IDCases 14 (2018) xxx–xxx

Contents lists available at ScienceDirect

IDCases

journal homepage: www.elsevier.com/locate/idcr

Case study

Successful prevention of perinatal HIV transmission utilizing direct observation therapy in the setting of Acquired Immunodeficiency Syndrome (AIDS) and progressive multifocal leukoencephalopathy

Shontreal Cooper[a,*], Hyacinth Norris[a], Joy Lander-Roe[a], Gregg Alleyne[a,b]

[a] Hahnemann University Hospital, Drexel University College of Medicine, Philadelphia, PA, United States
[b] Children's Hospital of Philadelphia, Philadelphia, PA, United States

ARTICLE INFO

Article history:
Received 15 July 2018
Received in revised form 1 September 2018
Accepted 1 September 2018

ABSTRACT

We report a case of a 22-year-old G1P0010 African-American female with poorly controlled perinatally acquired HIV/AIDS and recent diagnosis of progressive multifocal leukoencephalopathy (PML) by magnetic resonance imaging (MRI). She presented to a tertiary care facility for prenatal care and direct observation therapy after poor medication adherence during pregnancy. After multiple attempts at outpatient ART management, the patient was admitted at 35 weeks' gestation for direct observation therapy for both antiretroviral therapy and anti-seizure medication. Viral load at that time was 22,487 copies/mL and she was admitted and started on a salvage regimen which included: dolutegravir, tenofovir disoproxil fumarate/emtricitabine, darunavir, ritonavir, and trimethoprim/sulfamethoxazole for Pneumocystis jirovecii prophylaxis. The patient remained on direct observation therapy throughout her two-week hospital stay with final viral load of 1211 copies/mL, CD4 284/uL at time of delivery at 37 weeks' gestation, with minimal seizure activity. The infant received postnatal antiretroviral therapy including three doses of zidovudine and nevirapine with negative HIV PCR at birth, 2, 4, and 6 months postpartum and is currently HIV negative.

Introduction

Adherence to antiretroviral therapy (ART) in pregnancy is an important aspect to concerning in order to decrease maternal viral load and decrease the risk of mother-to-child transmission (MTCT) of HIV. Studies have shown that maternal viral load has a direct correlation with the risk of MTCT during pregnancy, thus lowering the maternal viral load lowers the risk of MTCT [1,2]. While antiretroviral therapy (ART) has led to declines in HIV-associated morbidity and mortality, non-adherence to ART has resulted in treatment failure in many patients [3]. Any interventions which focuses on improvement of ART adherence must consider all barriers including: social, emotional, behavioral, and cognitive associated with risk of nonadherence. For such patients, directly observed therapy (DOT) has been used to improve the self-administering of ART. Directly observed therapy is a direct method to measure adherence of self-administered ART regimen [4]. Observed therapy was originally use for treatment of tuberculosis (TB) with rates of completion of anti-TB therapy increasing significantly in New York City and other places [5]. It has also been shown to be effective in pediatric asthmatic patients with non-adherence to medication [6]. Short, hospital based DOT has been shown to be helpful for high-risk with non-adherence to antiretroviral medications and should be considered in pregnant women with poor virological control and those that have failed outpatient management.

Progressive multifocal leukoencephalopathy (PML) is a progressive demyelinating disease involving the central nervous system which is due to infection of oligodendrocytes by polyomavirus JC (JC virus) [7,8]. It is almost exclusively diagnosed in immunocompromised patients; however, there have been isolated reports of patients without apparent immunosuppression [9]. There have been limited studies on management of PML in pregnancy. However, other studies have shown that with increasing use of antiretroviral therapy (ART), the overall incidence of PML has decreased significantly [10,11]. Progressive multifocal leukoencephalopathy is diagnosed both by clinical findings and radiographic images with magnetic resonance imaging (MRI). Magnetic resonance imaging typically shows findings of progression of focal neurological deficits and distinct white matter lesions in certain regions of the brain [12].

