

Acute HIV infection comes with a missed opportunity

If you miss acute HIV infection, you miss a chance to prevent transmission of HIV as well. Patients are highly infectious, so a quick diagnosis is essential.

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CASE

The patient was a 31-year-old single male who worked in a hospital and had previously been in good health. He presented to primary care concerned that he might have “strep throat” or some other infection. He had been ill for 1 week with fevers as high as 103.5°F. In addition, he reported headache, congestion, mild cough, myalgias, and malaise. He also admitted to swollen, painful glands and night sweats. The patient reported some nausea but denied any other GI symptoms and denied any urinary symptoms.

A purified protein derivative skin test had been negative 5 weeks earlier. Three months earlier, the patient had traveled to Mexico but had since been well. He was taking ibuprofen, acetaminophen, and a course of azithromycin (Zithromax) that a coworker had given him, but his symptoms were not improving.

On examination, the patient’s temperature was 98.3°F. He appeared slightly anxious but was in no acute distress. Palpation of the neck revealed moderate anterior cervical lymphadenopathy, and examination of the oropharynx revealed swollen red tonsils without exudates. No rash was appreciated. Lung sounds were clear, and there were no signs of meningeal irritation.

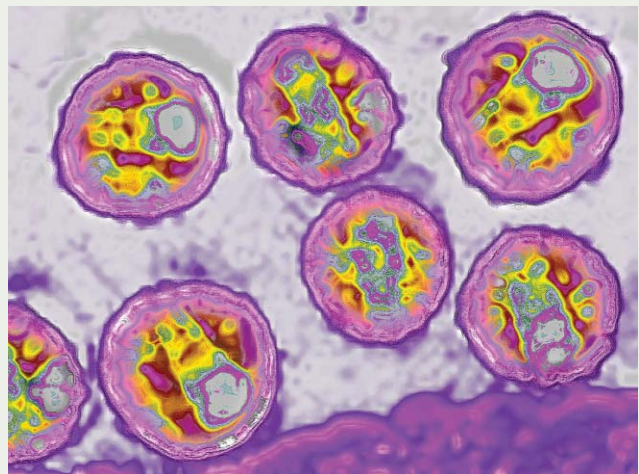
Initial laboratory studies included a routine throat culture, CBC with differential, Epstein-Barr virus (EBV) panel, and HIV antibody test (because the patient’s history was consistent with established HIV infection). Results were reported in 48 hours. The throat culture and HIV tests were negative. The EBV panel was consistent with past mononucleosis infection, and the WBC and platelet counts were slightly below normal levels (WBC count, $3.1 \times 10^3/\mu\text{L}$; platelet count, $85 \times 10^3/\mu\text{L}$). The patient was informed of his test results and given a presumptive diagnosis of viral infection. At that time, he reported that he was feeling better. However, he returned to the office 5 days later.

The sore throat had resolved, but the patient was experiencing persistent headaches and night sweats, ongoing fevers up to 103°F, and extreme fatigue. He now denied cough but had developed some mild diarrhea. At this sec-

ond visit, a more detailed history revealed that the patient was a sexually active gay male who usually practiced safe sex but had recently had an unprotected sexual encounter. Pertinent physical examination findings included a temperature of 99.4°F and diminished tonsillar swelling. Otherwise the examination findings were unchanged from the initial visit.

Although the initial HIV test was negative, the recent unprotected sexual encounter raised the possibility of acute HIV syndrome. Accordingly, a test for HIV p24 antigen, a blood test that detects HIV viral particles, was ordered. Additionally, a repeat CBC, a comprehensive metabolic panel, and urine and blood cultures were performed. Results for this second set of tests showed a diminished WBC count of $3.3 \times 10^3/\mu\text{L}$, an elevated AST level (198 U/L), and an elevated ALT level (322 U/L). Blood and urine cultures were negative. The HIV p24 antigen test was positive, however, indicating acute HIV infection.

The diagnosis was confirmed with a second antibody test and a polymerase chain reaction (PCR) HIV RNA viral load. The patient had an extremely high HIV RNA level of greater than 750,000 copies/mL, and he did seroconvert 2 weeks after his initial negative antibody test. By this time, his



Human immunodeficiency virus, the virus that causes AIDS

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CASE REPORT | Acute HIV infection

TABLE 1. Frequency of symptoms and findings associated with acute HIV-1 infection

Symptom or finding	Percentage of patients
Fever	>80-90
Fatigue	>70-90
Rash	>40-80
Headache	32-70
Lymphadenopathy	40-70
Pharyngitis	50-70
Myalgia or arthralgias	50-70
Nausea, vomiting, or diarrhea	30-60
Night sweats	50
Aseptic meningitis	24
Oral ulcers	10-20
Genital ulcers	5-15
Thrombocytopenia	45
Leukopenia	40
Elevated hepatic enzyme levels	21

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symptoms were improving. The WBC count, platelet count, and liver function normalized over the next few weeks.

