Case Report

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A 6-year-old child with a new diagnosis of perinatal human immunodeficiency virus infection

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Abstract

Perinatal human immunodeficiency virus transmission, while rare in the United States, should be considered in children with a history of recurrent infections, chronic respiratory symptoms and developmental delay. A delayed diagnosis of human immunodeficiency virus in children can lead to significant morbidity and mortality. We present a 6-year-old male who presented for evaluation and management of antibiotic refractory chronic cough and purulent nasal secretions, with a history of recurrent bacterial pneumonias and sinus infections, disseminated varicella zoster, and global developmental delay. He likely had perinatally acquired human immunodeficiency virus. At the time of his human immunodeficiency virus diagnosis, he met the criteria for acquired immunodeficiency syndrome and was ultimately diagnosed with lymphocytic interstitial pneumonia (LIP). Our case illustrates the importance of universal human immunodeficiency virus screening of pregnant women, consideration of human immunodeficiency virus, and the prompt initiation of treatment. We believe this case serves as an important reminder for all medical providers who care for pregnant women and children.

Keywords

Human immunodeficiency virus, pediatrics, immunodeficiency, HIV/AIDS

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Introduction

From the peak incidence of perinatal human immunodeficiency virus (HIV) infection cases in 1991 (n = 1760) in the United States, the incidence has decreased 97%.[1] The Centers for Disease Control and Prevention (CDC) recommends third trimester HIV testing of all pregnant women who are at risk for HIV, or who live in areas with a high HIV prevalence.[2] This strategy has decreased the risk of perinatal HIV transmission to less than 1%.[3] Missed third trimester HIV screening is a neglected opportunity to prevent perinatal HIV transmission.[2] Initiating antiretroviral therapy (ART) for pregnant women with HIV is a key strategy for preventing perinatal HIV.[4]

Case presentation

A 6-year-old, African American male with a past medical history (PMH) significant for difficult-to-control moderate persistent asthma, eczema, seasonal allergies, and learning delays presented to his primary care physician for evaluation of chronic cough and persistent, thick, nasal discharge. He lacked fevers, facial pain, and otalgia. His cough was productive and limited his activity due to exertional fatigue and frequent interruptions due to breathlessness. Three months prior to presentation, his primary care physician (PCP) started him on a daily inhaled corticosteroid for asthma, without improvement in his cough. His nasal discharge did

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not improve following a course of amoxicillin–clavulanic acid therapy.

Additional PMH was significant for three prior episodes of pneumonia requiring hospitalization for intravenous antibiotic therapy at 7 months, 2 and 4 years of age. He had a history of six sinus infections, which occurred independently of his episodes of pneumonia, that were each treated with antibiotics without improvement. Five months prior to his presentation, he was diagnosed with a disseminated varicella-zoster viral rash that crossed dermatomes which required treatment with antiviral therapy. Due to his learning delays, he was enrolled in a special education program at school and received at home speech therapy twice weekly.

On physical exam, he was afebrile and normotensive with a heart rate of 115 beats per minute, a respiratory rate of 20 breaths per minute, and pulse oximeter 100% on room air. His weight was 20.5 kilograms (CDC, 20.93%, Z = −0.81), his height was 111 cm (CDC, 2.62%, Z = −1.94), and his body mass index was 16.64 kg/m^2 (75.74%, Z = 0.70). On exam, he had thick, green nasal secretions and bilateral, painless, mobile, cervical lymphadenopathy. He was breathing comfortably and had clear breath sounds. He had no hepatosplenomegaly. He had a healed dermatomal rash along the right lower trunk that crossed midline. He had speech delay with phonological and receptive language disorders. His cranial nerves were grossly intact. He had normal strength, tone, reflexes, and gait.

Initial laboratory and imaging studies are reported in Table 1 and Figure 1, respectively. He was admitted to the hospital for further evaluation.

Table 1. Patient lab values.