* Corresponding author at: 230 North Broad Street, OBGYN Bobst Building 15th Floor, Philadelphia, PA, 19102, United States.
E-mail address: scooper_16@yahoo.com (S. Cooper).

https://doi.org/10.1016/j.idcr.2018.e00454

Case presentation

First hospital admission

The patient is a 22-year-old G2P0010 African-American female at approximately 35 weeks gestation with perinatally acquired HIV/AIDS, presenting to the hospital after poor compliant with ART therapy, and recently diagnosed PML which was previously diagnosed by MRI at an outside tertiary care facility. On admission, she reported fatigue, weakness, dizziness, and frequent new onset seizures. She was alert and oriented with a normal level of consciousness and responded appropriately to questions. Her speech was slow and slurred with impairment of fine motor skills and numbness in lower extremity, however, she was able to walk with limited difficulty. Deep tendon reflexes were 2+ throughout. Her viral load on presentation was 211,683 copies/mL and CD4 count 219/uL. The MRI showed scattered bilateral asymmetric areas of subcortical encephalomalacia and multiple non-specific T2 hyperintensities in the subcortical and deep white matter which was unchanged from prior MRI upon initial diagnosis. However, neurological testing showed a decline in her nonverbal intellectual capacity and attention deficiency. Of note, prior to this admission, the patient had multiple ER visits for seizure activity and presumed worsening or reactivation of PML because of immunosuppression. Her genotype resistance testing showed multiple drug resistance and thus she was started on a highly active ART therapy regimen was started which included: dolutegravir, tenofovir disoproxil fumarate/emtricitabine, darunavir, ritonavir, and trimethoprim/sulfamethoxazole for Pneumocystis jirovecii prophylaxis.

Second hospital admission

Clinically, the patient deteriorated after multiple attempts at outpatient ART therapy management, obtaining home nursing through Medicaid, direct daily contact with HIV and obstetric provider and case-worker. At 35 weeks gestation, she was admitted for direct observation therapy with both aggressive antiretroviral therapy and anti-seizure management. Viral load at that time was 22,487 copies/mL. Neurology was consulted, and she was, subsequently, started on 500 mg twice daily of levetiracetam. The patient remained on direct observation therapy throughout her two-week hospital stay with final viral load of 1211 copies/mL, CD4 284/uL and minimal seizure activity. Fig. 1 shows the patient's viral load pattern throughout pregnancy.

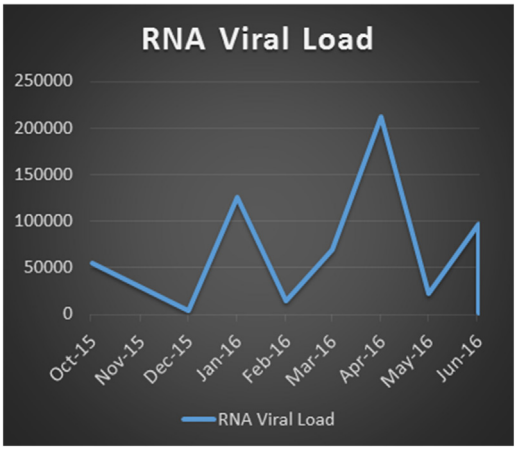

Fig. 1. RNA Viral Load throughout the course of pregnancy.

She was delivered at 37 weeks gestation, with infant receiving postnatal antiretroviral therapy including three doses of zidovudine and nevirapine. The infant was successfully followed with negative HIV PCR at birth, 2 months, and 4 months postnatal and is now considered HIV negative. The mother decided on the long acting reversible contraception, Nexplanon, for contraception at the time of discharge. At her six week, postpartum visit, the mother reported adherence to ART therapy with viral load 139 copies/mL and CD4 count 300/uL and 15%. Both mother and baby are receiving outpatient care.

Discussion

This case report is the first to our knowledge which demonstrates effective management of PML in an AIDS-infected pregnant patient. This patient's case demonstrates the fundamental need for direct observation therapy services in prevention of MTCT. This type of therapy is especially important in perinatally infected pregnant patients that are more likely to be nonadherent with antiretroviral therapy. ART has been shown to reduce MTCT transmission at approximately 1–2% in resource rich countries [13]. Nonadherence could thus increase these rates and result in suboptimal viral suppression. Some studies have also suggested that proactively addressing the concerns of pregnant would as it relates to teratogens and the safety of ART in pregnancy could help avoid medication nonadherence [14]. Interventions such as DOT thus become necessary to prevent MTCT in nonadherent pregnant women. One study used a simulation model to demonstrate that DOT in women receiving highly active antiretroviral therapy (HAART) in the 3rd trimester had a MTCT relative risk of 0.39 compared to conventional HAART. This study also showed that DOT was projected to be highly cost-effective [15].

