

CASE REPORT

DELAYED PROGRESSION AND INEFFICIENT TRANSMISSION OF HIV-2

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Abstract. We report a case of HIV-2 infection with delayed progression, taking approximately one and a half decades to develop HIV related symptoms. The spouse was still negative for HIV with a history of having regular unprotected sex with the index case which highlights the inefficient transmissibility of HIV-2. Continued surveillance is needed in screening of HIV-2 infection, especially in cases with a high index of suspicion and risk factors for HIV-2, as these patients develop AIDS related symptoms quite late due to delayed progression.

Key words: HIV-2 infection, delayed progression, inefficient transmissibility, India

INTRODUCTION

In 1984, 3 years after the first report of the disease that would become known as AIDS, researchers discovered the primary causative viral agent, HIV-1. In 1986, HIV-2, was isolated from AIDS patients in West Africa. Approximately 2.4 million people are currently living with HIV AIDS in India (UNAIDS, 2008). The first documented HIV infection in India was among sex workers in Chennai in 1986 (Simoes *et al*, 1987). Infection rates soared throughout the 1990s, the epidemic being most extreme in the southern half of the country and in the far north-east. Today the epidemic affects all sectors of Indian society, not just specific groups – such as sex workers and truck

drivers – with which it was originally associated. The first evidence of HIV-2 infection in India was provided in 1991 (Rubsamen-Waigmann *et al*, 1991). Since then it has been sporadically reported from various states of India (Kulkarni *et al*, 1999). A recent 3 year study at two HIV centers in southern India reported HIV-2 prevalences of 0.32% and 0.13% (Murugan and Anburajan, 2007). HIV-2 appears to be transmitted principally by sexual contact, with prostitutes being the well-studied group. The virus can also be spread by contact with infected blood as a transfusion. Early evidence indicates the transmission pattern of HIV-2 differs in at least one significant manner from HIV-1: at least 30% of babies born to mothers infected with HIV-1 become infected themselves, but no more than 10% of infants born to HIV-2 infected mothers become infected (Kanki, 1991).

We report a case of HIV-2 infection in which delayed progression of disease and

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inefficient transmissibility are suspected.

CASE REPORT

A 49 year old mechanic presented to an integrated counseling and testing center (ICTC) as a direct walk-in for HIV testing in October 2008 with unexplained chronic diarrhea for longer than one month and weight loss of >10% of presumed body weight. He was asymptomatic until January 2008 when he developed oral plaque-like lesions, which later healed after receiving treatment from a local medical practitioner. The patient was specifically questioned about having experienced acute retroviral syndrome, but he was unable to recall any symptoms. The ICTC is in the Department of Microbiology, Maulana Azad Medical College and is associated Lok Nayak Hospital, which is a tertiary care hospital in New Delhi, India. The patient was a resident of Kerala and stayed with his spouse in Mumbai from 1994 to 2006 and then moved to Delhi. The patient gave a history of frequent contacts with commercial sex workers (CSW) and multiple male sexual partners. He revealed he was first tested for HIV in 1995 in a private laboratory. At that time he had a positive HIV test. To confirm his HIV status he gave another blood sample at another private laboratory and that test was negative; no copies of these test results are available. The patient stated he did not indulge in any high risk sexual behavior after that. Most private laboratories at that time were performing single HIV antibody tests and did not use the rapid test to detect HIV-2.

Following the guidelines of the National AIDS Control Organization (NACO) (WHO, 2007), after informed consent and pre-test counseling, his blood sample was tested for HIV using a rapid test

(Immunocomb, J Mitra, Delhi) following manufacturer's instructions. Test was reactive for HIV, following which two more rapid tests (Retroquic QUALPRO Diagnostics Goa; Acon Trilene ACON BIOTECH, China) were carried out on the same sample (one test was able to differentiate between HIV-1 and 2). The sample was reactive on all three tests and was further confirmed by Western blot. The patient was found to be HIV-2 positive and was registered with the anti-retroviral therapy (ART) Center. His CD4 and CD3 counts (FACSCCount system, Becton Dickinson) were 364 cells/ μ l and 1,749 cells/ μ l, respectively. Other investigations were within normal limits. The patient was investigated for chronic diarrhea, but a definitive diagnosis was not made since three stool samples revealed no pathogens. The case was clinically diagnosed as a case of unexplained chronic diarrhea, per NACO guidelines (WHO, 2007) since he had watery stool more than three times daily for longer than one month. VDRL and HCV test were negative but the HBsAg was positive. The patient's repeat CD4 and CD3 counts were 247 cells/ μ l and 1,650 cells/ μ l, respectively, on 14-02-09.

