Interstitial lung disease in perinatally-acquired HIV infection: A case report

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Abstract

Human immunodeficiency virus (HIV) infection can lead to a wide range of lung disorders. These pulmonary manifestations include both infectious and non-infectious conditions, These lung disorders can manifest as interstitial lung disease in children and adolescents living with HIV. We report the case of a 4-month-old female infant admitted for febrile dyspnea requiring intubation and mechanical ventilation. Computed tomography of the lungs showed diffuse interstitial infiltrates. Bronchoalveolar lavage showed multiple Pneumocystis jirovecii cysts. Molecular testing for HIV infection and Cytomegalovirus PCR assay were positive. The patient received Trimethoprim / Sulfamethoxazole, corticosteroids, folinic acid supplementation and Ganciclovir, and later antiretrovirals. She succumbed later to progressive respiratory failure, marking the progression of lung fibrosis despite the successful treatment of opportunistic infections.

Mots clés: Human immunodeficiency virus, Children, Interstitial lung disease

Pneumopathie interstitielle révélant une infection par le VIH: A propos d'un cas

RÉSUMÉ

L'infection par le virus de l'immunodéficience humaine (VIH) peut se declarer par des manifestations respiratoires, dont l'origine peut être infectieuse ou non infectieuse. Chez les enfants et les adolescents vivant avec le VIH, ces troubles peuvent se manifester sous forme de pneumopathie interstitielle. Nous rapportons le cas d'une fillette de 4 mois admise pour dyspnée fébrile nécessitant une intubation et une ventilation mécanique. La tomodensitométrie des poumons a révélé des infiltrats interstitiels diffus. Le lavage bronchoalvéolaire a mis en évidence de multiples kystes de Pneumocystis jirovecii. Les tests moléculaires pour l'infection par le VIH ainsi que le test PCR pour le cytomégalovirus se sont avérés positifs. La patiente a reçu un traitement à base de triméthoprime/sulfaméthoxazole, de corticostéroïdes, une supplémentation en acide folinique et du ganciclovir, en association avec les antirétroviraux. L'évolution était fatale par une insuffisance respiratoire progressive, marquant la progression de la fibrose pulmonaire malgré le traitement réussi des infections opportunistes.

Mots clés: Virus de l'immunodéficience humaine, Enfants, Pneumopathie interstitielle

Introduction

Human immunodeficiency virus (HIV) infection can lead to a wide range of lung disorders, contributing significantly to morbidity and mortality. These pulmonary manifestations encompass both infectious and non-infectious conditions, with their incidence varying based on access to treatment [1]. These complications often stem from systemic and pulmonary inflammation, either directly related to HIV or secondary to opportunistic infections [2]. These mechanisms can be interrelated and occur concurrently in patients. Early detection of HIV-related lung disease is crucial for optimizing care, especially to children and adolescents living with HIV (CALWHIV) in order to reduce physical impairment in these populations. These diverse lung disorders can manifest as interstitial lung disease in CALWHIV, requiring a thorough evaluation to determine their underlying etiology.

Case

We present a case of a 4-month-old female infant, with no prior medical history, admitted for febrile dyspnea.

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Acute Bronchiolitis was initially suspected and the patient recieved symptomatic treatment with oxygen supplementation. Subsequently, she was transferred to the paediatric intensive care unit due to acute respiratory failure, where she required intubation and mechanical ventilation. Chest X-Ray showed alveolar-interstitial syndrome at the lung bases (Figure 1).

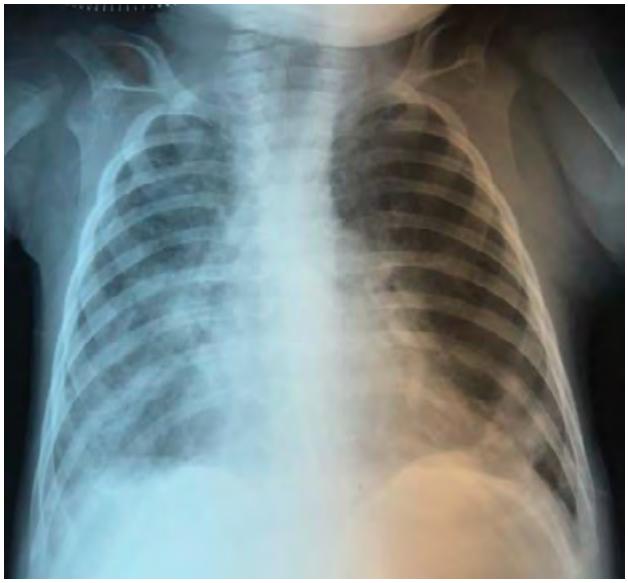

Figure 1: Chest X-Ray showing alveolar-interstitial syndrome at the lung bases

Computed tomography (CT) of the lungs showed diffuse interstitial infiltrates with multiple alveolar condensations (Figure 2).