Pregnancy results in a relative state of immunosuppression. It is generally thought that patients with progressive multifocal leukoencephalopathy (PML) have cellular immunity deficiency. It has previously been shown that the cellular immune response, mediated by CD4+ and CD8 + T lymphocytes, plays a crucial role in the containment of JCV [16].

In the setting of AIDS in pregnancy, DOT was necessary to prevent MTCT but also to prevent worsening of AIDS and neurological complications related to PML. DOT helps to provide early recognition for adherence to guidelines and treatment regimens in reducing the risk of fetal transmission.

Credit author's statement

Shontreal Cooper
Credit Roles: Original Draft, Review and Editing, Conceptualization.
Hyacinth Norris
Credit Roles: Resources, Software, Data curation.
Joy Lander-Roe
Credit Roles: Project Administration.
Gregg Alleyne
Credit Roles: Supervision, Review and editing.

Conflict of interest

No competing interest declared.

Acknowledgements

1. Drexel College of Medicine.
2. Drexel Obstetrics/Gynecology Department.

References

[1] Cohen M.S., Hellmann N, Levy JA, DeCock K, Lange J. The spread, treatment, and prevention of HIV-1: evolution of a global pandemic. J Clin Invest 2008;118:1244–54.

[2] Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission. Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States. May 24, 2010. http://aidsinfo.nih.gov/ContentFiles/PerinatalGL.pdf. [Feb 13;2012]. pp. 1–117.http://aidsinfo.nih.gov/ContentFiles/PerinatalGL.pdf

[3] Glikman D, Walsh L, Valkenburg J, et al. Hospital-based directly observed therapy for HIV-Infected children and adolescents to assess adherence to antiretroviral medications. Pediatrics 2007;119:1142–3.

[4] Sherer R. Adherence and antiretroviral therapy in injection drug users. JAMA 1998;280:567–8.

[5] Frieden TR, Fujuwara PI, Washko RM, et al. Tuberculosis in New York City—turning the tide. N Engl J Med 1995;333:229–33.

[6] Shields MD, ALQahtani F, Rivey M, McElnay J. Mobile direct observation of therapy (MDOT) - a rapid systematic review and pilot study in children with asthma. PLoS One 2018;13(2)e0190031.

[7] Amend KL, Turnbull B, Foskett N, et al. Incidence of progressive multifocal leukoencephalopathy in patients without HIV. Neurology 2010;75:1326.

[8] Astrom KE, Mancall EL, Richardson EP. Progressive multifocal leuko-encephalopathy; a hitherto unrecognized complication of chronic lymphatic leukemia and Hodgkin's disease. Brain 1958;81(93).

[9] Bolton CF, Rozdilsky B. Primary progressive multifocal leukoencephalopathy. A case report. Neurology 1971;21:72.

[10] d'Arminio Monforte A, Cinque P, Mocroft A, et al. Changing incidence of central nervous system diseases in the EuroSIDA cohort. Ann Neurol. Mar 2004;55(3):320–8.

[11] Casado JL, Corral I, Garcia J, et al. Continued declining incidence and improved survival of progressive multifocal leukoencephalopathy in HIV/AIDS patients in the current era. Eur J Clin Microbiol Infect Dis 2014;33(February (2)):179–87.

[12] Cinque P, Koralnik IJ, Gerevini S, Miro JM, Price RW. Progressive multifocal leukoencephalopathy in HIV-1 infection. Lancet Infect Dis. Oct 2009;9(10):625–36.

[13] Siegfried NL, van der Merwe L, Brocklehurst P, Sint TT. Antiretrovirals for reducing the risk of mother-to-child transmission of HIV infection. Cochrane Database of Systematic Reviews (Online.) 2011 7, article CD003510.

[14] Matsui Doreen. Obstet Gynecol Int 2012;2012:796590 Published online 2011 Dec 26.

[15] McCabe CJ, Goldie SJ, Fisman DN. The cost-effectiveness of directly observed highly-active antiretroviral therapy in the third trimester in HIV-infected pregnant women. PLoS One 2010;5(4)e10154.

[16] Coleman DV, Wolfendale MR, Daniel RA. A prospective study of human polyomavirus infection in pregnancy. J Infect Dis 1980;142:1–8.