



Report of a False Positive Rapid HIV Test Due to Hepatitis A in a U.S. Army Soldier

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Abstract

A 25 year old, single, active duty soldier presented to a clinic in Afghanistan complaining of malaise, fatigue, acholic stools, and mild jaundice over a 5- to 7-day period. He had significantly elevated liver transaminase levels approaching 5000 U/L and a positive rapid human immunodeficiency (HIV) 1 antibody test. Ultimately, the patient was found to have a false positive rapid HIV-1 antibody test due to acute hepatitis A virus infection. This case report describes his evaluation and outcome, in addition to exploring possible causes of false positive HIV screening.

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Introduction

Human immunodeficiency virus (HIV) is a well-known sexually transmitted disease that accounts for significant morbidity and mortality. A report by the Centers for Disease Control and Prevention (CDC) approximated 1,144,400 cases of HIV in 2010 in the United States with about 21,278 cases of death from known HIV.¹

Although HIV in the military is not of particular concern, all active duty personnel are required to have biennial HIV testing unless they are already HIV-positive. From 2008 to 2012, the incidence of HIV diagnosis among U.S. Army active component increased 22%. In 2012, 416,715 soldiers were tested and 111 (108 male) were found to be HIV-positive.²

Rapid HIV antibody testing allows for obtaining preliminary results within 20 to 30 minutes. This is advantageous in many populations including the military where early diagnosis can positively affect soldier and unit readiness. If positive, a rapid test is only considered a "preliminary positive" as confirmatory immunoassays and Western blots are necessary.³ Like conventional screening antibody immunoassays, a positive rapid result requires confirmatory testing. As with all screening tests, false-positive results occur. We describe the first case report of a false positive HIV antibody test due acute hepatitis A infection.

Materials and Methods

Case

A 25 year old, single, white, male Army soldier presented to a clinic in Afghanistan complaining of fatigue, malaise, nausea, chills, and acholic stools. He denied any sexual contact within the previous year and denied alcohol, tobacco, illicit drugs or supplement use. His only medication was doxycycline prescribed for malaria prophylaxis for which he was compliant. He worked closely with Afghani soldiers and frequently ate local food.

Physical examination was remarkable for normal vital signs, mild hepatomegaly, and marked jaundice and scleral icterus. Initial laboratory testing was significant for aspartate aminotransferase (AST) and alanine aminotransferase (ALT) at nearly 5000 U/L. Hepatitis B

and C testing was negative. HIV testing using OraQuick[®] Rapid HIV-1 Antibody Test (OraQuick[®]) (OraSure Technologies, Bethlehem, Pennsylvania, USA) was positive. Prior to deployment, the patient had a negative conventional HIV-1/2 antibody test.

The patient was evacuated to Landstuhl, Germany and then to Womack Army Medical Center (WAMC), Fort Bragg, NC for further evaluation. At WAMC, laboratory investigation included a hemoglobin of 13.8 g/dL, white blood cell count of 4.3 k/uL and platelet count of 213 k/uL. Prothrombin time and activated partial thromboplastin time were normal. Testing for hepatitis B, C, and E virus were negative. Hepatitis A IgM was positive. Conventional HIV enzyme immunoassay (EIA), Western blot and HIV-1 RNA quantitative assay were also negative. No record of hepatitis A vaccination was found. Four months after discharge, his AST and ALT were normal.

Discussion

In 2013, the US Preventive Services Task Force recommended universal HIV screening among patients age 15-65 years.⁴ Such screening allows the detection of asymptomatic infected patients thus providing the opportunity to prevent disease transmission and reduce morbidity with early anti-retroviral therapy. Previously, rapid HIV testing was advocated by the Centers for Disease Control and Prevention in their initiative, "Advancing HIV Prevention: New Strategies for a Changing Epidemic".⁵ Early diagnosis can be helpful in several populations to include high risk individuals, especially if they have infrequent follow-up and following accidental needlestick injuries to health care workers. Similarly, for pregnant women with unknown HIV status, rapid diagnosis is crucial for prompt treatment of mothers and infants.