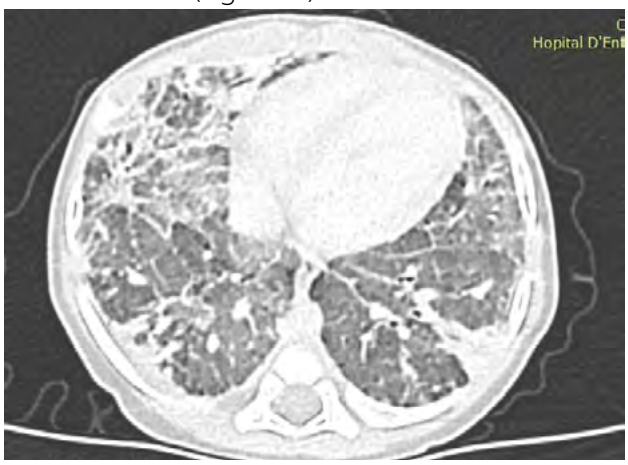

Figure 2: Computed tomography of the lungs showing diffuse interstitial infiltrates with multiple alveolar condensations

Interstitial pneumonia was suspected, and bronchoalveolar lavage (BAL) was performed. Giemsa stain showed multiple Pneumocystis jirovecii cysts. Molecular testing for HIV infection was positive with a viral load of 1000000 copies/mL. CD4 lymphocyte percentage was 26.3%. The mother's HIV serology was positive as well. Cytomegalovirus (CMV) PCR assay was positive on blood and in BAL liquid. Gene Xpert MTB/RIF ® PCR assay was negative in respiratory secretions. Pneumocystis pneumonia (PCP) and CMV disease complicating a perinatally acquired HIV infection was diagnosed, and the infant was put on Trimethoprim / Sulfamethoxazole, corticosteroids, folinic acid supplementation and Ganciclovir. Dolutegravir, Abacavir and Lamivudine based antiretroviral (ART) was initiated two weeks later. The patient was extubated but still required heated humidified high-flow therapy. Follow-up CT scan showed the persistence of bilateral dense lung infiltrates with ground-glass opacification suggestive of interstitial lung disease. HIV viral load was controlled one month after ART initiation and showed virological failure. Baseline genotypic resistance testing showed resistance to Abacavir and Lamivudine. Treatment backbone was switched to Zidovudine/Lamivudine and was reinforced with Lopinavir/ritonavir. Inhaled corticosteroids were initiated. Initial clinical improvement was noted but the infant would later succumb to progressive respiratory failure after 3 months, marking the progression of lung fibrosis despite the successful treatment of opportunistic infections.

Discussion

Our vignette illustrates a case of multifactorial interstitial lung disease in HIV infection in perinatally infected children. The usual focus on opportunistic infections in HIV-related lung disease is warranted by the frequency of these pathogens in patients without ART. PCP remains a major AIDS-defining infection in CALWHIV with a peak incidence during the first year of life [3]. Clinical presentation usually includes subacute or abrupt respiratory distress and substantial hypoxia [4]. In our case, the diagnosis of PCP was not initially suspected due to the lack of knowledge regarding the underlying immunosuppression. The analysis of BAL liquid remains the diagnostic gold standard, and treatment is based on Cotrimoxazole with the adjuvant corticosteroids in severe cases [4]. Concomitant CMV disease and PCP was a common condition in the pre-ART era [1]. Assessing the involvement of CMV in respiratory complications is usually difficult and requires histopathological evidence [4]. In most cases, CMV is regarded as a mere passenger if end-organ disease is not demonstrated [1]. In our case, treatment for CMV disease was initiated in light of the severe presentation. The persistence of interstitial pneumonia with deteriorating lung function in our patient could have been caused by lymphocytic interstitial pneumonitis. Lymphocytic interstitial pneumonitis is more common in HIV-infected children and requires a histologic diagnostic confirmation [5,6]. This complication is now less prevalent among CALWHIV since the advent of ART [7]. Ground-glass opacities can be seen on CT imaging [6,8] , which is consistent with our case. Another possible diagnosis, although less characterised than lymphocytic interstitial pneumonitis, is nonspecific interstitial pneumonitis (NSIP), which is more common among HIV-infected individuals with a higher probability of developing fibrosis than uninfected individuals [9]. HIV-induced immunological disruptions and nonspecific response, with an up-regulation of fibrosis-inducing markers is the suggested mechanism for NSIP [6,9,10]. We suggest that the multiple opportunistic infections and the initially uncontrolled

