CASE REPORT **Open Access**

A Child with HIV (Human Immunodeficiency Virus) Infection Accompanied by Severe Acute Malnutrition: A Case Report

Sidrah Darma[1,2]*, Herry D. Nawing[1], Ninny Meutia Pelupessy[1], Husein Albar[1]
[1]Department of Pediatrics, Faculty of Medicine, Hasanuddin University, Makassar, Indonesia
[2]Department of Nutrition, Faculty of Medicine, Universitas Muslim Indonesia, Makassar, Indonesia
*Corresponding Author. E-mail: sidrah.darma@umi.ac.id, Mobile number: +6285340478557

ABSTRACT

Joint United Nations Programme in HIV/AIDS (UNAIDS) reported that 1.8 million children under 15 years old had HIV with 150,000 new pediatric cases in 2015, and only 49% had an antiretroviral (ARV) therapy. Mortality in HIV-infected children with severe acute malnutrition was 30.4% in Africa. A 1-year and 8-months-old girl was hospitalized due to diarrhea, vomiting, oral thrush, and recurrent fever before admission. She has been hospitalized for HIV infection one month ago and treated with ARV. Her mother was treated with ARV before. Physical examination showed a severely ill, poorly nourished, stunting, and conscious child with normal vital signs. There was oral thrush. The evidence of nutritional marasmus was old man face, piano sign, wasting, and baggy pants**.** Laboratory findings revealed anemia, positive antigen and antibody of HIV infection, and low Cluster of Differentiation 4 (CD4). She was treated with ARV, Cotrimoxazole, and management of malnutrition and diarrhea. The prognosis of the patient was poor. A 1-year and 8-months-old girl with HIV infection complicated with severe acute malnutrition, acute diarrhea, oral thrush, and anemia of chronic disease were reported. The diagnosis was based on clinical and laboratory findings. Management focused on the therapy of HIV and accompanying illness. The prognosis was poor.

Keywords: HIV infection; severe acute malnutrition; child; diarrhea

Article history:
Received: 1 November 2020
Accepted: 23 December 2020
Published: 30 December 2020

GREEN MEDICAL JOURNAL
E-ISSN 2686-6668

Published by :
Faculty of Medicine
Universitas Muslim Indonesia

Address:
Jl. Urip Sumoharjo Km. 5, Makassar
South Sulawesi, Indonesia

Mobile number:
+62822 9333 0002

Email:
greenmedicaljournal@umi.ac.id

Introduction

HIV-induced Acquired Immuno Deficiency Syndrome (AIDS) pandemic has been a major medical and public health problem globally. Pediatric HIV infection can present in neonates, children, or adolescents.[1] The number of cases of AIDS among children in the United States is decreasing because of the increasingly successful prevention of perinatal transmission and the availability of effective treatment. Prompt diagnosis and adherence to effective treatment are critical to change the face of HIV infection from a fatal disease to a chronic, manageable infection. Globally in 2016, an estimated 2.1 million children were living with HIV, and < 50% of these children receiving antiretroviral (ARV) treatment.[2]

Currently, all pregnant women should be offered counseling and testing for HIV infection during pregnancy. The risk of HIV transmission from the mother to baby range from 15-25% in the developed nations and 25-35% in developing countries.[3]

This case is interesting because the patient's mother routinely controlled her pregnancy at the primary health care and hospital, but she was not screened for HIV infection at that time.

Case

The patient, RP, a one-year and eight-month-old girl, presented to the hospital with a 3-days history of watery stool, 3-5 times a day. The stool contained some grounds, mucus, but no blood. She also had a history of non-projectile vomiting three times, contained liquid and food residue. She looked thirsty but had no appetite. There were white patches on the mouth noticed in the past five days, especially on the tongue and inner buccal. There was fever developed in the two days before admission, not continuously. She has frequently had a fever, diarrhea, cough, and white patches in her mouth since the age of 3 months. The body weight did not gain appropriately due to frequent infection.

The patient was diagnosed with the Human Immunodeficiency Virus (HIV) 1 month before at Jumpandang Baru Primary Health Center and treated with Antiretroviral (ARV) and Cotrimoxazole. the patient's mother routinely controlled her pregnancy at primary health care, but unfortunately, she missed the screening examination of HIV. The patient was breastfed from birth until 15 months of age since her mother was diagnosed with HIV infection. Her mother has tattoos and lived with her drug user boyfriend before marriage. The patient's father had a non-reactive HIV test. The patient was born full-term, spontaneous vaginal delivery, assisted by midwives. The baby cried immediately, no cyanosis. The birth weight was 2500 grams, while the birth length and the head circumference were not recorded. The patient got complete basic immunization.

