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Case Report

Severe HIV Disease in a Rapid Antibody Negative Infant Infected After Late Maternal Incident HIV Infection: A Case Report from Lilongwe, Malawi

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- Early infant diagnosis

Abstract

The World Health Organization (WHO) places priority on initiation of antiretroviral therapy (ART) in all children less than 24 months of age with a confirmed diagnosis of HIV and those who meet criteria for presumptive diagnosis of severe HIV disease. A four-month old breastfed infant, HIV-exposed after mother was infected during pregnancy or breastfeeding (i.e. late maternal incident infection), presented to Kamuzu Central Hospital in Lilongwe, Malawi with respiratory distress and was diagnosed with Pneumocystis pneumonia versus severe pneumonia and thrush. These diagnoses were consistent with clinical criteria set forth by the WHO for presumptive diagnosis of severe HIV disease, however, the infant did not meet laboratory criteria due rapid antibody negative status. Despite not meeting WHO indications, he was empirically started on ART while awaiting the results of the HIV DNA PCR as well as broad-spectrum antibiotics. He improved, his DNA PCR was positive, and 3 weeks into treatment, he developed BCG-lymphadenitis suggestive of immune reconstitution. This case illustrates the limitations of WHO criteria for presumptive diagnosis of severe HIV disease in infants born to mothers with late maternal incident infection given their lack of circulating maternal antibody and their risk of developing severe disease before sero converting themselves. As Prevention of Mother to Child Transition (PMTCT) programs are optimized globally, an increasing proportion of vertical HIV transmission will be attributable to missed PMTCT, including women with late maternal incident infection, and this presentation of pediatric HIV infection may become relatively more common.

ABBREVIATIONS

ART: Antiretroviral Therapy; HIV: Human Immunodeficiency Virus; PMTCT: Prevention Of Mother To Child Transmission; WHO: World Health Organization

INTRODUCTION

HIV-infected infants have rapid disease progression and most will die before their second birthday if not treated with antiretroviral therapy (ART) [1,2]. To prevent morbidity, WHO places priority on early initiation of ART for all children less than 24 months old with confirmed HIV infection [1,2]. However, infant diagnosis of HIV is complicated by presence of maternal anti-HIV IgG, which is received transplacentally and can remain detectable for up to 18 months of age, resulting in false positive rapid antibody testing. Virological testing, such as HIV DNA PCR, should be used for infants under 18 months of age [1] but is often unavailable in resource poor settings or it may take several weeks to obtain results. Recognizing these widespread diagnostic limitations, the World Health Organization (WHO) outlines criteria for making a presumptive diagnosis of severe HIV disease in infants less than 18 months old (Table 1) and recommends starting ART once this diagnosis is madet [2,3]. In most scenarios, these criteria are appropriately sensitive to detect severe HIV disease in HIV-positive children at high risk of death and in need of ART without delay [3]. However, the following case illustrates that these criteria are may be insufficient to identify ill infants vertically infected with HIV after late maternal incident infection.

CASE PRESENTATION

A four-month old, exclusively breastfed infant presented with fever and several days of worsening respiratory distress to Kamuzu Central Hospital, a referral hospital in Lilongwe, Malawi where clinician's from the Baylor College of Medicine Clinical Center of Excellence-Malawi serve as HIV consultants. The infant's mother initiated antenatal care in her second trimester and had documentation of negative rapid HIV antibody testing in her second trimester and in labor. Pregnancy and delivery were uncomplicated. The infant had received regular immunizations including BCG and two doses of pneumococcal vaccine.

Exam revealed a febrile, hypoxic infant (peripheral capillary oxygen saturation 85%) with tachypnea (80-90 breaths per minute), and tachycardia (180 beats per minute). He was alert

Table 1: World Health Organization criteria for presumptive diagnosis of severe HIV disease in infants and children < 18 months of age where viral testing is not available [1].

A presumptive diagnosis of severe HIV disease should be made if:	
1. The child is confirmed as being HIV antibody-positive AND	2a. The infant is symptomatic with two or more of the following: • oral thrush[b] • severe pneumonia[b] • severe sepsis[b] OR 2b. A diagnosis of any AIDS-indicator condition(s)[a]a can be made
Other findings that support the diagnosis of severe HIV disease in an HIV-seropositive infant include: – Recent HIV-related maternal death or advanced HIV disease – Child's % CD4+ <20%	
Confirm the diagnosis of HIV infection as soon as possible.	

