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Case Report

AIDS in a three-year old girl

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The acquired immunodeficiency syndrome in children was first recognized in 1982, one year after the initial description in adults.[1,2] WHO estimates that 2 million children had been infected with human immunodeficiency virus (HIV) by the year 2000.[3] Pediatric AIDS threatens child survival in developing countries.[4] At the end of 1999, 34.3 million individuals were estimated to be infected globally, of which 1.3 million (3.8%) were children below 15 years old.[5] Until September 2005, no children with HIV AIDS in Indonesia was found.[6-8]

Approximately 80% of children acquired HIV-1 infection from vertical maternal transmission; the rest are infected from contaminated blood products, infected organs, breastfeeding, or sexual abuse.[3,4,9] Two general patterns of congenital infection are recognized. Twenty percent of infected infants develop early disease, while the rest progress slowly, developing into AIDS in adolescents. The most successful approach in the management of children with HIV requires a multidisciplinary team approach.[7]

Report of the case

A three-year old Balinese girl was referred to Sanglah Hospital in March 26, 2004, from a private clinic with the diagnosis of hyperemesis, cachexia, dehydration, HIV (+), and CD4 (+). She suffered from mild diarrhea for 3 months; for the last 2 days the diarrhea became worse and she also started to vomit. She was anorexic since 3 months and had cough about 35 days before admission. She has mild fever since 2 months before admission. There was no history of shivering and convulsion. The last void was 4 hours before admission. The urine was yellow and clear.

The patient was the second child, born at term assisted by a midwife. Her mother was an injected drugs user ("putaw") since January 1999, but she had quit for the last 6 months. She had an contacted HIV (+) friend. Her father was also injected drugs user since 5 years and also diagnosed as HIV (+). Both did not take anti-retroviral therapy (ART).

On February 2004, HIV diagnosis for both the patient and her mother was confirmed by ELISA method in a private clinic. CD4+ and CD 8+ were 23 cells/μl and 627cells/μl, respectively. When she developed cough, an HIV specialist prescribed co-trimoxazole syrup one teaspoon per day for 2 weeks. Chest x-ray at that time showed bronchopneumonia.

On physical examination she looked weak and skinny, the pulse rate was 130x/minute, regular; respiration rate 40x/minute, regular; rectal temperature 37.5^{0}C. Her body weight was 9.5 kg (1 month before, it was 11 kg), her height was 110 cm. Positive findings were decreased skin turgor, dry mouth, oral thrush,

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and increased bowel sounds. Other signs were within normal limits.

Laboratory findings showed Hb 10.6 g/dl, MCV 68 fl, MCH 23.5 pg, MCHC 34.5 g/dl, Ht 30.7%, WBC 9.1 K/ml with dominant granulocytes (57.2%) and platelet count 590,000 /ml. Blood glucose was 142 mg/dl. Liver function tests were as follows: total protein 6.0 g/dl, albumin 2.5 g/dl, total bilirubin 1.13 mg/dl, direct bilirubin 0.25 mg/dl, AST 51 IU/l, ALT 29 IU/l, and ALP 115 IU/l. Blood electrolyte were Na 143.9 mmol/l, K 3.57 mmol/l, and Cl 114.6 mmol/l. The chest x-ray showed increased vascularisation of the right and left lungs, consistent with chronic bronchitis.

The diagnoses of HIV-AIDS, chronic diarrhea with mild dehydration and moderate malnutrition were established. The patient was rehydrated with intravenous Lactated Ringer's solution. Ampicillin 3x300 mg was administered and a diet of 950 kcal per day and Pedialyte were given. There were no bacteria in the stool. She was consulted to the Department of Dermato-Venerealogy, and was given Nystatin drop 1 ml three times a day. After 2 days of treatment, the diarrhea stopped and 2 days later she was discharged. Her weight was 9.6 kg. One week later (April 6th 2004) she was brought to the outpatient clinic, she had lost weight of 1 kg. There was no history of diarrhea, fever, cough, or vomiting during the week. She was readmitted to improve her nutritional status. The Department of Nutrition put her on a 1000 kcal diet per day with a combination of i.v. Dextrose 10% and oral nutrition. Six days later, her body weight became 9 kg and she was discharged. One month later she was taken to Gilimanuk where she died on June 19th 2004.

Discussion

HIV infection is caused by human RNA retroviruses, HIV type 1 (HIV-1) and, less commonly, HIV type 2 (HIV-2).[3,10,11] Vertical transmission from mother to child is the main route; the risk of perinatal acquisition is 25%. Perinatal transmission may occur *in utero,* during peripartum period, or from breast feeding.[3] The risk of infection for an infant born to an HIV-seropositive mother who did not receive antiretroviral therapy during pregnancy is between 13% and 39%.[11]

Maternal viral load is a critical determinant of perinatal HIV transmission.[10] A higher rate was found in seroconverted woman during pregnancy. Other associated factors include low CD4+ T-lymphocyte counts, advanced maternal illness, intrapartum events resulting an increased exposure to maternal blood, placental membrane inflammation, premature delivery, prolonged labor, and longer duration of rupture of membrane.[10,12]

Postnatal infection may be transmitted through breast milk, giving a 14% additional risk.[12,13] Worldwide, an estimated of one-third to one-half of mother-to-child transmission may occur through breastfeeding.[10] The median age of onset is approximately 12 to 18 months for perinatal infected infants, though, some remained asymptomatic for more than 5 years, or even until puberty. Approximately 15% to 20% of untreated children die before reaching 4 years of age, with a median age of death of 11 months, whereas most children survive beyond 5 years of age.[10]

Our patient was born spontaneously and breastfed by her mother who had been a drug user for 4 years, and proven to be HIV (+) at the same time as her daughter. The patient was almost three years old when clinical manifestations appeared at the time of diagnosis. Since incubation period is between 12 - 18 months, HIV transmission might be from breast milk, probably the mother had HIV since then.