Lab test	Value	Reference range and units
White blood cell count	6.34	4.27–11.40 × 10^3/μL
Red blood cell count	4.40	3.90–5.03 × 10^6/μL
Hemoglobin	11.6	10.6–13.4 g/dL
Hematocrit	33.7	32.2%–39.8%
Platelet count	569	199–369 × 10^3/μL
Absolute neutrophil count	1.93	1.63–7.87 × 10^3/μL
Absolute lymphocyte count	3.37	0.97–4.28 × 10^3/μL
Absolute monocyte count	0.69	0.19–0.85 × 10^3/μL
Absolute eosinophil count	0.32	0.03–0.52 × 10^3/μL
Absolute basophil count	<0.03	0.01–0.06 × 10^3/μL
Sodium	139	136–145 mmol/L
Potassium	3.4	3.5–5.5 mmol/L
Chloride	107	95–105 mmol/L
Carbon dioxide	25	20–28 mmol/L
BUN	17	2–23 mg/dL
Creatinine	0.29	0.30–0.60 mg/dL
Glucose	86	70–100 mg/dL
Alkaline phosphatase	136	134–346 U/L
Calcium	9.1	8.8–10.1 mg/dL
Total protein	10.2	6.7–8.1 g/dL
Albumin	4.0	3.5–4.7 g/dL
Total bilirubin	0.2	0.2–1.0 mg/dL
Alanine transaminase	11	10–41 U/L
Aspartate aminotransferase	72	15–50 U/L

BUN: blood urea nitrogen; μL: microliter; d: deciliter; L: liter; mmol: millimoles; mg: milligrams; g: grams; U: units.

Hospital course

During her pregnancy, his mother lived in a state with a high prevalence of HIV and she was treated for gonorrhea. Her HIV testing in the first trimester of pregnancy was negative, and her testing was not repeated in the third trimester, nor at the time of his delivery. He was born vaginally at 35 weeks gestational age without complications. He was a breastfed infant. His mother was diagnosed with HIV when he was 2 years old. He had never been tested for HIV.

Upon his admission, a fourth-generation antigen/antibody HIV test, which includes HIV-1 and HIV-2 antibodies and P24 antigen, was performed at Texas Children's Hospital (Architect instrument, Abbott Diagnostics Division) and was reactive with a HIV viral load of 132,152 copies/mL (<80 copies/mL). His absolute CD4 count was 648 cells/mL (⩾500 cells/μL), and CD4% was 19.4% (⩾26%). He had normal immunoglobulin levels. He was started on ART with raltegravir and emtricitabine/tenofovir. Based on his developmental history, a diagnosis of HIV encephalopathy was suspected.[5] He saw a Pediatric Neuropsychologist, who diagnosed him with a mild neurocognitive disorder, most likely attributable to long-term untreated HIV infection.

During his hospitalization, he underwent work-up for opportunistic pathogens (Table 2). Positive findings included a quantitative Epstein–Barr virus (EBV) polymerase chain reaction (PCR) in whole blood of 4871 international units (IU)/mL (<261 IU/mL) and 13,500 IU/mL (<25 IU/mL) in bronchioalveolar lavage (BAL) fluid. Both *Haemophilus influenzae* and methicillin-sensitive *Staphylococcus aureus* were isolated from a middle meatus sinus culture. He received a course of sulfamethoxazole–trimethoprim. BAL cytology was negative for malignancy.

Based on his symptoms, CT scan findings, and infectious work-up, his working diagnosis was lymphocytic interstitial pneumonia (LIP). He was discharged on antiretroviral therapy (ART) therapy with outpatient follow-up.

Five months after initiation of ART, his viral load was undetectable, his CD4 count and CD4% increased to 1295 cells/mL (⩾500) and 41% (⩾26%), respectively. His cough and exercise intolerance improved over time. Repeat computed tomography (CT) chest 9 months into treatment revealed complete resolution of the interstitial lung disease (Figure 2).

Discussion

We present a case of a 6-year-old child who had a delayed diagnosis of perinatal HIV infection resulting in acquired immunodeficiency syndrome (AIDS), lymphocytic interstitial pneumonia (LIP), and presumed HIV encephalopathy.