Approximately 10 days after this patient's diagnosis, his sexual partner presented for testing. This second patient had tested negative for HIV antibodies 1 month earlier, before the first patient developed viral symptoms. Unfortunately, repeat testing now revealed positive HIV antibodies and an HIV RNA level greater than 750,000 copies/mL, indicating that the second patient had also recently been infected with HIV. The possibility is strong that one of these men transmitted HIV to the other during acute HIV syndrome. This is not surprising: high levels of circulating virus render the patient with acute HIV syndrome highly infectious to others.

DISCUSSION

Each year in the United States, approximately 40,000 people become infected with HIV,^{1,2} and within 4 weeks of contracting the virus, as many as 90% will experience an acute illness known as primary or acute HIV syndrome.² During this acute phase, before HIV antibodies develop, the patient suffers a burst of viremia associated with a peak in HIV RNA levels. Levels remain high and an HIV antibody test will be negative for approximately 3 weeks, but as the body mounts an antibody response, HIV RNA levels subsequently decline and reach a relative steady state within 3 to 6 months.³ People with acute HIV infection who seek medical care during this so-called *window period* pose a diagnostic challenge. Indeed, clinicians miss the diagnosis of acute HIV syndrome the majority of the time.^{4,5} As this case demonstrates, failure to recognize acute HIV syndrome represents a significant missed opportunity—not only to manage the patient appropriately but also to prevent the patient from transmitting HIV to others.

Acute HIV syndrome manifests in variable ways and is difficult to distinguish from common infections such as mononucleosis, influenza, and streptococcal pharyngitis.⁶ Signs and symptoms most strongly associated with acute HIV infection are listed in Table 1.^{5,7} A viral syndrome with a rash and/or oral ulcers is particularly suspicious. Leukopenia, thrombocytopenia, and elevated hepatic enzymes may also be present. The acute illness usually subsides within 14 days but may persist for several weeks.⁵ Patients recover without intervention and may not seek medical attention.

Those who do seek treatment will usually present to primary and emergency care providers. In fact, research at one urban urgent care center revealed that 1 in 100 patients who presented with a viral syndrome and at least one HIV risk factor actually had acute HIV infection.⁸ Because of the variable manifestations, misdiagnosis is common. It is likely also true that patients are often told incorrectly that they do not have HIV infection based on a negative HIV antibody test result. Clinicians must maintain a high index of clinical suspicion, be familiar with signs and symptoms, and know which tests to order to make the diagnosis.

If the presentation is compatible with acute HIV infection, the provider should obtain a detailed history to determine if the patient could have been exposed to the virus within the

