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Drug resistance during follow up of a case with HIV infection

Dear Editor,

Human immunodeficiency virus (HIV) continues to cause a high rate of morbidity and mortality despite drug and vaccine studies conducted with a high speed worldwide. According to the data of the World Health Organization the number of HIV positive pregnant women who receive antiretroviral treatment increase each day in countries with low-moderate income level. Infection is acquired during pregnancy, during delivery or in the breastfeeding period in more than 90% of the children infected with human immunodeficiency virus (1). Therefore, prevention of transmission from infected women to their infants in addition to prevention of infection in women who are in the child-bearing period is important (2). Treatment may be required in case of transmission from the mother to the infant which occurs in spite all precautions. In follow-up of infection acquired at youger ages, noncomplicance with treatment or drug resistance frequently leads to problems. With this case we would like to draw attention to development of drug resistance and its management in cases who are followed up because of HIV infection and in whom drug resistance develops.

HIV was found to be positive in a subject in screening performed at the age of 11 because of presence of HIV infection in the mother. After this date lamivudine, nevirapine and zidovudine combination treatment was started. The patient used this treatment for two years irregularly and was lost to follow-up for a period of one year. Afterwards, viral load was found to be increased as 6,67 E2 copies/ml at presentation. Transaminase levels and renal function were found to be normal, total white blood cell count was found to be 3510/mm3 and the rate of CD(4) T cells was observed to be decreased to 29% (534/mm3). There was no special finding in the personal medical history except for hospitalization because of lung infection 2 years ago. In the familial history, it was learned that HIV infection was found in the father during investigations performed bacause of intracranial abcess and the father died because of this. It was also learned that HIV infection was also found in the mother simultaneously. On physical examination, growth and development were found to be normal and no extraordinary finding was observed. No diagnostic test for HIV infection had been performed before, but transmission from the mother was considered, since the mother had HIV infection. Since irregular drug use was reported, it was anticipated that drug resistance might have been developed. Drug resistance test was done in Refik Saydam Hıfzısıhha Institute. Lamuvidine was shown to have methionine valine transition (M184V) high resistance mutations against nucleoside reverse transcriptase inhibitors (NRTI) and valine alanine transition (V106A) resistance mutations against non-nucleoside reverse transcriptase inhibitors (NNRTI). Considering antiretroviral treatment protocol used for children, treatment was arranged as 2 NRTI (Zidovudine+Tenofovir) and one protease inhibitor (Lopinavir/Ritonavir) selected according to resistance results in subjects who previously received 2 NRTIs and 1 NNRTI treatment, if resistance developed (3). No problem has been observed in the one-year follow-up of the subject whose viral load decreased at the end of a follow-up period of one month, viral load test was found to be negative at the second month and CD4 positive lymphocyte level was normal.

Resistance develops during treatment of human immunodeficiency virus because of incomplete compliance with treatment and this affects the survival negatively, if early intervention is not performed. Introduction of the approach of use of NRTIs initially and combined antiretroviral treatment (cART) afterwards has substantially decreased the mortality and morbidity related to HIV (4). Although successful results are obtained with treatment regimes containing lamivudine (3TC), mutations at a single position including M184V cause a decrease in drug sensitivity by 100-1000 fold (5). Methionine valine transition mutation is mainly responsible of development of resistance against lamivudine with a high rate, but is also responsible of resistance against other drugs in this group (6,7). Valine alanine transition mutation is associated with resistance against non-nucleoside reverse transcriptase inhibitors and especially with resistance against nevirapine (8).

Address for Correspondence: Başak Yıldız MD, Ege University Medical Faculty, Division of Pediatric Infectious Diseases, İzmir, Turkey
E-mail: basakyildiz@gmail.com **Received:** 12.23.2011 **Accepted:** 01.02.2011

Since development of new resistance against the drugs used during treatment is possible, subjects who receive HIV treatment should be followed up closely. If any minor suspicion of resistance is present, resistance tests should be performed and a new treatment regime should be started without losing time evaluating treatment options in line with the results of these tests.

Başak Yıldız, Deniz Gökengin, Dilek Yılmaz Çiftdoğan, Fadıl Vardar

Ege University Medical Faculty, Division of Pediatric Infectious Diseases, İzmir, Turkey

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