The manifestations of pediatric HIV infection/AIDS are different from those of adults. Lymphocytic interstitial pneumonitis, chronic parotid swelling, and HIV encephalopathy are encountered more in young children. Kaposi's sarcoma is hardly ever reported in children.[2] Opportunistic infections in children are usually pneumocystis carinii, and recurrent bacterial infections.

The National AIDS Control Organization has devised a clinical definition of AIDS in children aged below 12 years of age. WHO provides clinical classification for suspected HIV infections. For epidemiological surveillance in Indonesia, the diagnosis of AIDS is confirmed if HIV test is positive with the presence of at least 2 major symptoms and 1 minor symptom.[2,14,15] In our case, prolonged fever (intermittent), diarrhea (intermittent), loss of weight, oropharingeal candidiasis and persistent cough were all presence over 1 month.

The HIV virus attaches to the host cell by a surface glycoprotein to the CD4 molecule; therefore,

it primarily infects $CD4^+$ lymphocytes and macrophages. The reduction in cell-mediated immunity and secondary ß-cell dysfunction result in immuno compromised state and proliferation of opportunistic infections and malignancies. An elevated level of activation-induced cell death from apoptosis of T cell occurs in HIV (+) patients.[3,11]

The diagnosis of HIV infection or AIDS depends on the presence of HIV infection, the immunological status of the child, the pattern of clinical illnesses that occurs secondary to the infection and loss of immune function. In children older than 18 months, a standard anti-HIV immunoglobulin G (IgG) antibody test is used and then confirmed by Western blot analysis. Enzyme immunoassays (EIA) are highly sensitive and specific, but repeated EIA of initially reactive specimens is required to decrease the small likelihood of laboratory error. This should be followed by Western blot or indirect immunofluorescence antibody assay to exclude false-positive EIA result.[9] A positive HIV antibody test in an 18-month old child or older usually indicates infection.[10] Polymerase chain reaction (PCR) and virus culture are currently the most sensitive and specific assays for detection of HIV infection in children.[1,9-11]

As the disease progresses, there is an increasing loss of cell-mediated immunity.[9-11] The peripheral blood lymphocytes count at birth and during the first year of infection can be normal, but eventually lymphopenia resulting from a decrease in the total number of circulating CD4+ lymphocytes, develops. The T-suppressor CD8+ lymphocytes count usually increases initially and CD8+ cells are not depleted until late in the course of the disease. These changes result in a decrease of CD4+ to CD8+ cell ratio. This nonspecific finding, although characteristic for HIV infection, also occurs with other acute viral infections, i.e. CMV and Epstein-Barr virus. The normal values of peripheral CD4+ lymphocyte counts are age related.[10]

Our patient had HIV (+) with CD4 less than 25cells/μl, PCR was not done because it was not available in Bali. Based on physical examinations and laboratory findings the diagnosis for this patient was AIDS.

Successful treatment requires a multidisciplinary team approach, the objectives fall into three categories: supportive care and adequate nutrition, prevention of infectious complication, and specific ART.[3,9] The National Pediatric Resource Center Working group on Retroviral Therapy recommends that CD4+ cell count or percentage be used as a criteria for initiation of antiretroviral therapy. Several clinical conditions merit ART regardless CD4+ cell count,[3,9] namely failure to thrive, AIDS-defining opportunistic infection, progressive HIV encephalopathy, HIV-associated malignancy, chronic or recurrent bacterial infection, thrombocytopenia and hypogammaglobulinemia.[9] WHO emphasizes the importance of clinical parameters and immunological markers in the decision making.[16]

Decision about therapy in such situation is complex and requires consultation with an HIV specialist. When selecting appropriate ART regimen, the age of the child, potential for maintenance of future treatment options, anticipated patient adherence, availability and cost effectiveness, side effect profile, and etc should be considered.[16,17,18]

Combination of antiretroviral therapy has been shown to be more effective than monotherapy. A good HIV suppression can be achieved with triple therapy including a protease inhibitor or a nonnucleoside reverse transcriptase inhibitor.

Suppression of virus to undetectable levels is the desired goal. A change in antiretroviral therapy should be considered if there is evidence of disease progression (virologic, immunologic, or clinical), toxic effects or intolerance to the drugs, or data suggesting a superior regimen.[9] Azidothymidine (zidovudine, AZT) and didanosine (ddI) are currently used alone or in combination. Although HIV infection is usually fatal especially in developing countries, the development of new antiretroviral drugs is promising. The nutritional status and the thoroughness to control viral replication are principal in determining the outcome. The social setting of children and the stressors to which they are exposed have also been linked to the progression of the disease.[3,10]

Our patient was not treated with ART because the parents were unwilling to come regularly and buy the medicine. The socioeconomic condition (the father was jobless and a drug user) and attitude (the mother did not tell the father about their daughter's illness) made this case hopeless. The patient was taken by her grandmother to Gilimanuk and she died 3 months (June 19th) later. Both her parents condition were also deteriorated since then. The only

one left was her healthy 8 years old sister, who is HIV negative.

In summary, we report a case of HIV-AIDS in a three-year old girl. The diagnosis was based on clinical manifestations and laboratory findings. This patient was not treated with ART because of unaffordable reasons and subsequently she died.

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