Essential findings at presentation included a chronically ill-looking girl and undernourished, with bodyweight, was 6.4 kg (between -2 SD and -3 SD of weight for length, WHO Z-score chart). Her vital signs were within normal limits. There was a whitish plague in her mouth and buccal (oral thrush). There was evidence of nutritional marasmus on physical examination consisted of old man face, piano sign, wasting, and baggy pants. She had dehydration signs such as sunken eyes, dry lips, increased bowel sound, and no tenderness.

The result of the laboratory examination was anemia of chronic disease and hyponatremia describe in Table 1. Because the hemoglobin level was 8.9 mg/dl, we continued by examining the ferritin level, and the result was 288.15 ng/ml. We also confirmed that she had HIV by examining the antigen/antibody of HIV and CD4, and the result was reactive antigen/antibody HIV and 131 cell/ml, respectively.

Table 1. Laboratory examination

Blood Test	27/12/2019	1/1/2020	Normal Range
WBC (/uL)	12000	10240	4000-10000
HGB (g/dL)	8.9	9.1	11-14
MCV (fL)	82	80	73-89
MCH (pg)	29	31	24-30
PLT (/uL)	448000	214000	150000-400000
Sodium (mmol/l)	133	138	136-145
Potassium (mmo/l)	4.6	4	3.5-5.1
Chloride (mmol/l)	111	98	97-111

Note : Abbreviations: WBC, White Blood Cell; HGB, Haemoglobin: MCV, Mean Corpuscular Volume; MCH, Mean Corpuscular Hemoglobin; PLT,Platelet

She was commenced on antiretroviral (ARV) therapy with a fixed drug combination (lamivudine, nevirapine, and zidovudine) 1 tablet daily, cotrimoxazole 240 mg daily, and nystatin 100.000 IU twice a day. The patient was also placed on rehydration and got zinc 20 mg daily (10 days) for diarrhea, and malnutrition management. On day 6th, no more signs of diarrhea and oral thrush but still with Severe Acute Malnutrition (SAM). She was given oral feeding and medications. On day 9th, laboratory evaluation became normal except for SAM and bone age, similar to a one-year-old child. Therapy with zinc, antiretroviral, cotrimoxazole, and malnutrition management was continued.

Discussion

Data from the Joint United Nations Programme in HIV/AIDS (UNAIDS) related to 160 countries reported 36.7 million HIV worldwide in 2015. There were 1.8 million children under 15 years old living with HIV, 150,000 new pediatric cases. Only 49% had a retroviral therapy in 2015.[4]

Data from the Health Ministry of Republic Indonesia until September 2014, the amount of AIDS were 238 children under one-year-old, 969 children in 1-4 years old, 441 children in 5-14 years old, and 1,717 children in 15-18 years old.[5]

Most of HIV infection in children is caused by mother to baby transmission. This vertical transmission was first reported in 1983. There is direct or indirect evidence of three pathways of HIV transmission from mother to baby: intrauterine, intrapartum, and transmission through breast milk. Most infections occur during late pregnancy or intrapartum. With a Polymerase Chain Reaction (PCR) examination of HIV DNA (Deoxyribonucleic Acid), nearly a third of infants infected with HIV can be identified 48 hours after birth. The baby is estimated to be infected in utero. The remaining two-thirds occur during labor because HIV DNA can be detected approximately two weeks later.[6] The rate and time of HIV transmission are 5-10% during pregnancy, 10-15% during delivery, and 5-20% during breastfeeding. In general, there are 15 – 45% HIV transmissions from mother to child.[3] In this case, the transmission of HIV from breastfeeding and probably from the intrauterine and delivery transmission, but the mother not screening HIV at that time.

