RESEARCH LETTER

A case of rilpivirine drug-induced liver injury

Liver toxicity is a frequent adverse event following antiretroviral therapy for HIV, ranging from asymptomatic increases in liver enzymes to fulminant liver failure.[1 2] Rilpivirine is a second-generation non-nucleoside reverse transcriptase inhibitor with low rates of liver enzyme elevations.[3] We report a case of acute hepatitis secondary to rilpivirine with histological documentation.

A 27-year-old Mediterranean man was diagnosed with HIV, with a baseline CD4 count of 0.359×10^9/L and an HIV-1 viral load of 21 525 copies/mL. His last negative HIV test was 2 years prior. His medical history included depression, G6PD deficiency and a beta thalassaemia carrier status. He reported minimal alcohol intake. His baseline liver markers were normal.

Abacavir/lamivudine 600/300 mg once daily and raltegravir 400 mg two times per day were started on week 4 following diagnosis. Raltegravir was switched to rilpivirine 25 mg once daily on week 11 due to symptoms of fatigue.

His liver markers were abnormal on week 25, 14 weeks following switch, with alanine transaminase (ALT) of 231 IU/L (reference range 4–51 IU/L) and total bilirubin of 31 µmol/L (0–21 µmol/L). A summary trend of his liver markers is presented in figure 1. An extended liver panel, including hepatitis A, B, C and E, syphilis, autoimmune antibodies, ferritin, alpha-1 antitrypsin and caeruloplasmin screen, was negative or normal. HIV-1 viral load remained undetectable (under 20 copies/mL) throughout.

He received a 7-day course of doxycycline, as well as metronidazole and clindamycin for an asymptomatic chlamydia infection and a perianal abscess during this period, respectively; however, both diagnoses and treatments were given after the increase in liver markers. He reported no regular prescription, over-the-counter or herbal medications, and no increased alcohol intake. Liver ultrasound showed an echogenic liver in keeping with mild fatty infiltration. On liver transient elastography, the median liver stiffness was 5.4 kPa and the controlled attenuation parameter was 205, suggesting no significant fibrosis or steatosis.

Histology revealed diffuse confluent centrilobular necrosis, which is a typical lesion of drug-induced liver injury but not specific, present also in new-onset autoimmune hepatitis or in some cases of hepatitis virus infection, the two main differential diagnoses. Both conditions were reasonably excluded in our patient.

The patient remained asymptomatic apart from mild nausea after antiretrovirals. Rilpivirine was switched to raltegravir 1200 mg once daily on week 66. His ALT showed an improvement soon after the switch; however, raltegravir was switched to boosted darunavir with ritonavir on week 71 due to poor mood. Abacavir/lamivudine was subsequently switched to tenofovir disoproxil fumarate/emtricitabine on week 74 due to nausea. By week 92, liver markers had normalised and his nausea resolved.

Low rates of liver toxicity have been reported with rilpivirine. In the ECHO and THRIVE studies comparing rilpivirine with efavirenz, rilpivirine had significantly lower incidence of grade 2–4 ALT and aspartate transaminase levels,[3] with no serious treatment-related hepatic adverse events. One other case of possible drug-induced allergic hepatitis secondary to rilpivirine has been reported[4]; however, the patient was severely immunosuppressed with disseminated *Mycobacterium avium* infection, multiple comorbidities and concomitant medications, without histological evidence of underlying liver pathology. While rilpivirine-induced liver damage is rare, further monitoring and reporting of such events are important to better understand the safety profile of this drug.

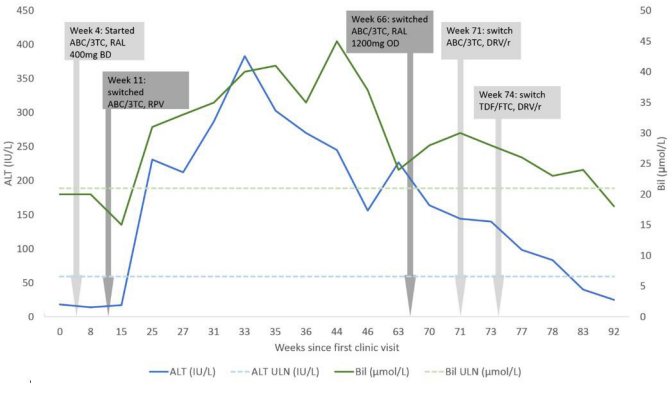

Figure 1 Liver markers and association with antiretroviral switches over time. ABC/3TC, abacavir and lamivudine fixed-dose combination; ALT, alanine transaminase; BD, twice daily; Bil, total bilirubin; DRV/r, boosted darunavir with ritonavir; IU, international unit; OD, once daily; RAL, raltegravir; RPV, rilpivirine; TDF/FTC, tenofovir disoproxil fumarate and emtricitabine fixed-dose combination; ULN, upper limit of normal range.

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