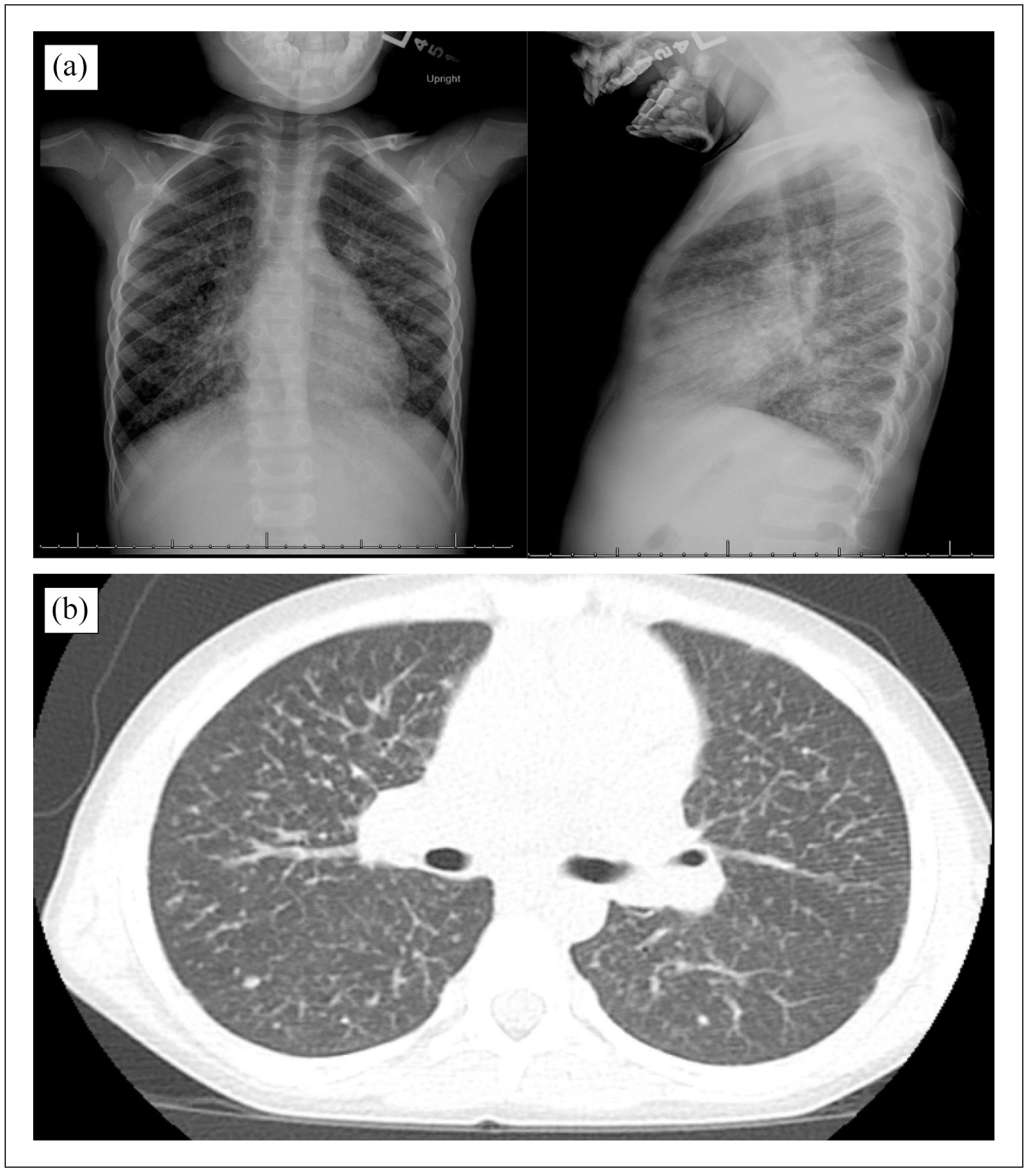

Figure 1. (a) Chest radiograph showing bilateral, tiny, nodular shadows. (b) Chest computed tomography showing miliary micronodules scattered throughout both lungs. These nodules are predominately random in distribution but some demonstrate perilymphatic/peribronchial distribution.

Table 2. Infectious disease work-up.

