Contradictory diagnostic investigation results of an unusual skin lesion in a man with HIV-HBV coinfection – A diagnostic and management conundrum

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Abstract

This case report highlights the potential ramifications of an error in the diagnosis of an unusual skin lesion due to misguided interpretation of conflicting investigation results, in a treatment-experienced patient with HIV-HBV co-infection. The ramifications include potential life threatening limitation of therapeutic options for 2nd line antiretroviral therapy due to potential drug-drug interactions.

Keywords: HIV, tuberculosis, antiretroviral therapy, molluscum contagiosum, drug-drug interaction.

Introduction

The management of HIV-positive patients with opportunistic infection (OI) is challenging, especially if there are multiple OIs. The successful management of these conditions hinges on two main criteria – an accurate diagnosis and good knowledge of potential drug-drug interactions (DDIs). We report the case of a 24-year-old man with HIV, Hepatitis B (HBV) and latent syphilis with contradicting investigation results of an unusual skin lesion affecting a therapeutic dilemma when the treatment of OIs was combined with antiretroviral therapy (ART) for HIV.

Case Summary

A 24-year-old HIV-positive man was diagnosed with pancytopenia, hepatitis B and latent syphilis when he presented with an episode of syncope. At the time, he had an exophytic lesion on the dorsum of his right ankle (Figure 1) which was biopsied for histopathological examination (HPE) and polymerase chain reaction (PCR) for suspected cutaneous tuberculosis. His nadir CD4 count was 2 cells/mm^3. He was commenced on 1st line ART-regimen consisting of two nucleoside reverse transcriptase inhibitors (NRTIs), tenofovir-emtricitabine (TDF + FTC), and a non-nucleoside reverse transcriptase inhibitor (NNRTI), efavirenz (EFV). Itraconazole was prescribed for the exophytic lesion presumed to be cutaneous fungal infection.

At his review after two months, the HPE of the biopsy showed Molluscum contagiosum (MC) but the PCR was positive for tuberculosis (TB). No change was made to his medications until he was reviewed another two months later by the respiratory medicine team. At this point, itraconazole was ceased and he was started on anti-TB consisting of isoniazid (INH), rifampicin (RIF), and ethambutol (ETH) for cutaneous TB infection or tuberculosis verrucose cutis (TVC) based on the PCR result. Pyrazinamide was not added as his alanine transaminase (ALT) was elevated (90 U/L), presumably due to itraconazole.

Upon review one month later, the exophytic lesion had increased in size. His CD4 remained low (1.9 cells/mm^3) with HIV viral load of >3-million copies/mL suggesting failure of ART. The usual course of action is to cease ART in totality while awaiting HIV viral resistance testing to be done. However, because of his hepatitis B positivity, only EFV was ceased while TDF + FTC were continued to avoid triggering an acute hepatic flare of hepatitis B from abrupt cessation of TDF.[1] At this juncture, he was referred to our centre for commencement of 2nd line ART.

The choice of 2nd line ART regimen in a treatment-experienced patient on anti-TB presents a therapeutic dilemma due to potential DDIs. The conflicting investigation results and the lack of response of the skin lesion to anti-TB raised the question about the accuracy of the original diagnosis of TVC. These issues are explored under 'Discussion'. These dilemmas were serendipitously resolved when the PCR result was

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confirmed to be a false positive due to contamination at the original testing laboratory. Anti-TB was immediately ceased while TDF and FTC were continued, pending the results of the HIV resistance test. The ankle lesion was managed with liquid nitrogen cryotherapy initially and surgically excised soon after it became infected.

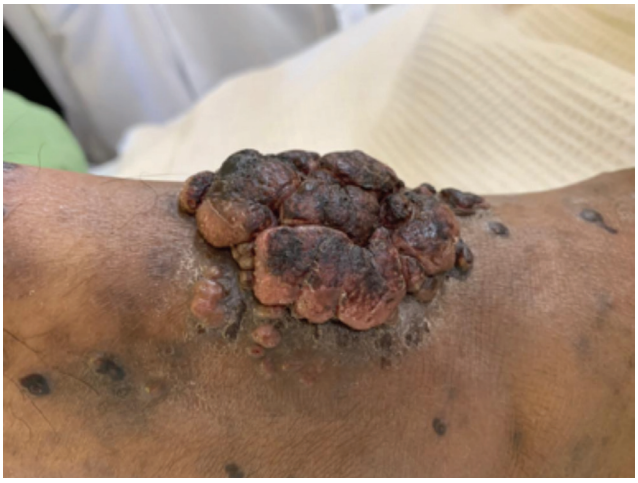

Figure 1: Lateral view of the exophytic growth measuring 8 x 7 x 2 cm on the dorsum of the right ankle.

