Early diagnosis of an acute HIV infection in a primary care setting: the opportunity for early treatment and prevention

Marinko Dobec[a], *Juerg Frei*[b], *Alois Flaviano*[a], *Franz Kaeppeli*[a]

[a] medica, medizinische Laboratorien Dr. F. Kaeppeli, Zurich, Switzerland
[b] Permanence Hauptbahnhof Practice, Zurich, Switzerland

Introduction

Despite the fact that today over 40 million individuals worldwide are living with HIV, fewer than 1,000 cases have been diagnosed in the first month of infection [1].

Due to clinical reasons (acute retroviral syndromes mimic many common febrile illnesses) and because confirmatory HIV antibody tests will typically remain negative during the diagnostic window beyond the onset of acute retroviral symptoms, acute HIV infections are still missed [2, 3].

Case report

In May, 2005, a 54-year-old man, who had recently returned from a vacation in Cuba, presented to us with high fever (39.8 °C), tonsillopharyngitis, fatigue and myalgia of one week's duration. No rash or lymphadenopathy were observed. At that point in time a lymphopenia (0.58×10^3 cells/µL), a thrombocytopenia (65×10^3 cells/µL) and elevated C-reactive protein (64/5) were encountered. Slightly elevated liver enzymes were noted (alanine aminotransferase 41.8; aspartate aminotransferase 56.7; alkaline phosphatase 174; gamma-GT 104 and total bilirubin 45.5 µmol/L).

In the control examination 3 days later, leucopenia (3.3×10^3 cells/uL), neutropenia (1.4×10^3 cells/uL), continuing thrombocytopenia (70×10^3 cells/µL) and an increase of lymphocyte count (1.05×10^3 cells/µL) were encountered. CD4 (467 cells/µL) and CD8 (332 cells/µL) count were found normal as was the CD4/CD8 ratio (1.41). After introduction of Moxifloxacin (Avalox; 1 × 400 mg/day) the patient become afebrile and his general condition improved, except for newly diagnosed aphthous ulcera on the left palatum molle.

Malaria, dengue, Streptococcus pyogenes group A, enteroviruses, Shigella, Salmonella, Epstein-Barr virus, cytomegalovirus, hepatitis B virus, hepatitis C virus and Treponema pallidum were excluded as causes of this clinical condition.

In the history at that time the patient denied any risk exposure known to be associated with HIV transmission.

Nevertheless, because of the lymphopenia and thrombocytopenia, an HIV screening test was suggested and the patient agreed. A third-generation HIV test gave a negative result and two fourth-generation HIV EIA Tests, which simultaneously detect antigen and antibodies, were reactive. A negative immunoblot test result was received from an external, designated confirmatory laboratory and a control testing in 3–6 months was suggested by them. In spite of this, we performed an HIV nucleic acid amplification test (NAT) on the first sample, which revealed a positive HIV-1 result of 4,150,000 copies/mL. Follow-up results are summarized in table 1.

At that point the patient confirmed an unprotected heterosexual contact on May 11 during his vacation in Cuba.

Discussion and conclusions

Many countries have recently placed significant emphasis on the identification of people with acute HIV infection [1, 4–6].

In our case we have shown that an early HIV infection can still be missed, in spite of clinical suspicion, by using immunoblot as the sole confirmatory method in patients with an early HIV infection in whom only the HIV antigen is detectable and antibodies have not yet been produced [5, 7, 8].

We can conclude that, in cases of leucopenia with thrombocytopenia and fever, an acute HIV infection has to be considered as the differential diagnosis and should be excluded.

For the diagnosis of an early HIV infection, fourth-generation EIA should replace the third-generation and NAT for HIV should be introduced into the confirmatory algorithm at the first sample stage in addition to the standard HIV fourth-generation EIA if the confirmatory immunoblot is negative.

In patients with reactive fourth-generation HIV EIA, with or without clinical illness, a negative immunoblot result should be followed by NAT.

This would optimise early HIV diagnosis without a significant cost increase, considering the benefits accruing in terms of opportunities for earlier treatment, source identification and introduction of preventive measures.

