
Case Report

Central Nervous System Involvement in a Child with Human Immunodeficiency Virus Infection: A Case Report

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ABSTRACT

HIV has infected 4.4 million children worldwide and has resulted in 3.2 million deaths. The progression of vertically acquired HIV infection appears to have a trimodal distribution. Approximately, 15% of children have rapidly progressive type of disease, while the remainders have either a chronic progressive course or an infectious pattern typical of that in adults. Mean survival is about 10 years. Children can be asymptomatic for many years, and the appearance of an opportunistic infection in a 10-year-old child in whom AIDS is subsequently diagnosed is not rare. Neurologic findings in an infected child are: Motor delay, hypotonia, hypertonia, and/or pyramidal tract signs which may indicate progressive HIV encephalopathy or opportunistic infection of the CNS. Our case was an 8-year old boy presented with fever, vomiting, and loss of consciousness. The patient was a known case of HIV infection due to mother's infection in perinatal period and was on treatment from 3 years before his referral. He was presented to our hospital for the fever which had started one month earlier and refractory vomiting. The patient got in coma on the chest examination; tachypnea, crackles and heart murmur were auscultated. In neurologic examination, anisocoria, right-sided hemiparesis, increased deep tendon reflexes in the right side and extensor plantar reflex, Kernig and Brudzinski signs were detected. Eventually, the patient died after 46 days of hospitalization in pediatric intensive care unit because of full sepsis.

Keywords: Encephalopathy, HIV infection, Central nervous system

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INTRODUCTION

Human Immunodeficiency Virus (HIV) has infected 4.4 million children worldwide and has resulted in 3.2 death million children so far. The progression of vertically acquired HIV infection

appears to have a trimodal distribution. Approximately 15% of children have rapidly progressive type of disease, and the remainders have either a chronic progressive course or an infection

pattern typical of that in adults. Mean survival is about 10 years (1-4).

Vertical HIV infection occurs during one of 3 below-mentioned periods:

Period 1: Prenatal, the fetus can be genically infected by means of transmission across the placenta or across the amniotic membranes, especially if the membranes are inflamed or infected.

Period 2: Most vertical infections occur during delivery, and many factors affect the risk of infection during this period. In general, the longer and the greater contact the neonate has with maternal blood and cervicovaginal secretions, the greater the risk of vertical transmission. Premature and low birth-weight neonates appear to have an increased risk of infection during delivery because of their reduced skin barrier function and immunologic defenses.

Period 3: Postnatal vertical transmission occurs with the ingestion of HIV in the breast milk. The age of presentation can be highly variable in a high-risk child who was previously unidentified (4-7).

Children can be asymptomatic for many years, and the appearance of an opportunistic infection in a 10-year-old child in whom AIDS is subsequently diagnosed is not rare. Children who acquire HIV by means of nonvertical transmission may have an illness during the acute phase of the retroviral syndrome, or they may present many years later with opportunistic or recurrent infections (7-10).

Neurologic findings in an infected child are: motor delay, hypotonia, hypertonia, and/or pyramidal tract signs which may indicate progressive HIV encephalopathy or opportunist infection of the CNS. Spastic diplegia and motor dysfunction in the mouth are early signs of encephalopathy. Acquired microcephaly with accompanying cerebral atrophy is a poor prognostic sign. Subacute combined degeneration of the spinal cord with higher

cortical dysfunctions occur in vitamin B-12 deficiency (5-10).

CASE REPORT

Our case was an 8-year old boy presented with fever, vomiting, and loss of consciousness. The patient was a known case of HIV infection due to mother's infection in perinatal period and was on treatment since 3 years before his admission. He had history of several admissions because of pneumonia and meningitis, and had been treating with zidovudine, biovudine and nelfinavir for his HIV infection.

He was referred because of fever from one month earlier and refractory vomiting. His signs and symptoms had worsened from 5 days ago and headache, neck pain, aphasia and finally loss of consciousness were seen. On physical examination, the patient was in coma and febrile. On chest examination, tachypnea, crackles and heart murmur were auscultated. In neurologic examination anisocoria, right-sided hemiparesis, increased deep tendon reflexes in right side and extensor plantar reflex and Kernig and Brudzinski signs were seen.

Laboratory findings were as below:

ESR=135 and hypergammaglobulinemia (IgG>2800). Lumbar puncture revealed WBC=50 (PMN: 70%, lymphocyte: 30%), RBC=20, protein= 410 and glucose=15. Cultures of CSF, urine and blood were negative.

