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Letter to the Editors

A non-affective psychotic syndrome after starting antiretroviral therapy

Dear Editors,

It is very well known that various antiretroviral agents may induce neuropsychiatric disorders.[1,2] The more frequent symptoms include insomnia, disturbing dreams, nervousness and depression. Other antiviral agents such as interferon α[3] or zidovudine[4] may precipitate similar neuropsychiatric effects. Psychotic reactions have also been described, mostly associated with manic affective states.[5] The case observed was a non-affective psychotic syndrome associated with an antiretroviral regimen containing tenofovir plus emcitrabine which had not been previously described for any of these drugs. Suppression of these antiretroviral agents led to remission of symptoms, but not the antipsychotic treatment.

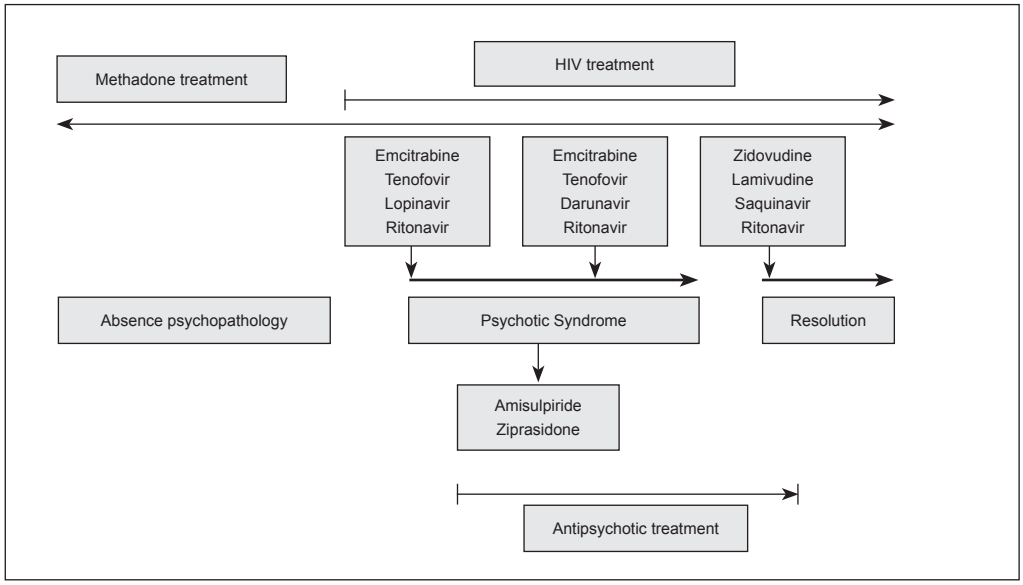
Case report

Ms. A, a 24-year-old antiretroviral-naive woman who had asymptomatic HIV infection, a virus load of 87,082 copies/mL, and a $CD4^+$ lymphocyte count of 490 x 10^6 cells/L, began receiving antiretroviral treatment with emcitrabine 200 mg plus tenofovir disoproxil 245 mg q24h and lopinavir 400 mg q12h plus ritonavir 100 mg q12h. Ms. A had been diagnosed HIV positive two years ago. She had no history of opportunistic diseases or other disorders related to HIV infection. She had a history of three years dependence on opiates with methadone 90 mg/day replacement therapy. Moreover, she reported an attention-deficit hyperactivity disorder when she was a child and a father with alcohol dependence.

Approximately one month after initiation of antiretroviral regimen, Ms. A started experiencing ideas of being observed and followed by somebody. She was hearing voices and believed in some plot against her. She partially preserved insight of these beliefs and showed no expression of harm to herself or others at that time. The results of neurological and general physical examinations as well as those of routine laboratory tests showed no significant disturbances. The brain MRI showed no significant changes. Because she also complained of diarrhoea, her lopinavir treatment was switched to danuravir 600 mg q12h. When Ms. A was referred to our psychiatric department she was already treated with amisulpiride 800 mg/day and ziprasidone 60 mg/day prescribed by physicians in the Methadone Maintenance Programme one month ago. We increased amisulpiride to 1,200 mg/day and gave her a new appointment in four weeks.

Then, Ms. A mentioned taking this dose during three weeks with improvementof her anxiety levels, but no resolution of psychotic symptoms. At that time, she knew she was pregnant, and the antiviral treatment was switched to combivir (zidovudine 300 mg and lamivudine (3TC) 150 mg) q12h, ritonavir 100 mg q12h and saquinavir 1,000 mg q12h. Moreover, she decided to stop antipsychotic treatment as psychotic symptoms did not ameliorate. At the next visit, the patient and her family explained that two weeks after starting the new antiviral regimen and stopping antipsychotic therapy, her mental state began to improve and the previous psychotic symptoms disappeared. The psychopathological assessment showed that she was in clinical remission. Two months later, in a follow-up, she continued in remission and under the same antiretroviral treatment.

In our opinion, the occurrence of the psychotic syndrome clearly implicates the antiretroviral therapy. We discarded methadone-antiretroviral drug interactions as the patient did not mention opioid withdrawal syndrome during this period. Ritonavir remained constant throughout. Psychiatric symptoms persisted after lopinavir was stopped, and danuravir was introduced later. Therefore, these agents were not the cause and psychosis could be either a consequence of an



unexplained interaction between tenofovir-emcitrabine, or a rare tenofovir or emcitrabine-related side effect. The incidence of these side effects needs to be evaluated in large databases or pharmacokinetics studies.

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