Since the patient was in an advanced stage of HIV, WHO clinical stage 3, and his CD4 count was <350 cells/ μ l, he was started on ART (ZDV + 3TC + NVP). Since the index case gave a history of regular unprotected sex with his spouse, we suggested the wife to be tested for HIV. She was found to be negative for HIV per NACO guidelines (WHO, 2007). She tested negative for HIV infection 3 years earlier under the Prevention of Parent to Child Transmission (PPTCT) program. Under NACO guidelines, pregnant women are offered the HIV test under the PPTCT program and those who give consent for HIV testing are tested after pre-test counselling. Their 2^{1/2} year

old daughter was also tested for HIV and found to be negative. Adherence to ART was >95% for the index case and he reported no side effects due to ART. The index case was monitored for ART per NACO guidelines (WHO, 2007). He reported weight gain and his diarrhea resolved by 3 and 4 months after initiation of ART, respectively. He had an adequate immunological response per NACO guidelines (WHO, 2007) and his CD4 count increased to 400 cells/ μ l after six months of ART.

DISCUSSION

Although HIV-2 infection is mostly confined to West African countries it has been identified in other continents following sexual contact with foreigners with a history of frequent contact with CSWs or multiple male sexual partners, as in our case. These CSWs provide a bridge for transferring HIV-2 infection from high prevalence regions, such as West African countries, to low prevalence countries, such as India. In our case there is a possibility the CSW may have had contact with a sexual partner from Western Africa, who then transferred the disease to the index case. One study (Leaño *et al*, 2003) found a large number of travelers to and from different regions of the world plays an important role in introduction of diverse HIV strains into a country, and further suggests overseas contract workers be included in surveillance programs.

Studies of HIV-2 infection are limited, but to date comparisons with HIV-1 show both viruses share properties, such as CD4 cell tropism, mode of transmission and morphology, but differ at molecular, clinical and epidemiological levels. Though human infection with HIV-2 is associated with eventual immunologic failure, dis-

ease progression has been reported to be much slower. A prospective 8 year study concluded HIV-1 infected women had a 67% probability of AIDS-free survival 5 years after seroconversion, in contrast with 100% probability for HIV-2 infected women. The rate of developing abnormal CD4+ lymphocyte counts with HIV-2 infection was also significantly lower, which demonstrates HIV-2 has lower virulence than HIV-1 (Marlink *et al*, 1994). Our patient also presented with unexplained chronic diarrhea for longer than one month and weight loss of >10% of presumed body weight almost 14 years after a history of a first sexual contact with a CSW, before which he was apparently healthy. Persons infected with HIV-2 are less infectious early in infection. Infectiousness increases as disease progresses, however, the duration of this infectiousness is shorter than with HIV-1. Knowing this incidence is epidemiologically significant; >95% of infected individuals followed for at least 8 years fit a clinical definition of long-term non-progression.

With HIV-2 infection, both heterosexual and vertical transmissions have been reported to be rare. More discordant couples exist with HIV-2 infection than HIV-1 infection as was seen in our case and his spouse in spite of having regular unprotected sex with her husband for almost over 10 years. One study recently reported the levels of viral RNA in plasma are much lower in HIV-2- infected individuals despite similarities in age at infection and time infected (Popper *et al*, 2000). Another study showed HIV-2 infection is characterized by a significantly lower plasma viral level (Andersson *et al*, 2000).

Given the slower development of immunodeficiency and the limited clinical experience with HIV-2, little is known about the best approach to manage these

patients. More clinical experience is needed to determine the most effective treatment for HIV-2 patients, the optimal timing for ART is unclear.

Although the prevalence of HIV-2 infection is very low, the potential risk for obtained HIV-2 infection in some populations justifies routine HIV-2 testing for all people from areas with high HIV-2 prevalence, people sharing needles or having sexual partners known to be infected with HIV-2, people receiving transfusions or other non-sterile medical care from endemic areas and children of women with risk factors for HIV-2 infection (O'Brien *et al*, 1992).

In conclusion, continued surveillance is needed to monitor for and develop special guidelines for HIV-2 in the Indian population. Physicians involved in screening for HIV need to have a high index of suspicion in patients with risk factors for HIV-2 infection, to appropriately diagnose and treat the disease since these patients develop AIDS related symptoms late due to delayed progression. Guidelines should be created for HIV testing of spouses with HIV-2 infection to diagnose and treat the disease, since these cases have inefficient transmission.

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