An HIV Diagnostic Paradox in Late Pregnancy

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CASE DESCRIPTION

A 28-year-old female at 37 weeks gestation presented to the emergency department with painless vaginal bleeding, fever, and cramp-like lower abdominal pain. She had received most of her prenatal care outside of the United States monthly until 4 weeks prior to this presentation. Fetal monitoring revealed signs of fetal distress and arrested labor, and an uncomplicated cesarean delivery was performed. As part of maternal evaluation, a fourth-generation human immunodeficiency virus type 1 and 2 [HIV-1/2 antigen/antibody (Ag/Ab) screen; ADVIA Centaur HIV Ag/Ab Combo, Siemens] was performed and repeatedly returned a result as reactive. Reflex testing with the HIV-1/2 Geenius supplemental assay (Bio-Rad) was positive for HIV-1 (Fig. 1). Therefore, a confirmed reactive HIV-1 result was reported. The mother had no history of symptoms suggesting acute or chronic HIV infection and denied prior HIV diagnosis or antiretroviral treatment. Laboratory evaluation revealed no evidence of immunodeficiency, with normal CD4 and CD8 counts, lymphocyte percentage, and white blood cell count (Table 1). Maternal serological studies were negative for active hepatitis A, B, and C, as well as syphilis. However, a positive hepatitis B virus core and surface antibody, with negative core IgM and surface antigen, was consistent with past exposure (Table 1).

Following the reactive HIV-1 result, a peripartum dose of zidovudine was administered to the mother, and an infectious disease consultation was requested. The consulting infectious disease physician requested a baseline viral load to guide postpartum antiretroviral therapy. Unexpectedly, quantitative plasma HIV-1 RNA nucleic acid amplification test (NAAT; Alinity M, Abbott) with a limit of quantitation of 20 copies/mL, yielded an “not detected” result. A repeat HIV-1/2 Ab/Ag screening test remained reactive. Given the discordance between serologic and nucleic acid results, the infectious disease team deferred neonatal prophylaxis pending clarification and asked the clinical laboratory, “How reliable is the Geenius result in pregnancy?”

Upon review, the Geenius supplemental assay demonstrated strong reactivity to all 4 HIV-1 bands, including gp160, gp41, p31, and p24, with a clearly positive control band. All HIV-2 bands were absent (Fig. 1). While false positives on HIV-1/2 Ag/Ab screening tests are not uncommon during pregnancy (1, 2), such cases typically resolve at the differentiation step by the Geenius supplemental assay and are not accompanied by this degree of band reactivity. In this case, the intense, multiband Geenius profile argued strongly against a pregnancy-related false positive. To our knowledge, this was the first documented case at our institution of a reactive fourth-generation HIV-1/2 Ag/Ab screening test and reactive HIV-1 differentiation assay with an undetectable plasma HIV-1 RNA viral load.

After discussion, the clinical team considered the possibility of a rare phenotype in which individuals maintain serologic evidence of HIV infection yet suppress plasma viremia to low or undetectable viral loads for an extended period without receiving antiretroviral therapy (ART), known as an HIV elite controller. A subsequent plasma HIV-1 RNA NAAT (COBAS Ampliprep/COBAS Taqman, Roche Diagnostics) performed at another laboratory was reported as “detected, <20 copies/mL,” indicating the presence of viral RNA but at a level below the assay’s limit of quantitation and consistent with very low-level viremia,

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supporting the elite controller phenotype. An HIV-1 proviral DNA test was also reported positive by a reference laboratory using a laboratory-developed test, with whole blood as the specimen to detect integrated HIV DNA (provirus) within host cells, a method most commonly applied in patients with suppressed viremia on ART or in infants (1, 2). For the neonate, HIV-1 RNA NAAT (Hologic Aptima, limit of quantitation 30 copies/mL, reported qualitatively) was negative. Although the infant was considered at relatively low risk given maternal viral suppression, the absence of maternal ART precluded classification as low-risk and the infant still received triple ART prophylaxis (1).