Lab test	Value	Reference range
Blood		
Peripheral blood culture	No organisms isolated	No organisms isolated
Peripheral mycobacteria blood culture	No acid fast bacilli isolated	No acid fast bacilli isolated
Peripheral fungal blood culture	No yeast or filamentous fungus isolated	No yeast or filamentous fungus isolated
Quantiferon gold in-tube	Negative	Negative
Toxoplasma antibody panel	Negative	Negative
Syphilis Screen	Negative	Negative
Aspergillus antigen	Not detected	Not detected
Fungitell	<31 pg/mL	<80 pg/mL

(Continued)

Table 2. (Continued)

Lab test	Value	Reference range
Histoplasma antigen	Not detected	Not detected
Fungal complement fixation		
Aspergillus	<1:8	<1:8
Blastomyces	0.4 IV	<0.9 IV
Coccidioides	<1:2	<1:2
Histoplasma mycelial	<1:8	<1:8
Histoplasma yeast	<1:8	<1:8
Ql herpes simplex virus 1/2 PCR	Not detected	Not detected
Qn varicella-zoster virus PCR	Not detected	Not detected
Qn Epstein–Barr virus PCR	4871 IU/mL	<261 IU/mL
CSF		
Cell counts		
WBC	2 CU/mm	0–5 CU/mm
RBC	170 CU/mm	170 CU/mm
Aerobic culture	No organisms isolated	No organisms isolated
Mycobacterial culture	No acid fast bacilli isolated	No acid fast bacilli isolated
Fungal culture	No yeast or filamentous fungus isolated	No yeast or filamentous fungus isolated
Ql VDRL	Non-reactive	Non-reactive
Cryptococcal antigen	Negative	Negative
Epstein–Barr virus PCR	Not detected	Not detected
Bacteria broad range PCR	Not detected	Not detected
Mycobacteria broad range PCR	Not detected	Not detected
Fungal broad range PCR	Not detected	Not detected
MTB complex PCR	Not detected	Not detected
Bronchioalveolar lavage		
Aerobic culture	No organisms isolated	No organisms isolated
Mycobacterial culture	No acid fast bacilli isolated	No acid fast bacilli isolated
Fungal culture	No yeast or filamentous fungus isolated	No yeast or filamentous fungus isolated
Anaerobic culture	No organisms isolated	No organisms isolated
Viral respiratory culture	No virus isolated	No virus isolated
Bacteria broad range PCR	Not detected	Not detected
Mycobacteria broad range PCR	Not detected	Not detected
Fungal broad range PCR	Not detected	Not detected
Pneumocystis jiroveci PCR	Not detected	Not detected
Histoplasma antigen	Not detected	Not detected
MTB complex and rifampin resistance PCR	Not detected	Not detected
Qn adenovirus PCR	Not detected	Not detected
Qn cytomegalovirus PCR	Not detected	Not detected
Qn Epstein–Barr virus PCR	13,500 IU/mL	<25 IU/mL
Middle meatus sinus culture	Rare methicillin-susceptible *Staphylococcus aureus*; moderate *Haemophilus influenzae*	No organisms isolated

Qn: quantitative; IU: International units; mL: milliliter; PCR: polymerase chain reaction; CSF: cerebrospinal fluid; WBC: white blood cell; CU/mm: cubic millimeter; RBC: red blood cell; Ql: qualitative; VDRL: venereal disease research laboratory; MTB: mycobacterium tuberculosis; CT: computed tomography.

Our patient acquired HIV perinatally. The exact timing of perinatal transmission (i.e. in utero, at the time of labor and delivery, or postnatally via breastfeeding) is unknown. His mother was at high risk for HIV given her residence in a high HIV prevalence state and the diagnosis of gonorrhea during pregnancy.[2] Despite the CDC's HIV screening guidelines for pregnancy,[2] a third trimester HIV test was not obtained and the child was not tested for HIV at age 2 years when his mother was diagnosed with HIV infection. At the time of his diagnosis of HIV, at age 6, he met clinical criteria for a diagnosis of AIDS.[6] A diagnosis of LIP was made after excluding other infectious etiologies.