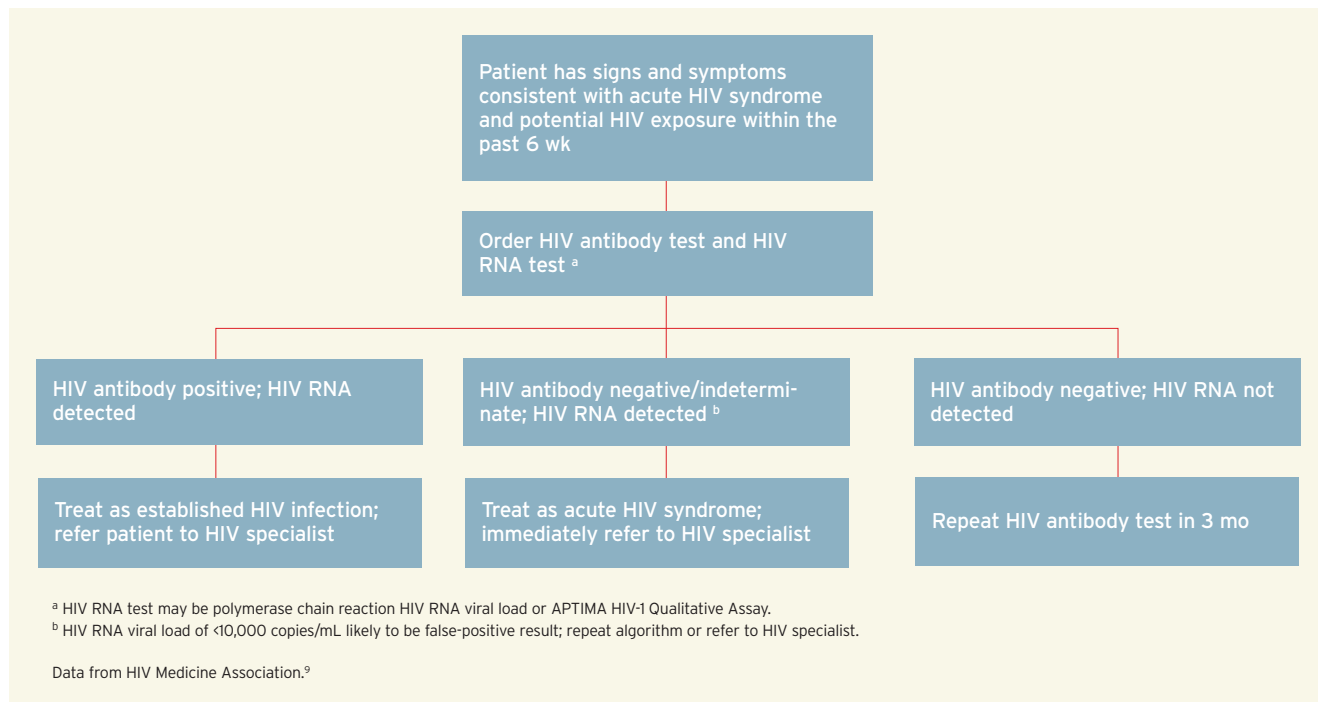
TEACHING POINTS

- Within 4 weeks of contracting HIV, up to 90% of people will experience acute HIV syndrome. The patient suffers a burst of viremia associated with a peak in HIV RNA levels. Levels remain high and an HIV antibody test will be negative for approximately 3 weeks.
- People with acute HIV infection who seek medical care during this *window period* pose a diagnostic challenge, and clinicians typically miss the diagnosis of acute HIV syndrome.
- Failure to recognize acute HIV syndrome represents a significant missed opportunity—not only to appropriately manage the patient but also to prevent the infection of others.
- The rate of HIV transmission is highest within the first 2.5 months of contracting HIV, and a disproportionate number of new infections can be attributed to persons with acute HIV syndrome. Most HIV-infected persons will substantially reduce sexual behaviors that transmit the disease once they have received a diagnosis.

COMPETENCIES

- Medical knowledge
- Interpersonal & communication skills
- Patient care
- Professionalism
- Practice-based learning and improvement
- Systems-based practice

ALGORITHM. Testing for acute HIV syndrome



past 6 weeks. If risk factors are present, appropriate laboratory tests should be ordered. However, given that a history of risk may not be elicited because the patient or provider does not recognize a potential exposure as “high risk,” clinicians should also consider testing in the absence of a definite history of exposure.² Providers should bear in mind that people aged 13 to 24 years account for at least half of new cases of HIV infection.² In order to make the diagnosis of acute HIV syndrome, an HIV antibody test and an HIV RNA test such as the quantitative PCR HIV RNA test should be obtained.^{2,9}

Current guidelines for testing have incorporated the option of using the APTIMA HIV-1 RNA Qualitative Assay as an alternative to quantitative HIV RNA testing. This assay received FDA clearance for clinical use in October 2006 and is the first test approved to detect HIV RNA for the purpose of diagnosing acute HIV infection. A reactive result on this assay, in conjunction with a negative HIV antibody test, suggests the diagnosis.¹⁰ Currently, the APTIMA assay is not available in all areas.

When the PCR HIV RNA viral load test is used to identify acute HIV, a high titer viral load obtained in conjunction with a negative HIV antibody test indicates acute infection^{2,9} (see the algorithm). HIV RNA levels are generally markedly elevated during the acute infection period, so a low HIV RNA titer (less than 10,000 copies/mL) obtained during a suspected case of acute HIV syndrome suggests a false-positive result.² Although the HIV p24 antigen test can detect the presence of primary HIV, it is less sensitive than the HIV RNA tests. Regardless of methodology, all diagnoses of

acute HIV syndrome should be followed by HIV antibody testing at a later time to document seroconversion.^{2,10}

As this case demonstrates, a delayed or missed diagnosis of acute HIV infection can have serious consequences in part because the patient can so easily infect others. The rate of HIV transmission is highest within the first 2.5 months of contracting HIV,¹¹ and a disproportionate number of new infections can be attributed to persons with acute HIV syndrome.¹² Most HIV-infected persons will substantially reduce sexual behaviors that transmit the disease once they have received a diagnosis.¹³ Identifying a patient during the early period thus provides a crucial opportunity to prevent the spread of the virus.

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TABLE 2. Current guidelines for HIV testing

HIV screening is recommended for patients aged 13-64 years in all health-care settings after the patient is notified that testing will be performed unless the patient declines (opt-out screening)
Persons at high risk for HIV infection should be screened at least annually
Separate written consent for HIV testing should not be required; general consent for medical care should be considered sufficient to encompass consent for HIV testing
Prevention counseling should not be required with HIV diagnostic testing or as part of HIV screening programs in health-care settings
Data from Centers for Disease Control and Prevention. ¹⁴

Comment Patients who have acute HIV syndrome should be immediately referred to an experienced HIV specialist. These providers can perform confirmatory testing at the appropriate time and can effectively counsel the patient about the most appropriate treatment options. Nevertheless, HIV disease should still be regarded a major health concern by primary and emergency care providers. Despite significant advances in treatment of these diseases in recent years, the CDC continues to report that HIV infection and AIDS are leading causes of illness and death in the United States.¹⁴

Recently revised CDC recommendations for HIV testing advise health care providers to incorporate routine HIV screening as "... a normal part of medical practice"¹⁴ (see Table 2, page 37). The guidelines address a number of important objectives, which include fostering earlier detection of HIV infection and identifying people with unrecognized infection and linking them to clinical and preventive services. Clinicians must remain vigilant, through routine screening and accurate diagnosis, in order to meet these objectives, provide appropriate care to infected patients, and reduce HIV transmission. [JAAPA](#)

Bettie Coplan is an instructor in the PA program at Midwestern University, Glendale, Arizona. She has indicated no relationships to disclose relating to the content of this article.

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