Performance of Alere Determine HIV-1/2 Ag/Ab Combo rapid test for acute HIV infection: a case report

Performance del test rapido Alere Determine HIV-1/2 Ag/Ab Combo nell'infezione acuta da HIV: un caso clinico

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INTRODUCTION

Early diagnosis of acute human immunodeficiency virus (HIV) infection by rapid HIV tests allows identification of patients who may be candidates for antiretroviral treatment, quick confirmation of HIV status in patients presenting with an AIDS-defining illness and prevention of the spread of HIV infection [1, 2].
"Fourth-generation or combo" rapid tests (detecting both antibodies and p24 antigen) have recently been found to be less accurate in identifying the acute phase of HIV infection in respect of conventional "fourth-generation" tests [3, 4].
We report our experience in a patient with acute HIV infection (Fiebig III stage), in whom the rapid Alere Determine HIV 1/2 Ag/Ab Combo assay (Alere, Milan,Italy) test became positive only two weeks after the first positivity of conventional "fourth generation" immunoassays and over 30 days after HIV exposure [5, 6].

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CASE REPORT

A 20-year-old man was admitted at the Infectious Diseases Unit, G.B. Rossi Hospital in Verona (Italy) in December 2013. He had been hospitalised elsewhere two days earlier with a one week history of fever, sore throat, arthromyalgias and fatigue, and found to be HIV-infected by Ag P24/Ab anti-HIV 1-2: CLIA assay (ADVIA CENTAUR HIV AG/AB COMBO, Siemens Healthcare Diagnostics Inc., USA) and ELFA assay (VIDAS HIV DUO, Quick bioMérieux, France). The patient had had unprotected sexual intercourse with an HIV-infected man 10 days prior to the onset of symptoms. When he presented to us he had fever (40°C), sore throat, arthralgias and headache. On physical examination a trunk macular rash and bilaterally palpable, tender cervical and inguinal lymph nodes were present. Blood tests showed anemia, leukopenia and increased transaminases. At arrival in our Unit the Alere Determine HIV 1/2 Ag/Ab Combo test on whole blood was negative, while ADVIA CENTAUR HIV AG/AB COMBO and VIDAS HIV DUO were positive on serum. HIV1 and 2 immunoblot on serum (INNO-LIA HIV-1/2, Innogenetics N.V., Belgium) was also negative. The first positive result of the rapid test Alere Determine on whole blood (Ag p24

Table 1 - Days after sexual exposure and temporal trend of laboratory tests.

Days after sexual exposure	*Laboratory tests*					
	Alere Determine ™ HIV-1/2 Ag/Ab Combo		*ADVIA CENTAUR HIV*	*VIDAS HIV DUO*	*INNO-LIA HIV-1/2*	*HIV-RNA (copies/mL)*
	Ag p24	*Antibodies*				
17 days	not performed	not performed	+	+	negative	not performed
18 days	-	-	+	+	negative	>10,000,000 copies/mL
21 days	-	-	+	+	negative	not performed
31 days	-	+	+	+	HIV-1 indeterminate gp41++, p31+	not performed
66 days	not performed	not performed	+	+	HIV-1 positive gp41+++, p31++, p24+++, p17+++	1,350 copies/mL

negative and HIV antibodies positive) was two weeks after admission (31 days after the likely acquisition of HIV infection), when Immunoblot became indeterminate (positivity for antibodies to -gp41 and p31) for the first time. Immunoblot was positive late in January 2014. At admission the patient had a viral load >10,000,000 copies/mL and a CD4 cell count of 188 cells/µL (Table 1). We had started HAART (tenofovir/emtricitabine, atazanavir, ritonavir) three days after admission and 45 days later the CD4 cell count had risen to 610/µL while HIV RNA had decreased to 1,310 copies/mL.