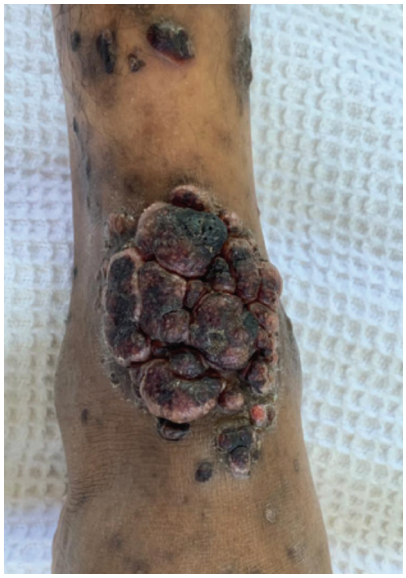

Figure 2: Superior view of the exophytic growth surrounded by several smaller lesions.

Discussion

The management of this patient with latent syphilis and HIV-HBV co-infection requiring 2nd line ART while on anti-TB for TVC presented a therapeutic dilemma. The recommended ART regime for treatment-experienced patients require either a protease inhibitor (PI) or an integrase inhibitor (INSTI) as part of the regimen.[1]

Unfortunately, PI is contraindicated in patients who are on RIF as the latter induces cytochrome-P3A (C3PA) and interferes with metabolism of PIs.[2,3] When co-administered with RIF, the concentration of standard-doses of PI diminish by more than 80% and significantly reduces its therapeutic efficacy.[1,4] Increasing the dosage of PI to counter the inductive effect of RIF is not recommended due to high incidence of PI-induced hepatotoxicity.[1,3] Similarly, RIF reduces the trough concentration of INSTI by more than 50%, even with the doubling of INSTI dosage.[4] Ideally, RIF should have been replaced with rifabutin, a less potent CP3A inducer. Unfortunately, rifabutin is not readily available in this country. It would appear at this juncture that as long as the patient was on anti-TB, there was no feasible 2nd line ART options. The option to wait until the completion of anti-TB before initiating ART could not be considered given the severely immunocompromised state of this patient. Delaying ART could be potentially fatal.

The apparent non-response of the skin lesion to anti-TB therapy raised doubts on the initial diagnosis of TVC and the veracity of the PCR result. How reliable is the PCR result compared to HPE?

The differential diagnoses of such a lesion in an immunocompromised person include Molluscum contagiosum (MC), cryptococcosis, histoplasmosis, squamous cell carcinoma, condylomata lata on account of his latent syphilis, and TVC.

MC is an infection caused by poxvirus transmitted via skin-to-skin contact or fomites, presenting as smooth-surfaced dome-shaped pearly papules between 3 mm to several cm in diameter with the characteristic central umbilication.[5,6] Its presence in HIV positive patients indicates advanced stage disease. Cutaneous cryptococcosis are similar to MC except for central haemorrhagic crust.[6] Primary cutaneous histoplasmosis lesions are chancre-like lesions with associated lymphadenopathy while the disseminated variety presents as either papules, umbilicated nodules, plaques, ulcers or abscesses.[6]

Squamous cell carcinoma is found on sun-exposed areas of the body. They are dull-red in colour, round and indurated with an elevated base which may ulcerate and bleed.[6] Condylomata lata are soft papular red mushroom-like masses of 1-3cm in diameter found usually around the genitalia and anus.[6] TVC presents initially as a small papule which grows peripherally to become hyperkeratotic with fissuring of its surface with exudative purulent discharge. Typically, it presents solitarily on the dorsa of fingers and hands in adults.[6]

The diagnosis of MC is usually made clinically by its characteristic appearance. Histologic examination may be necessary in patients with HIV as the lesions may be atypical. Hematoxylin and eosin staining of a molluscum contagiosum lesion typically reveals keratinocytes containing eosinophilic cytoplasmic inclusion bodies or Henderson-Paterson bodies.[7] Although PCR may be useful in the diagnosis of TVC in cases where biopsy and culture fail to detect evidence of mycobacteria, its low sensitivity and specificity (25% and 74%, respectively in one study) suggest PCR results should be interpreted with clinical and histopathological findings.[8] Therefore, the decision to favor the PCR over HPE results in this case and treating this patient with anti-TB was an error in diagnosis.

Conclusion

The accurate diagnosis of opportunistic infections in patients with HIV infection is crucial and should be based on sound clinical judgement and careful evaluation of available evidence. The diagnostic error from favouring PCR over histopathological evidence could have led to potentially fatal DDI and serious limitation of 2nd line ART options for this patient.

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Conflict of interest

None.

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