HIV transmission can be facilitated by breastmilk directly and indirectly. A high concentration of inflammatory molecule (e.g., CXCL12, CCL5 IL-8, RANTES, IL-8, IL-15, macrophage inflammatory protein 1a) are associated with increased risk of transmission by breastmilk.[6]

Signs and symptoms of HIV infection in children were nonspecific, such as weight loss, failure to thrive, chronic diarrhea, recurrent fever, cough, anemia, lymphadenopathy, liver and spleen enlargement, and opportunistic infection.[7] Willians et al reported that clinical manifestations often appeared in HIV children are recurrent fever (44.6%), malnutrition (37.6%), lymphadenopathy (34.4%), respiratory tract infection (34.4%), diarrhea (24.5%), oral thrust (6.6%) and anemia (4.9%). The common first manifestation of HIV infection in the pediatric patient is oral mucosal lesion and important prognostic values. [8]

Diagnosis of HIV in children is established from previous HIV infection, clinical signs direct to HIV infection, and supporting the investigation. There is no superior or inferior algorithm in proving HIV diagnosis. HIV antibody and virology tests help to establish the diagnosis better.[9]

Table 2. Diagnose of HIV infection [9]

Methode	Recommendation
Serology test (DNA, RNA)	To diagnose HIV children <18 months old, recommended initial examination in 6-8 week old.
Antibody HIV test	In diagnosing HIV mother or identification exposure in baby ≥ 18 months old Identification HIV infection <18 months

Recommendation of examination method in diagnosing HIV infection in < 18-month-old children is a serology test while in ≥ 18-month-old children is antibody HIV test as described in Table 2.

World Health Organization (WHO) had classified HIV based on clinical stage.[8] Immunology parameter was used to measure immunodeficiency, began antiretroviral (ARV), and its use is accompanied by clinical examination. The differentiation (CD4+) absolute and lymphocyte total in the healthy baby is higher than adults and decreased until adult value. CD4+ percentage almost does not change at any age, and this is used as an immunology measurement for children less than five years old.[10]

SIn this case report, we found a history of recurrent fever, diarrhea, and oral candidiasis. Anthropometrics measurement also showed wasted children. Based on the WHO clinical stage of HIV, this patient was classified into stage 3. The patient had severe immunodeficiency based on the immunodeficiency stage, due to CD4+ of 131 cell/ml. Table 3 shows the severity of HIV infection by CD4 value based on the children's age.

Table 3. WHO HIV Associated Immunodeficiency [11]

	CD4+ value by Age			
	<11 months (%)	**12-35 months (%)**	**36-59 months (%)**	**>5 years (cell/ml)**
Negative	>35	>30	>25	>500
Mild	30-35	25-30	20-25	350-499
Moderate	25-29	20-24	15-19	200-349
Severe	<25 Or <1500cell/ml	<20 Or <750cell/ml	<15 Or <350cell/ml	<200 Or <15%

Immediately after the diagnosis of HIV was established and clinical staging was specified, Antiretroviral (ARV) therapy should be given. The first-line regimens recommended to the patients who had never received any antiretroviral treatment are presented below. [11]

Children ≤ 3 years old:

- Zidovudin (AZT) + Lamivudin (3TC) + Nevirapin (NPV), or
- Stavudin (D4T) + Lamivudin (3TC) + Nevirapin (NPV)

Children ≥ 3 years old and weighing ≥ 10 kgs

- Zidovudin (AZT) + Lamivudin (3TC) + NPV or Efavirenz (EFV)
- Stavudin (D4T) + Lamivudin (3TC) + NPV or Efavirenz (EFV)

In this case, the patient received three regimens of ARV therapy consisting of zidovudine, lamivudine, and nevirapine. A Randomized Controlled Trial of short-cycle intermittent compared to continuous ARV therapy in Uganda, 2010, reported that short cycle five days on/two days off intermittent ARV was at least as effective as continuous therapy.

The success of ARV treatment in children requires the cooperation of the caregivers or parents. They have to understand the treatment goals, adhere to treatment programs, and the importance of control. Non-adherence to the medications is the main reason for treatment to be failed.[12]

It is not easy for infants and children to remain adherent to ARV, so the caregiver must perform effective strategies and interventions that can support and simplify ARV adherence for children. A range of behavioral and biomedical interventions are recommended by WHO, including the use of peer counselors, mobile phone text messages, reminder devices, cognitive-behavioral therapy, behavioral skills training, medication adherence training, Fixed-Dose Combinations (FDC), and once-daily regimens.[13]

Opportunistic infections are mostly happened in HIV and related to the amount of CD4+. Cotrimoxazole is a broad-spectrum antibiotic that is mainly used to prevent bacteria or secondary parasites in HIV children. Daily prophylaxis of cotrimoxazole is proven to increase the long-term survival rate in children with HIV and decrease comorbidity incidence. WHO recommends giving cotrimoxazole prophylaxis to all HIV children below 12 months without considering CD4+ level, 1-5 years old children with clinical stage 2-4, or CD4+ <25% for any stage, >5 years old children with clinical stage 3-4 or CD4+ <350 cell/mm^3. [14] This current patient got cotrimoxazole as prophylaxis.

