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P 217
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Idiosyncratic drug liver injury during long-acting HIV treatment: A Case Report

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Background

Transaminase elevation is a recognized, yet usually transient and rare adverse effect of long-acting injectable antiretroviral therapy (ART) drugs like cabotegravir and rilpivirine in people living with HIV (PLWH)[1,2]. We report a case of hepatopathy in a patient transitioning to long-acting injectable (LAI) ART and subsequently returning to oral therapy due to liver toxicity.

Case Presentation

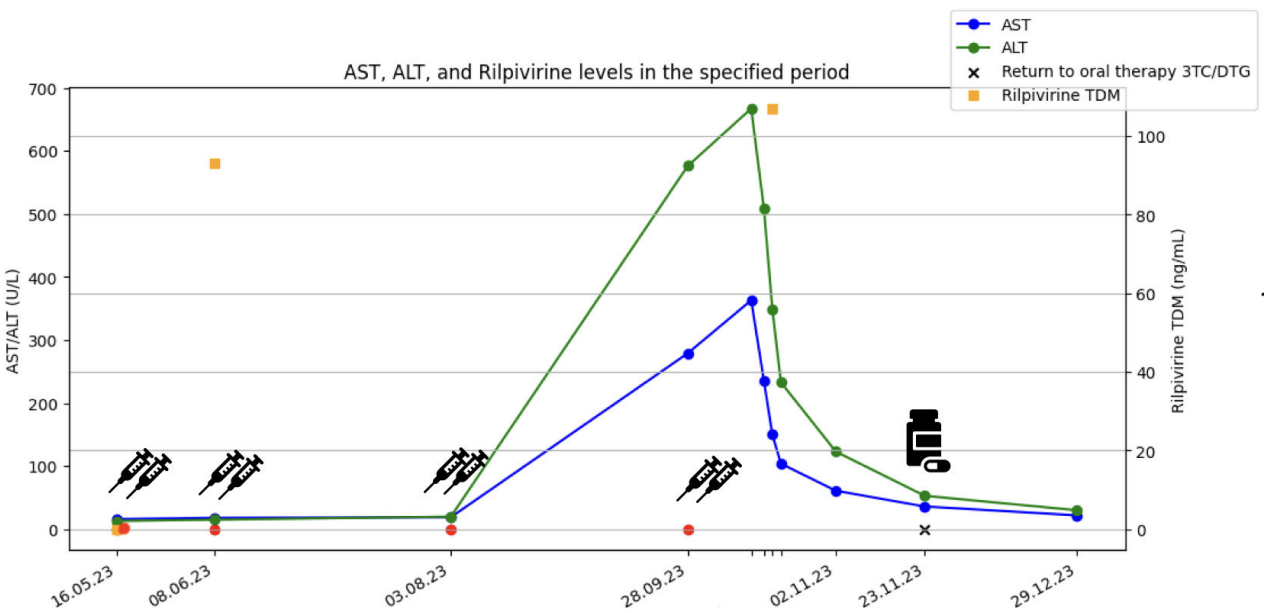
We describe a 68-year-old man diagnosed with HIV since 2015, with a nadir CD4 count of 122 cells/mm³ and peak HIV-RNA of 302174 cp/mL (CDC stage A3). Virologically suppressed for years, he had been on combination ART since diagnosis with 3TC/DTG since 2019.

In May '23, he switched to LAI with intramuscular cabotegravir 600 mg/3mL and rilpivirine 900mg/3mL without oral bridging. The patient weighed 59 kg and was 170 cm tall (BMI 20.4 kg/m²). He received the second injection after 21 days due to personal reasons, but was still within the suggested time window of injection. Rilpivirine therapeutic drug monitoring (TDM) showed a trough concentration of 93 ng/mL (target >48 ng/mL) after the first injection. TDM for cabotegravir was not performed. The third and fourth injections followed at 8-week intervals. Asymptomatic transaminase elevation (AST 279 U/L, ALT 578 U/L) with stable immunovirological parameters occurred at the fourth injection.

Repeated tests after 2 weeks confirmed elevated transaminases, prompting follow-up with supportive therapy and investigations. Rilpivirine TDM was rechecked, resulting in 107 ng/mL. Transaminases gradually decreased. **Figure 1** shows AST and ALT levels, rilpivirine concentration, and dates of cabotegravir and rilpivirine injections. Hepatic stasis indices and bilirubin were always within normal limits. The patient was vaccinated against HAV and HBV while HCV antibodies were negative. Serologies for T. pallidum, HEV, and Parvovirus B19 were negative, with negative HCV-RNA and CMV-DNA, and irrelevant EBV-DNA (42 cp/mL). Liver ultrasound was normal. Autoimmune disease investigations yielded inconclusive results.

In November '23, following a rapid decrease in transaminase levels, we proposed to continue LAI with a fifth dose, but the patient preferred to revert to oral 3TC/DTG regimen.

Figure 1



Discussion

This case highlights the importance of monitoring hepatic function during the transition to LAI. Rilpivirine TDM may be useful in assessing drug toxicity, but the lack of a universal reference range, particularly in the upper range, hinders dose adjustment in singular cases. Additionally, the patient received the second loading dose three weeks after the first, which, although clinically feasible, may have contributed to drug accumulation.

References

1. Moti N Ramgopal et al. Efficacy, safety, and tolerability of switching to long-acting cabotegravir plus rilpivirine versus continuing fixed-dose bictegravir, emtricitabine, and tenofovir alafenamide in virologically suppressed adults with HIV, 12-month results (SOLAR): a randomised, open-label, phase 3b, non-inferiority trial
2. Edgar T Overton et al. Long-acting cabotegravir and rilpivirine dosed every 2 months in adults with HIV-1 infection (ATLAS-2M), 48-week results: a randomised, multicentre, open-label, phase 3b, non-inferiority study