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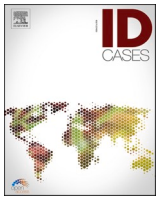

Case report

Repeated false-negative HIV rapid test results in a patient presenting to care with advanced HIV disease: A case report

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ABSTRACT

Severe immunosuppression has been reported as one of the causes of a false-negative HIV rapid test result. Guidelines on what tests should be performed in adult patients presenting with severe immunosuppression despite a negative HIV rapid test result are lacking. This is the second case report of a false-negative HIV rapid test results in a patient presenting with advanced HIV disease in Tanzania.

Introduction

Advanced HIV Disease (AHD) in adults, defined by the World Health Organization (WHO) as having a CD4 cell count below 200 cells/mm3 or being of WHO clinical stage 3 or 4 [1], persists in low- and -middle-income countries. A recent survey conducted in 9 African countries found up to 22% of adults had AHD at diagnosis [2]. Despite the high sensitivity and specificity of the HIV rapid tests, a systematic review assessing the HIV misdiagnosis and testing practices reported a prevalence of 3.1% and 0.4% false positive and negative results respectively; with AHD being among the reported causes for false negative results [2]. We report a case of a 45 yrs old HIV-infected male who received multiple false negative HIV rapid test results, leading to a delay in enrolment in care, denial of HIV positive status, and eventually death.

Case presentation

A 45 yrs old male from Dar es Salaam, the largest city in Tanzania, presented to our rural referral hospital outpatient department in September 2021 with a complaint of long-standing abdominal pain which was associated with the passing of loose stool three to four times per day. This was preceded by a 2-year history of unintentional weight loss and a six months history of intermittent low-grade fevers. During his illness, the patient had attended multiple hospitals without proper diagnosis and management. He reported having tested HIV-negative three times (in January, March, and June 2021) as per the Tanzanian National HIV Testing Services Guidelines; where a whole blood sample from a finger-prick would be tested for HIV using the SD BIOLINE HIV I/2–3.0 (Standard Diagnostics, Inc., Gyeonggi, Republic of Korea) rapid test, and only after a reactive result, a second HIV rapid test by the Uni-Gold HIV (Trinity Biotech Manufacturing Ltd., Bray, Ireland), would be conducted. If the first rapid test is negative, the patient is considered to be HIV-negative and if both are reactive, a positive HIV diagnosis is made [3]. The sensitivities of SD BIOLINE HIV I/2–3.0 and Uni-Gold HIV rapid tests are 99.76% (98.7%−100%) and 100% (99.2–100%), and the specificities are 99.85% (99.2%−100%) and 99.9% (99.2–100%) respectively [4,5]. His wife and 2 children also tested HIV-negative. His family had decided to bring him back to the village to seek alternative therapy thinking he was bewitched.

On examination, the patient was wasted with enlarged cervical lymph nodes and multiple Pruritic Papular Eruptions covering his trunk and limbs, suggestive of severe immunosuppression. With HIV being the most common cause, provider-initiated HIV testing and counseling were again offered. The results came back negative. However, following high suspicion of HIV, an HIV DNA PCR test was done which came back positive, and an HIV viral load test showed 33,122 copies/mL. Other Laboratory results were: a very low CD4 count, 23cells/mm^3; elevated Creatinine, 139.9micromol/l (estimated Glomerular filtration rate of

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60.2 mL/min/1.73 m^2, by Chronic Kidney Diseases Epidemiology formula (CKD EPI)); Haemoglobin, 12.4 g/dl; Alanine Aminotransferase (ALT), 45.4 IU/L; White Blood Cell count, 5200/mm^3; Platelet count, 258,000/mm^3; Venereal Disease Research Laboratory test (VDRL), Negative; Hepatitis B Surface Antigen Test, Negative; Plasma Cryptococcal Antigen Test, Negative; GeneXpert Ultra in urine, Negative; Stool analysis, no parasites seen. An abdominal ultrasound revealed an enlarged liver. Chest radiography was normal.

The patient was diagnosed with HIV WHO stage 4 and acute renal impairment secondary to dehydration because of continual diarrhea. He was counseled on his HIV status and initiated on the first line of antiretroviral therapy as per the Tanzanian National HIV Treatment Guidelines [6] which were Tenofovir, Lamivudine, and Dolutegravir. He was also started on Co-trimoxazole preventive therapy.

Despite repeated counseling sessions, the patient refused to accept his HIV status and opted for traditional medication instead of antiretrovirals believing he was bewitched. He later died from renal failure attributed to herbal intoxication, a cause that is not uncommon in African settings [7,8]. The possibility that he had underlying opportunistic infections that might have contributed to his death cannot be refuted.

Discussion

AHD continues as a challenge for HIV programs in developing countries. Delayed HIV diagnosis results in a lack of prompt treatment, fast disease progression, and increased mortality, hence the WHO treat-all approach [9]. With a CD4 count of 23 cells/mm^3, as previously postulated [2], we suspect severe immunosuppression from AHD resulting in low levels of HIV 1/2 antibodies, was the reason for a false negative result in our patient.

Despite multiple reports of false negative HIV test results in HIV-positive adults presenting with AHD [10–13], there are currently no guidelines on what tests should follow a high suspicion of HIV in sero-negative adult patients, in resource-limited settings. Because of the lack of such a recommendation, the prevalence of false negative results might be underrepresented.

Our patient had multiple encounters with the healthcare system but was not diagnosed timely. This led to his disbelief in the health care system, denial of his HIV status, and turning to herbal therapy which resulted in his death.

Since the HIV molecular tests remained positive, and to ensure that no one is left behind; we advocate HIV programs to review HIV testing algorithms, utilizing the existing platforms for HIV viral load monitoring and DNA PCR testing, to assist in the diagnosis of patients presenting with AIDS-defining illnesses despite a negative HIV rapid test result.

Conclusion

To our knowledge, this is the second reported case of a false negative HIV rapid test result associated with AHD in Tanzania. Despite it being a rare occurrence, the repercussions are fatal. Adapting the HIV testing guidelines to include molecular tests in the diagnosis of HIV, in adult patients presenting with severe immunosuppression, should be among the key components of the advanced HIV disease package for resource-poor settings.

Ethics approval

The patient had given written informed consent to participation in the Kilombero and Ulanga Antiretroviral Cohort (KIULARCO) which has ethical approval from both the Ifakara Health Institute Institutional Review Board, and the National Institute for Medical Research of Tanzania.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contribution

Francisca Chuwa and Bernard Kivuma were actively involved in the diagnosis and management of the patient, were responsible for data collection and wrote the first draft of the manuscript. Robert Ndege conceptualized the case report, supervised the management of the patient and reviewed the manuscript.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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