On neuroimaging with MRI, ventricular dilatation, brain edema, non-communicating hydrocephalus and normal fourth ventricle were seen and insertion of a ventriculoperitoneal shunt was considered for the patient. Because of the patient's hypertension crisis, stress-induced hypertension and syndrome of inappropriate antidiuretic hormone (SIADH) were suspected that the latest was ruled out. Bone marrow aspiration was normal and intravenous immunoglobuline (IVIG) was infused for

treatment of thrombocytopenia. In echocardiography, endocarditis was detected.

Eventually, the patient died after 46 days of hospitalization in the pediatric intensive care unit because of full sepsis although he had been receiving wide spectrum antibiotics, anti HIV drugs and supportive treatments.

DISCUSSION

HIV infection and AIDS have had a significant clinical impact on children world wide. Therefore, clinical and healthcare specialists (including primary care givers, pediatric subspecialists, nursing staff and social service professionals) who provide care to children should be familiar with HIV infection develop expertise and anticipate provision of services to this population. Prenatal transmission of HIV infection accounts for more than 90% of newly reported pediatric AIDS cases. The transmission rate for perinatally acquired HIV infection without perinatal antiretroviral intervention has been reported between 12 and 25 percent in the United States and Europe and is probably higher in Africa. Recent advances in perinatal primary antiretroviral therapy (antepartum, peripartum and postpartum delivery of zidovudine in HIV infected women without severe immunosuppression) have led to a decrease in perinatal transmission rates to approximately 8 percent. Maternal risk factors as identified through national surveillance in reported AIDS cases include drug abuse, heterosexual infection by sexual partner along with the risk factors for acquiring HIV disease. Perinatal HIV transmission can take place during the antepartum, peripartum and postpartum periods. However, the distribution of transmission across these timing periods has not been defined precisely (15).

Antiretroviral treatment (ART) is the mainstay of HIV treatment. Double- and triple-drug therapy should be started with 2 nucleoside reverse

transcriptase inhibitors (NRTIs) or 2 NRTIs plus a non-nucleoside reverse transcriptase inhibitor (NNRTI) or a protease inhibitor. Initial NRTI combinations may include zidovudine with didanosine or lamivudine. A 10 or 5-fold decrease in the viral load is expected following 2-3 months triple-drug therapy or double-drug therapy respectively, but not all infants have an undetectable viral load. Reduction in the mortality rate of perinatally acquired HIV-1 over the past 5 years is a result of improved antiretroviral therapy. Only triple combination therapy, however, appears to significantly reduce the relative hazard ratio of death, when compared with no treatment. For those at risk for vertical transmission, zidovudine therapy should be started after obtaining a baseline CBC count within 6-12 hours after delivery. Zidovudine therapy should be continued until the infants age is (reaches) 6 weeks, at which it may be discontinued if all HIV-DNA PCR results are negative. Pneumocystis Carinii Pneumonia (PCP) prophylaxis should be started in all infants aged 6 weeks who were born to HIV-infected mothers and continued until HIV infection is ruled out (13,15).

HIV-related encephalopathy is an important problem in vertically infected children with HIV. Infected infants may manifest early catastrophic encephalopathy, with loss of brain growth, motor abnormalities, and cognitive dysfunction. Even without evidence of AIDS, infected infants score lower than serorevertors on developmental measures, particularly language acquisition. Children with perinatal or later transfusion-related infection are roughly comparable developmentally to their peers until late in their course. Symptoms similar to adult AIDS dementia complex are occasionally seen in adolescents with advanced AIDS, including dementia, bradykinesia, and spasticity. Opportunistic CNS infections such as toxoplasmosis and progressive multifocal leukoencephalopathy are less

common in children and adolescents than in adults. Increasing evidence suggests that aggressive antiretroviral treatment may halt or even reverse encephalopathy. Neuroimaging changes may precede or follow clinical manifestations, and include early lenticulostriate vessel echogenicity on cranial ultrasound, calcifying microangiopathy on CT scan, and/or white matter lesions and central atrophy on MRI. Differential diagnosis of neurological dysfunction in an HIV-infected infant includes the effects of maternal substance abuse, other CNS congenital infections, and other causes of early static encephalopathy. Initial entry of HIV into the nervous system occurs very early in infection. The risk of clinical HIV encephalopathy increases with very early age of infection and with high viral loads. Virus is found in microglia and brain derived macrophages, not neurons. The neuronal effect of HIV is probably indirect, with various cytokines implicated. Apoptosis is the presumed mechanism of damage to neurons by HIV (14).

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