HIV infection may have accelerated the development of pulmonary fibrosis in our patient. Definite diagnosis can only be made via histology with an incidence varying according to the use of pulmonary biopsy during diagnostic work-up during HIV-associated interstitial lung disease [5]. Radiological findings can include ground-glass opacities, parenchymal areas of condensations and less predominantly, honeycombing [6]. The first case of PCP-induced fibrosing interstitial lung-disease was described by Suzuki & al. in a 68 years-old patient, with a persistent dyspnoea after completion of PCP treatment [11]. There are currently no clinical trials regarding NSIP treatment in CALWHIV. Treatment options can include corticosteroids, although case reports show inconsistent therapeutic outcomes [11–13].

Conclusions

This case demonstrates the multifaceted challenges in managing pediatric HIV, especially when complicated by opportunistic infections and drug resistance. It highlights the importance of early diagnosis, clear treatment strategies, and the need for ongoing research to improve outcomes for HIV-infected infants. Moreovern, interstitial lung disease can be the initial presentation of numerous pathologies in CALWHIV. Rigorous exclusion of opportunistic infections is required, considering the frequency of these disease in children who have yet to receive ART. Rigorous examination of radiological findings and lung biopsy are a useful tools for setting the diagnosis of non-infectious aetiologies. Establishing the right diagnosis is fundamental in order to initiate treatment and avoid the development of pulmonary sequelae and chronic lung disease in CALWHIV.

References

[1] Murray JF. Epidemiology of Human Immunodeficiency Virus–Associated Pulmonary Disease. Clinics in Chest Medicine. juin 2013;34(2):165-79.

[2] Cribbs SK, Crothers K, Morris A. Pathogenesis of HIV-Related Lung Disease: Immunity, Infection, and Inflammation. Physiological Reviews. 1 avr 2020;100(2):603-32.

[3] Williams AJ, Duong T, McNally LM, Tookey PA, Masters J, Miller R, et al. Pneumocystis carinii pneumonia and cytomegalovirus infection in children with vertically acquired HIV infection: AIDS. févr 2001;15(3):335-9.

[4] Guidelines for the Prevention and Treatment of Opportunistic Infections in Children with and Exposed to HIV.

[5] Crothers K, Morris A, Huang L. Pulmonary Complications of HIV Infection. In: Murray and Nadel's Textbook of Respiratory Medicine [Internet]. Elsevier; 2016 [cité 9 avr 2024]. p. 1583-1611.e31. Disponible sur: https://linkinghub.elsevier.com/retrieve/pii/B9781455733835000907

[6] Doffman SR, Miller RF. Interstitial Lung Disease in HIV. Clinics in Chest Medicine. juin 2013;34(2):293-306.

[7] Du Plessis A, Andronikou S, Machemedze T, Griffith-Richards S, Myer L, Mahtab S, et al. High-resolution computed tomography features of lung disease in perinatally HIV-infected adolescents on combined antiretroviral therapy. Pediatric Pulmonology. nov 2019;54(11):1765-73.

[8] Sharland M, Gibb DM, Holland F. Respiratory morbidity from lymphocytic interstitial pneumonitis (LIP) in vertically acquired HIV infection. Arch Dis Child. avr 1997;76(4):334-6.

[9] Huang WJ, Tang XX. Virus infection induced pulmonary fibrosis. J Transl Med. 7 déc 2021;19:496.

[10] George M, Singh V, Gladwin M. Noninfectious and Nonneoplastic Conditions Associated with Human Immunodeficiency Virus Infection. Semin Respir Crit Care Med. 14 mars 2016;37(02):289-302.

[11] Suzuki T, Shimoda Y, Teruya K, Gatanaga H, Kikuchi Y, Oka S, et al. Case report: new development of fibrosing interstitial lung disease triggered by HIV-related pneumocystis pneumonia. BMC Pulm Med. 18 mars 2019;19(1):65.

[12] Duggal L, Puri V, Vasdev N. Non-specific interstitial pneumonia in an HIV positive patient. J Assoc Physicians India. juin 2005;53:564-5.

[13] Collins B, Mulhall P, Travaline JM. Nonspecific Interstitial Pneumonia in a Patient with HIV. SN Compr Clin Med. mars 2019;1(3):203-4