DISCUSSION

Alere Determine™ HIV-1/2 Ag/Ab Combo is a fourth generation assay capable of detecting HIV-1 p24 antigen and HIV-1 and HIV-2 antibodies in serum, plasma and whole blood; it is therefore a conventional lateral flow rapid test device [6].
The sensitivity, as listed in the Alere Determine Combo package insert, is 99.9% using serum, plasma, and whole blood, while the specificity using all specimen types (serum, plasma, whole blood) is 100% for low risk subjects and ranges from 98.9% (serum) to 99.7% (whole blood) for high risk subjects [6].
CDC studies comparing all the FDA-approved tests on the same plasma specimens collected from persons during seroconversion found that Determine Combo detects infection one to two weeks before other rapid tests, and three to four days after fourth-generation laboratory antigen/antibody HIV tests [7]. Despite the industry indications, currently there are limited data on the relative sensitivity of Alere Determine Combo or other rapid HIV tests used with whole blood specimens like in our case.
International studies using Alere Determine Combo indicate that antibody sensitivity is comparable to package insert specifications, but that the antigen component does not detect most acute infections demonstrated by laboratory 4th generation p24 antigen/antibody immunoassays [8-10]. Alere Determine Combo can become reactive earlier than Western blot.
Our case indicates the inability of Alere Determine HIV 1/2 Ag/Ab Combo test to diagnose primary HIV infection during the earliest phase. Also, we did not find a correlation between a viral load > 10,000,000 copies/mL and a positive Alere Determine HIV 1/2 Ag/Ab Combo test, contrary to as the report by Faraoni and colleagues, probably because they tested serum samples [4]. Our data suggest that when acute HIV infection is suspected, a rapid test should be supplemented by conventional "fourth generation" tests and/or plasma HIV RNA assay.

Conflict of interest:
The authors declare that they have no conflict of interest

Keywords: rapid "fourth generation/combo" test, p24 antigen, HIV-specific antibodies, acute HIV infection, plasma HIV RNA.

SUMMARY

We describe a case of symptomatic acute HIV infection in a young man where a fourth-generation rapid screening test combining HIV-specific antibody and p24 antigen was negative. In highly suspicious cases of acute HIV infection, plasma HIV RNA assays together with conventional, non-rapid screening tests should be used.

RIASSUNTO

Descriviamo il caso clinico riguardante un giovane ragazzo con un'infezione acuta da HIV sintomatica non diagnosticata dal test rapido combo di quarta generazione. Nei casi altamente sospetti di infezione acuta da HIV si dovrebbero preferire la determinazione di HIV RNA plasmatico e i tests di screening convenzionali.

REFERENCES

[1] Kigozi G., Wawer M., Settuba A., et al. Foreskin surface area and HIV acquisition in Rakai, Uganda (size matters). *AIDS* 23, 2209-2213, 2009.

[2] Branson B.M., Handsfield H.H., Lampe M.A., et al.Revised recommendations for HIV testing of adults, adolescents, and pregnant women in health-care settings. Centers for Disease Control and Prevention (CDC). *MMWR* 5, 1-17, 2006.

[3] Fox J., Dunn H., O'Shea S. Low rates of p24 antigen detection using a fourth-generation point of care HIV test. *Sex. Transm. Infect*. 87**,** 178-179, 2011.

[4] Faraoni S., Rocchetti A., Gotta F., et al. Evaluation of a rapid antigen and antibody combination test in acute HIV infection. *J. Clin. Virol*. 57**,** 84-87, 2013.

[5] Cohen M.S., Gay C.L., Busch M.P., Hecht FM. The detection of acute HIV infection. *J. Infect. Dis*. 202, S270-S277, 2010.

[6] Alere, Determine™ HIV-1/2 Ag/Ab Combo Test package Insert, 30 September 2013.

[7] Masciotra S., Luo W., Youngpairoj A.S., et al. Performance of the Alere Determine HIV-1/2 Ag/Ab Combo Rapid Test with specimens from HIV-1 seroconverters from the US and HIV-2 infected individuals from Ivory Coast. *J. Clin. Virol*. 58, e54-e58, 2013.

[8] Laperche S., Leballais L., Ly T.D., et al. Failures in the detection of HIV p24 antigen with the Determine HIV-1/2 Ag/Ab Combo rapid test. *J. Infect. Dis.* 206, 1946-1947, 2012.

[9] Rosenberg N.E., Kamanga G., Phiri S., et al. Detection of acute HIV infection: a field evaluation of the determine® HIV-1/2 Ag/Ab combo test. *J. Infect. Dis.* 205, 528-534, 2012.

[10] Kilembe W., Keeling M., Karita E., et al. Failure of a novel, rapid antigen and antibody combination test to detect antigen-positive HIV infection in African adults with early HIV infection. *PLoS One* 7, e37154, 2012.