Malnutrition is the main problem for children with HIV infection. Malnutrition impairs the disease progress, increases morbidity, and decreases survival rate. HIV children with malnutrition are often followed by comorbidities and other complications such as tuberculosis, respiratory tract infection, diarrhea, and oral candidiasis, leading to decreased appetite.[15]

The patient's malnutrition resulted from the combination of chronic disease, infection, and inadequate intake since she was three months old. The patient has already given initial treatment and malnutrition management, including dieting and multivitamin. The patient, already in the rehabilitation phase, showed feeding tolerance and increased body weight.[16]

No controlled studies directly investigated diagnostic strategies or clinical interventions for HIV-infected children with severe malnutrition and diarrhea. However, diarrhea is common in both HIV-infected children and children with severe malnutrition. Cryptosporidium is suggested as a common pathogen causing diarrhea and that disaccharide intolerance.[17] Based on several journals, no direct evidence about the efficacy of zinc supplements in HIV children with diarrhea and severe acute malnutrition who have diarrhea. However, the effect of zinc on the prevention or management of diarrhea is yet to be established.[18]

Malnutrition always related to the deficiency of macro and micronutrients simultaneously causing growth and development failure. Malnutrition and chronic disease conditions correlate with the incidence of pathological stunting in children. Stunting is a condition of toddlers having less length or height compared to a similar age. This condition is defined by body height/length located below -2 Standard Deviation of WHO Z-score curve.

A stunted toddler is a chronic problem caused by many factors, including social-economy, pregnancy nutritional state of the mother, illness in the infancy period, and inadequate intake in the infancy period. Eventually, a stunted toddler will has a problem in gaining optimal physical and cognitive growth.[19] In this case, anthropometrics measurement revealed the length of age was below –3 SD of WHO Z-score curve. Its consequence of chronic malnutrition was accompanied by chronic infection. Thus, a diagnose of stunting, in this case, could be established.

Anemia is a common feature of HIV infection in children and becomes a predictor of morbidity and mortality associated with disease progression and poor clinical outcome. Anemia has been recognized as a significant clinical problem and HIV infected patients, with an estimated prevalence ranging from 10% in symptomatic HIV infected patients to 92% in patients with AIDS.[20] HIV is less likely to be affected directly by micronutrient deficiency compare to the general population. Micronutrient deficiency and inflammation become a risk factor for anemia in HIV infection. The treatment in acute or chronic disease includes detecting and treating the underlying cause.[21] Patients experienced anemia of chronic disease that is most likely caused by long-term HIV infection. The treatment, in this case, is to treat the underlying disease.

Low mortality and pleasing treatment outcomes can be achieved despite challenges associated with pediatric ARV therapy in developing countries. Outcomes are worse in younger patients and those with advanced disease at the time of ARV initiation. This condition is highlighting the importance of early diagnosis and treatment. Infants are at risk for rapid disease progression, and low CD4 count lead to poor predictive outcomes. Delaying ARV treatment initiation in infants results in higher mortality rates.[22]

In this case, the patient was a one-year and eight-months-old girl diagnosed with HIV 1 month ago and had started ARV. Furthermore, patients also suffered from recurrent infections that lead to malnutrition. The strength of this case report is a complete and thorough examination of the patient. However, this case report has a limitation of not doing a further follow-up on this patient after ARV therapy, including the side effect of the drugs and clinical condition after therapy.

In conclusion, A case of Human Immunodeficiency Virus Infection with Severe Malnutrition, Stunting, Acute Diarrhea, and Anemia of Chronic Disease in a 1 year and 8-months-old girl has been reported. The diagnosis was established based on anamnesis, physical examination, and laboratory testing. Treatments consisted of antiretroviral, secondary prophylaxis antibiotics, nutrition management, and rehydration. Since the birth of a child, the family plays the role of a caregiver. Children with HIV/AIDS need to have family support for their social and emotional development. The family caregivers need to be aware of the child's conditions and needs and the importance of adherence to therapeutic success. This case reminds us of the importance of HIV screening examination in pregnant women, although they look healthy. By so doing, we can plan the prevention program of transmission from mother to child.

Conflict of Interest

The authors have no conflict of interest.

Funding Sources

This case report received no specific grant from any agency in the public, commercial, or non-profit sectors.

