LACK OF RESPONSE TO THERAPY IN A PERSON LIVING WITH HIV WITH TUBERCULOSIS AND HEPATITIS C COINFECTION

Chen WB[1], Moso MA[1,2], Singh KP[1,2,3]

[1]Victorian Infectious Diseases Service, The Royal Melbourne Hospital at the Peter Doherty Institute for Infection and Immunity, Melbourne, VIC

[2]Department of Infectious Diseases, The University of Melbourne at the Peter Doherty Institute for Infection and Immunity, Melbourne, VIC

[3]Department of Infectious Diseases, Peninsula University Hospital, Frankston, VIC

Case Presentation: A 20-year-old Karen male was initially referred with HIV infection, hepatitis C and latent tuberculosis (TB) coinfection. Antiretroviral therapy (ART) was prescribed but clinic attendance was sporadic, with poor adherence to therapy. Six years later he presented with advanced HIV and disseminated TB. TB therapy was initiated, complicated by hepatotoxicity and peripheral neuropathy necessitating multiple regimen changes before stabilising on intensive phase rifampicin/levofloxacin/pyrazinamide with continuation phase rifampicin/levofloxacin. ART with emtricitabine/tenofovir and double-dose dolutegravir was introduced.

Four months later he re-presented with abdominal pain and fevers. HIV viral load remained elevated (log 5.7) with CD4 0.0 cells/μL raising questions around adherence to therapy. During admission, HIV viral load dropped to 69 copies/mL. He was discharged with regular nursing visits with apparent adherence to therapy. Five months later, he was re-admitted with seizures and new cerebral lesions on imaging. Biopsy was culture positive for TB without change in drug-susceptibility profile. This raised concerns about dosage, CNS penetration, absorption and metabolism of TB therapy. Treatment was changed to levofloxacin, linezolid and high-dose intravenous rifampicin. Pharmacogenomic testing did not reveal abnormalities in TB drug metabolism and therapeutic drug monitoring was inconclusive.

Despite apparent adherence to therapy, he experienced HIV virologic failure. Genotyping found resistance to integrase inhibitors, attributed to inadequate dolutegravir exposure due to hepatic enzyme induction with high-dose rifampicin. ART was changed to darunavir/cobicistat/emtricitabine/tenofovir together with a rifampicin-sparing TB regimen. Despite change in ART, his HIV viral load increased further. Next generation sequencing was performed which did not identify additional drug resistance mutations. Darunavir drug levels were adequate. His HIV viral load eventually responded without change in therapy and he completed 12 months of TB therapy with clinical and radiological improvement. Hepatitis C treatment was introduced but was followed by paradoxical increase in viral load which is currently under investigation.

Conclusion: This case highlights multiple factors that should be considered when disease unresponsiveness is encountered in HIV with coinfections, including medication adherence, drug-drug interactions and utility of therapeutic drug monitoring.

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