns and extent of radiological abnormalities and the consistent use of appropriate reporting terminology.

RESULTS

Forty-seven publications documented the CXR findings in 826 patients; 533(65%) patients were from sub-Saharan Africa. (Table 1)

Less than half the reports (n = 21;45%) had a radiologist as co-author and less than a quarter (n = 10;21%) were prospective studies.

Reporting methodology was defined in three studies (6%) [66–68]. Norton [67] utilized the forced-choice template of the Prospective Study of Paediatric Pulmonary and Cardiovascular Complications of Vertically transmitted Human Immunodeficiency Virus Infection (P2C2 HIV study) [69]. Nodule dimension was the basis of the documentation of LIP by Oldham [66], and Iriso [70] invoked clinico-radiological criteria for the identification of PTB.

Pulmonary tuberculosis (n = 581;70%) and lymphocytic interstitial pneumonitis (n = 128;15%) together accounted for over 85% of cases.

The CXR features of less than a dozen cases each of chronic PCP, pulmonary IRIS, mycobacterium avium complex (MAC) pneumonia, bronchiectasis, fungal pneumonia, interstitial pneumonitis, thoracic Kaposi's sarcoma, lymphoma and smooth-muscle tumours were recorded.

There were no reports of the CXR features of aspiration pneumonitis or pulmonary congestion and no studies of the chronic CXR features of young children on ART.

Pulmonary tuberculosis(TB):(studies = 14, patients = 581; Table 2)

Mediastinal lymphadenopathy (n = 266;46%) and homogeneous segmental or lobar opacification (n = 244;44%) have been the most consistently documented features, with pulmonary nodules recorded in a third of patients (n = 194;33%).

The non-specific term "infiltrate" was used to describe the parenchymal opacification in almost one-fifth of cases (n = 108;19%).

In all studies, a proportion showed more than one parenchymal abnormality. However, combinations of parenchymal involvement were reported in less than one-fifth of cases (n = 113;19%) [9,25,67,71,72] and no study systematically recorded the extent of parenchymal abnormality.

The distribution of mediastinal adenopathy was noted in less than forty percent of cases (n = 222;38%) [39,45,70,71] and the association of mediastinal adenopathy with parenchymal involvement in just over ten percent (n = 64;11%) [71,72].