Acknowledgment

This work support by Department of Pediatrics, Faculty of Medicine, Hasanuddin University.

References

1. ML, D. *et al.* HIV prevalence and risk factors in infants born to HIV positive mothers, measured by dried blood spot real-time PCR assay in Tigray, Northern Ethiopia. *BMC Pediatr.* (2019).
2. Penazzato, M. *et al.* A Global Research Agenda for Pediatric HIV. *J. Acquir. Immune Defic. Syndr.* **78**, S10–S15 (2018).
3. Birhane, T., Assefa Tessema, G., Addis Alene, K. & Dadi, A. F. Knowledge of pregnant women on mother-to-child transmission of HIV in Meket district, northeast Ethiopia. *J. Pregnancy* (2015)
4. Zhang, Y. & Lozada, J. S. Joint United Nations Programme on HIV/AIDS. *Encycl. Glob. Heal.* (2012)
5. Ditjen PP & PL. Kemenkes RI. Infodatin AIDS.pdf. *Situasi dan Analisis HIV AIDS* 1–6 (2014).
6. Tobin, N. H. & Aldrovandi, G. M. Immunology Of Pediatric HIV Infection. *Immunol. Rev.* **254**, 143–169 (2013).
7. Ogunbosi, B. O., Oladokun, R. E., Brown, B. J. & Osinusi, K. I. Prevalence and clinical pattern of paediatric HIV infection at the University College Hospital, Ibadan, Nigeria: a prospective cross-sectional study. *Ital. J. Pediatr.* **37**, 29 (2011).
8. Lauritano, D. *et al.* Oral manifestations in HIV-positive children: A systematic review. *Pathogens* **9**, 1–15 (2020).
9. Kementrian Kesehatan, R. I. Pedoman penerapan terapi hiv pada anak. *World Heal. Organ.* 1–81 (2014).
10. Suradi, R. Tata laksana Bayi dari Ibu pengidap HIV/AIDS. *Sari Pediatr.* **4**, 180 (2016).
11. Ikatan Dokter Anak Indonesia. *Infeksi HIV pada Bayi dan Anak. Pedoman Pelayanan Medis*. (IDAI, 2011).
12. Bernays, S. *et al.* Qualitative study of the BREATHER trial (Short Cycle antiretroviral therapy): Is it acceptable to young people living with HIV? *BMJ Open* **7**, 10–12 (2017).

13. Penazzato, M. *et al.* A Global Research Agenda for Pediatric HIV. *J. Acquir. Immune Defic. Syndr.* **78**, (2018).
14. Bourke, C. D. *et al.* Cotrimoxazole reduces systemic inflammation in HIV infection by altering the gut microbiome and immune activation. *Sci. Transl. Med.* **11**, (2019).
15. Okechukwu, A. Burden of HIV Infection in Children with Severe Acute Malnutrition at the University of Abuja Teaching Hospital Gwagwalada, Nigeria. *J. HIV Clin. Sci. Res.* (2015) doi:10.17352/2455-3786.000015.
16. Cloete, J. Management of severe acute malnutrition. *South African Med. J.* **105**, 1–4 (2015).
17. Irena, A. H., Mwambazi, M. & Mulenga, V. Diarrhea is a major killer of children with severe acute malnutrition admitted to inpatient set-up in Lusaka, Zambia. *Nutr. J.* **10**, (2011).
18. Pavlinac, P. B., Tickell, K. D. & Walson, J. L. Management of diarrhea in HIV-affected infants and children. *Expert Review of Anti-Infective Therapy* (2015) doi:10.1586/14787210.2015.981157.
19. Ghimire, U., Aryal, B. K., Gupta, A. K. & Sapkota, S. Severe acute malnutrition and its associated factors among children under-five years: A facility-based cross-sectional study. *BMC Pediatr.* **20**, 1–9 (2020).
20. Odhiambo, C. *et al.* Anemia and red blood cell abnormalities in HIV-infected and HIV-exposed breastfed infants: A secondary analysis of the Kisumu breastfeeding study. *PLoS One* **10**, (2015).
21. Ghozali, M., Sunjaya, A. F. A. & Indrati, A. R. Characteristics of Anemia in Children with HIV Infection. *Maj. Kedokt. Bandung* **50**, (2018).
22. Kabue, M. M. *et al.* Mortality and clinical outcomes in HIV-infected children on antiretroviral therapy in Malawi, Lesotho, and Swaziland. *Pediatrics* **130**, e591–e599 (2012).