Currently, several approved rapid HIV tests are available to patients: OraQuick[®] and OraQuick ADVANCE[®] Rapid HIV-1/2 Antibody Test (OraSure Technologies, Bethlehem, PA, USA); Reveal[™] Rapid HIV-1 Antibody Test, Reveal[™] G2 Rapid HIV-1 Antibody Test, and Reveal[™] G3 Rapid HIV-1 Antibody Test (MedMira Laboratories, Inc., Halifax, Nova Scotia); Uni-Gold Recombigen[®] HIV Test (Trinity BioTech, Bray,

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Ireland), Multispot HIV-1/HIV-2 Rapid Test (Bio-Rad Laboratories, Redmond, WA, USA), Clearview[®] HIV 1/2 STAT-PAK, Clearview COMPLETE[®] HIV1/2 Assay (Alere, Waltham, MA, USA); and Insti[™] HIV-1 Antibody Test Kit (bioLytical Laboratories, Inc., British Columbia). Since this case was conducted, OraQuick[®] In-Home HIV Test (Orasure Technologies, Bethlehem, PA, USA) and Chembio DPP[®] HIV 1/2 Assay (Chembio Diagnostic Systems, Inc., Medford, NY, USA) have also been approved. Delaney et al. compared 6 rapid HIV tests to conventional EIAs and found all to have statistically similar high specificity and sensitivity.⁶ The OraQuick ADVANCE[®], which is the only FDA-approved rapid test for oral fluid (can also be used with whole blood or plasma), had a sensitivity of 99.3% and specificity of 99.8% for oral specimens.⁶

A positive rapid HIV antibody test requires confirmation. Our patient, after having a positive screening test, had conventional EIA and confirmatory Western blot/HIV RNA testing that was negative. Hence he was assessed as having a false-positive rapid test due to acute hepatitis A infection.

A review of the literature reveals that false-positive conventional EIA testing has been reported to be associated with a variety of states to include vaccinations with rubella,⁷ influenza^{8,9}, rabies¹⁰, hepatitis B¹¹, and tetanus;¹² acute cytomegalovirus infection;¹³ systemic lupus erythematosus;¹⁴ and the presence of rheumatoid factor or anti-nuclear antibody.¹² For the military who deploy to numerous continents to include Africa, it is important to be aware that false-positive EIA testing can also occur with malaria,¹⁵ human African trypanosomiasis,¹⁶ visceral leishmaniasis,¹⁷ trypanosoma cruzi,¹⁸ and schistosomiasis.¹⁹ An important cause of false-positive test in the US is pregnancy. Chao et al. reviewed data from 47,794 pregnant women and found that 0.3% had a false positive test. The positive predictive value was 54.3%.²⁰ Younger and nulliparous women were more likely to have a false positive. Of note, Tung²¹ and Jamieson²² have shown that the false-positive rate among pregnant women is significantly lower using OraQuick[®] than with conventional EIA testing.

For false positive rapid tests, the literature documents reports only for OraQuick[®]. In January 2004, New York City started offering on-site rapid HIV testing

of finger-stick whole blood with OraQuick[®]. In March 2005, they switched to oral fluid testing using OraQuick ADVANCE[®]. In late 2005 and 2007, an unexpected increase in false-positive oral fluid rapid tests occurred; no clear cause was found.²³ Similarly, Jafa et al. reported on an investigation of 16 false positive oral specimens using the OraQuick ADVANCE[®]; no cause was identified.²⁴

False-positive OraQuick ADVANCE[®] results have been caused by dengue fever²⁵ and have been associated with O-negative blood and sex with an HIV-infected person.²⁶ Additionally, the package labeling for OraQuick[®] Rapid lists several potentially interfering medical conditions that are associated with false-positive testing: multiparous women, rheumatoid factor, Epstein Barr virus, and hepatitis A and B viruses.²⁷

For many of these conditions, infection and subsequent antibody response may result in cross-reactivity that produces a false-positive test.²⁸

Conclusion

HIV diagnosis in a time-efficient manner is readily available with rapid HIV testing. Upon diagnosis, a treatment regimen can begin earlier than determined by traditional testing methods. The benefits and timeliness of rapid tests for HIV diagnosis has led to their increased use, now including home testing. Physicians and health care providers should be aware that while these tests have high sensitivities and specificities, they can also falsely detect HIV antibody. All positive rapid HIV tests require confirmatory testing. If proven negative, clinicians should investigate for possible etiologies.

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Written consent for this case report was received from the patient and is available for review by the editorial office.

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Conflict of Interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

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