LIP is a benign lymphoproliferative disorder characterized by chronic cough and dyspnea with a negative infectious work-up. Lung biopsy is required for definitive diagnosis. Our patient's prolonged cough was likely due to his development of LIP, as the typical onset of LIP in children with perinatal HIV is 1–2 years of age.[7] This is further supported by

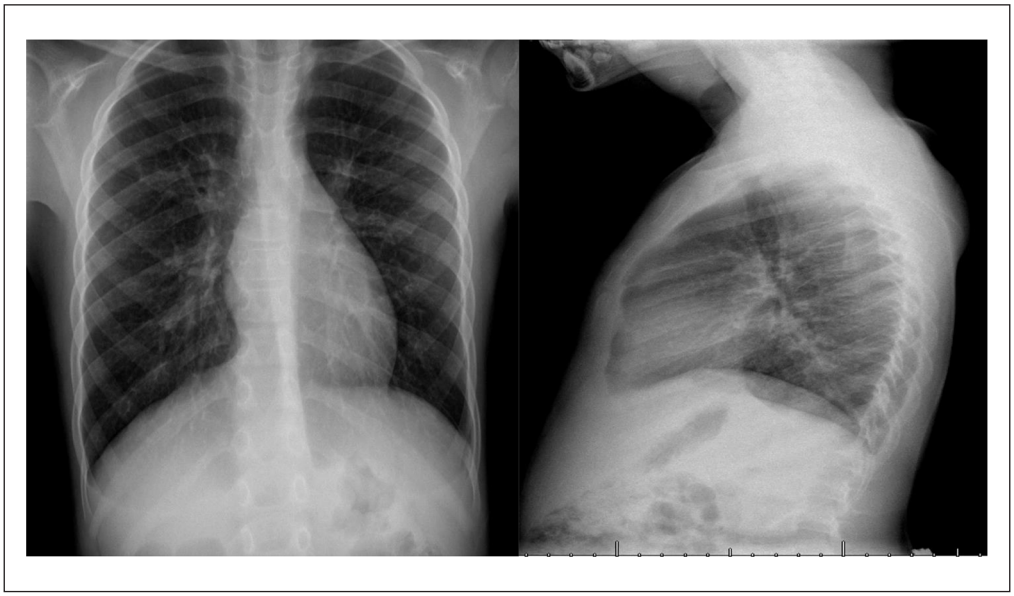

Figure 2. Chest radiograph showing resolution of LIP after ART therapy.

his history of multiple episodes of pneumonia, as acute lung infections are more common in children with LIP than those without.[8] He also had bilateral reticulonodular infiltrates on chest radiograph (CXR) and perilymphatic micronodules on high-resolution CT, both characteristic of LIP.[7]

Although the pathogenesis of LIP is currently unknown, there is evidence that EBV plays a role, particularly in the context of HIV. Our patient had evidence of EBV infection with a positive quantitative PCR in whole blood and BAL fluid. Studies have shown EBV positivity in lung biopsy samples as well as serology in patients with LIP.[9,10] The significance of a positive EBV BAL PCR based on literature review is unknown.[11]

Management of HIV-related LIP includes treatment of HIV with ART. Intravenous immunoglobulin has been used as therapy in children with immunoglobulin deficiencies as has prolonged corticosteroid therapy in severe or persistent cases.[12,13] Our patient's LIP symptoms improved with ART.

Conclusion

A history of chronic recurrent bacterial infections, developmental delay, and disseminated varicella-zoster virus in a child should prompt a work-up for immunodeficiency, including obtaining a fourth-generation HIV test. Perinatal transmission of HIV, while rare in United States, still occurs and requires a high index of suspicion and thorough maternal history. Providers should be aware of HIV screening guidelines in first and third trimesters of pregnancy for prevention of perinatal HIV transmission and prompt treatment with appropriate ART when indicated. LIP should be considered in untreated children with HIV infection and chronic respiratory symptoms. LIP is a diagnosis of exclusion, and therefore, these patients should have a broad work-up to rule out alternative etiologies. In most situations, children with LIP improve with supportive care and ART.

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Authorship

All authors contributed to the conceptualization, writing, and critical review of this case report.

Availability of data and materials

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

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Ethics approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed consent

Written informed consent was obtained from a legally authorized representative(s) for anonymized patient information to be published in this article.

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