QUESTIONS TO CONSIDER	
1.	What is an HIV elite controller, and how do they differ from other individuals living with HIV?
2.	What are the limitations of HIV-1 RNA PCR in the diagnosis of elite controllers?
3.	Why might pregnancy increase the risk of false-positive results on HIV-1/2 Ag/Ab screening tests, and how can this complicate diagnosis?
4.	What is the diagnostic utility of HIV-1 proviral DNA testing, and when should it be considered?
5.	How does your center test HIV-exposed neonates, particularly those born to mothers with undetectable viral load (including elite controllers)? Which type of NAAT (RNA, DNA, or both) do you use, and at what time points are tests obtained?

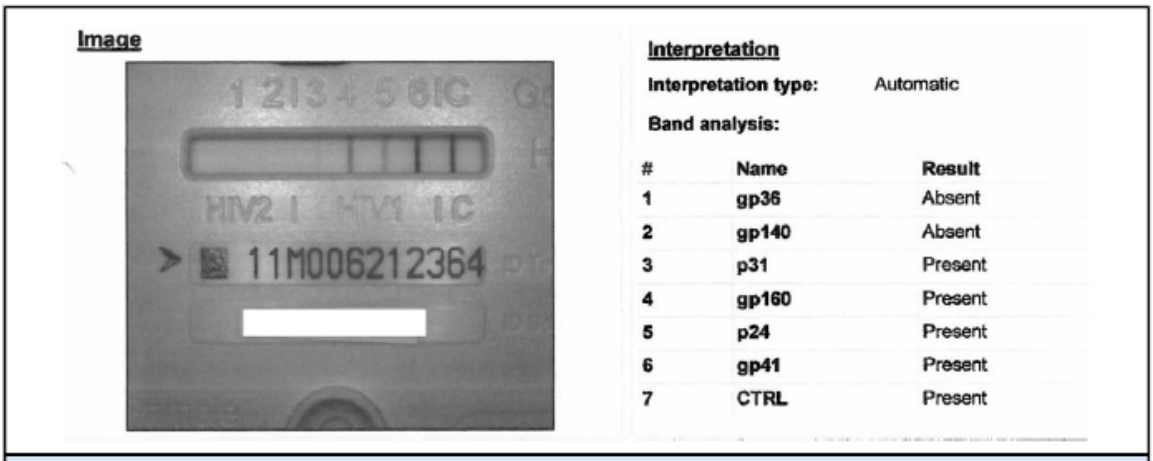

Fig. 1. Patient's Geenius supplemental assay result and interpretation. Bands 1 and 2 correspond to HIV-2, bands 3 to 6 represent HIV-1, and band C serves as the internal control.

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Table 1. Selected laboratory results.

Test	Result	Reference range
CD4 count	701 cells/μL	431–1623 cells/μL
CD8 count	747 cells/μL	170–1078 cells/μL
CD4/CD8 ratio	0.94	0.86–2.05
CD4%	30.5%	25.0–56.0%
CD8%	32.5%	14.2–35.8%
Lymphocyte %	44.2%	20.0–50.0%
Lymphs	2.31 × 10^3/μL	1.18–3.74 × 10^3/μL
WBC count	5.2 × 10^3/μL	4.5–11.0 × 10^3/μL
Syphilis screen (reverse algorithm)	Nonreactive	Nonreactive
Hepatitis B core Ab	Positive	Negative
Hepatitis B surface Ab	Positive	Positive indicates immunity
Hepatitis B surface Ag	Negative	Negative
Hepatitis B core IgM	Negative	Negative
HCV RNA (quantitative)	Not detected	Not detected
Hepatitis A IgG/IgM	Nonreactive	Nonreactive
Chlamydia/gonorrhea DNA	Not detected	Not detected
TSH	1.70 μIU/mL	0.45–5.33 μIU/mL
Urine drug screen	Negative	Negative

Abbreviation: WBC, whole blood cell.

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2. Joshi RP, Gomez CA, Steiner D, Aziz N, Pinsky BA. The brief case: confirmed positive HIV-1 serologic screening but undetectable RNA virus load in a pregnant woman. J Clin Microbiol 2017;55: 3316–20.

Final Publication and Comments

The final published version with discussion and comments from the experts will appear in the April 2026 issue of *Clinical Chemistry*. To view the case and comments online, go to https://academic.oup.com/clinchem/issue/72/4 and follow the link to the Clinical Case Study and Commentaries.

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