Correspondence:
Marinko Dobec, MD, PhD
medica
medizinische Laboratorien Dr. F. Kaeppeli
Wolfbachstrasse 17
CH-8024 Zurich
Switzerland
E-Mail: m.dobec@medica-labor.ch

References

1 Pilcher CD, Eron JJ, Galvin S, et al. Acute HIV revisited: new opportunities for treatment and prevention. J Clin Invest. 2004;113:937–45.
2 Sterling TR, Chaisson RE. General clinical manifestations of human immunodeficiency virus infection (including the acute retroviral syndrome and oral, cutanaeous, renal, ocular, and cardiac diseases). In: Mandel GL, Bennett JE, Dolin R, eds. Principles and practice of infectious diseases. 6th ed. Philadelphia: Churchill Livingstone, 2005: 1546–66.
3 Weintrob AC, Giner J, Menezes P, et al. Infrequent diagnosis of primary human immunodeficiency virus infection: missed opportunities in acute care settings. Arch Intern Med. 2003;163:2097–100.
4 McElborough D. Importance of using an HIV Ag/Ab combined assay in a UK population at high risk of acquiring HIV infection. Commun Dis Public Health 2004;7:312–4.
5 Pilcher CD, Fiscus SA, Nguyen TQ, et al. Detection of acute infections during HIV testing in North Carolina. N Engl J Med. 2005;352:1873–83.
6 Taylor MM, Hawkins K, Gonzalez A, et al. Use of the serologic testing algorithm for recent HIV seroconversion (STARHS) to identify recently acquired HIV infections in men with early syphilis in Los Angeles County. J Acquir Immune Defic Syndr. 2005;38:505–8.
7 Weber B, Thorstensson R, Tanprasert S, et al. Reduction of the diagnostic window in three cases of human immunodeficiency-1 subtype E primary infection with fourth-generation HIV screening assays. Vox Sang. 2003;85:73–9.
8 Schupbach J. SHCS and the laboratory diagnosis of HIV infection – from the development of the HIV Western blot to virus quantification and clinically relevant individual virus characterization. Ther Umsch. 2004;61:603–7.

Table 1

Comparison of HIV-EIA 4th generation, immunoblot and PCR in a serum initially negative by 3rd generation HIV EIA screening.

Collection Date	HIV 4th generation Antigen/Antibody test Combo AxSYM, Abbott*	HIV 4th generation Antigen/Antibody test VIDAS HIV Duo Quick, Biomerieux**	Immunoblot Inno-Lia HIV-Confirmation, Innogenetics	Cobas Amplicor HIV-1 Monitor Test Version 1.5, Roche Diagnostics
May 30, 2005	8.06	3.81	not done	4,150,000 copies / mL
June 3, 2005	5.25	4.89	negative	8,320,000 copies / mL
June 26, 2005	7.38	3.20	positive (p24, p31, gp41)	82,000 copies / mL

* cut off 1.0 ** cut off 0.25

Established in 1871

Formerly: Schweizerische Medizinische Wochenschrift

Swiss Medical Weekly

Official journal of the Swiss Society of Infectious diseases, the Swiss Society of Internal Medicine and the Swiss Respiratory Society

The many reasons why you should choose SMW to publish your research

What Swiss Medical Weekly has to offer:

- SMW's impact factor has been steadily rising. The 2005 impact factor is 1.226.
- Open access to the publication via the Internet, therefore wide audience and impact
- Rapid listing in Medline
- LinkOut-button from PubMed with link to the full text website http://www.smw.ch (direct link from each SMW record in PubMed)

- No-nonsense submission – you submit a single copy of your manuscript by e-mail attachment
- Peer review based on a broad spectrum of international academic referees
- Assistance of our professional statistician for every article with statistical analyses

- Fast peer review, by e-mail exchange with the referees
- Prompt decisions based on weekly conferences of the Editorial Board
- Prompt notification on the status of your manuscript by e-mail
- Professional English copy editing
- No page charges and attractive colour offprints at no extra cost

We evaluate manuscripts of broad clinical interest from all specialities, including experimental medicine and clinical investigation.

We look forward to receiving your paper!

Guidelines for authors:
http://www.smw.ch/set_authors.html

EMH FMH Schwabe
Editores Medicorum Helveticorum

All manuscripts should be sent in electronic form, to:

EMH Swiss Medical Publishers Ltd.
SMW Editorial Secretariat
Farnsburgerstrasse 8
CH-4132 Muttenz

Manuscripts:	submission@smw.ch
Letters to the editor:	letters@smw.ch
Editorial Board:	red@smw.ch
Internet:	http://www.smw.ch