[a]AIDS-indicator conditions include some but not all HIV pediatric clinical stage 4 conditions such as Pneumocystis pneumonia, cryptococcal meningitis, severe wasting or severe malnutrition, Kaposi sarcoma, extrapulmonary TB.
[b]As per the IMCI definition:
Oral thrush: Creamy white-to-yellow soft small plaques on red or normally colored mucosa which can often be scraped off (pseudomembranous), or red patches on the tongue, palate or lining of mouth, usually painful or tender.
Severe pneumonia: Cough or difficult breathing in a child with chest in drawing, stridor or any of the IMCI general danger signs; i.e. lethargic or unconscious, not able to drink or breastfeed, vomiting, and presence or history of convulsions during current illness; responding to antibiotics.
Severe sepsis: Fever or low body temperature in a young infant with any severe sign, e.g. fast breathing, chest in drawing, bulging fontanelle, lethargy, reduced movement, not feeding or sucking breast milk, convulsions.

and awake, but was in severe respiratory distress with subcostal and suprasternal retractions and nasal flaring. The lung exam was non-focal without wheezes, rhonchi or rales. Oral thrush was present. Infant was small-for-age but with normal weight/height ratio and normal nutrition Z-score. Patient had dry mucous membranes, but normal skin turgor and capillary refill.

Due to stock-outs and supply shortages, no radiographic diagnostics were available. A bedside echo was reassuring against structural heart disease and cardiac failure. Rapid HIV antibody testing was performed on the mother and infant at admission and repeated the next day. Both times, the mother's test was positive and the infant's test was negative. The father's HIV status remained unknown. An HIV DNA PCR was drawn on the infant at admission.

A clinical diagnosis of oral thrush and pneumocystis pneumonia was made with the consideration of an alternative diagnosis of severe pneumonia. Treatment was started with high-dose oral sulfamethoxazole/ trimethoprim, steroids, oxygen therapy, ceftriaxone IV and oral fluconazole. The infant did not meet WHO criteria for presumptive diagnosis of severe HIV disease due to laboratory rapid antibody negative status (Table 1), but because of his HIV exposure and strong clinical suspicion of HIV disease, ART was initiated empirically while awaiting the result of the DNA PCR, which returned several weeks later with a positive result.

Respiratory status improved gradually over the course of two weeks. The patient developed BCG-lymphadenitis after three weeks of ART consistent with immune reconstitution, which pointed to the infant's late stage immune suppression prior to ART despite his negative antibody test results. At six month follow up, he was growing well and clinically asymptomatic on ART.

DISCUSSION

As more countries optimize PMTCT efforts and follow WHO recommendations to offer combination ART to all HIV-infected pregnant women [1], overall vertical transmission will decrease and an increasing proportion of new pediatric HIV infections will be attributable to women who have missed PMTCT, for example, those who test negative early in pregnancy only to acquire HIV during pregnancy or breastfeeding, such as the infant-mother pair presented here. Studies across sub-Saharan Africa demonstrate that HIV incidence during pregnancy and breastfeeding is high [4]. Furthermore, the risk of perinatal transmission with late maternal incident infection is 2.8 times that seen with chronic HIV infection [4]. High viral load is also associated with rapid disease progression [5].

This case demonstrates that, unlike the limited acute infection seen in adults, infants acutely infected with HIV can become severely ill prior to mounting their own antibody response. It is conceivable that pathophysiological factors of late maternal incident infection, like high viral load and lack of maternal antibody protection, accelerate this process and lead to the presentation described. Therefore, infants vertically infected in HIV after late maternal sero conversion require urgent initiation of ART for survival, perhaps even more so than previous studies of vertically infected infects have suggested. However, because prompt virological testing is not available and antibody testing does not reflect HIV status or HIV exposure, they do not meet WHO definition of confirmed HIV infection or of presumptive diagnosis of severe HIV disease, and therefore do not meet WHO indications to start ART. In resource poor settings like Malawi, which base their own ART guidelines on WHO recommendations, these infants will go untreated and mortality will likely approach 100 percent.

In the era of improved PMTCT and the likely resultant shift in the epidemiology of new pediatric HIV infections as described above, further studies to examine the public health as well as the clinical impact on infants infected with HIV after late maternal incident HIV infection must be done. PMTCT and early infant diagnosis programs must include and individually evaluate the

efficacy of repeat HIV testing of mothers in late pregnancy, labor and/or during breastfeeding. In settings with high rates of late maternal incident HIV infection, point-of-care virological testing is necessary, but until it becomes widely available, the diagnosis of presumptive diagnosis of severe HIV disease may need to be reconsidered to include HIV-exposed infants with negative rapid antibody tests if mother tests positive or cannot be tested

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REFERENCES

1. World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection Recommendations for a public health approach- 2nd edition. Geneva. 2016.

2. World Health Organization. Antiretroviral therapy of HIV infection in infants and children: towards universal access. Geneva. 2010.

3. Grundman N, Iliff P, Stringer J, Wilfert C. Presumptive diagnosis of severe HIV infection to determine the need for antiretroviral therapy in children less than 18 months of age. Bull World Health Organ. 2011; 89: 513-520.

4. Drake AL, Wagner A, Richardson B, John-Stewart G. Incident HIV during Pregnancy and Postpartum and Risk of Mother-to-Child HIV Transmission: A Systematic Review and Meta-Analysis. PLoS Med. 2014; 11: e1001608.

5. Rich KC, Fowler MG, Mofenson LM, Abboud R, Pitt J, Diaz C, et al. Maternal and infant factors predicting disease progression in human immunodeficiency virus type-1 infected infants. Pediatrics. 2000; 105: e8.

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