Diagnostic dilemma for human immunodeficiency virus in a fatal case of acute myeloid leukemia

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Abstract

National Human Immunodeficiency Virus (HIV) testing programs utilize antibody-based tests for confirming HIV diagnosis which has a diagnostic window period of 23–90 days. In Fiebig acute HIV Stage I–II, an individual has antibody-negative but RNA-positive test results. Here, we present a case of a 54-year-old complete remission acute myeloid leukemia patient, who was recently reported HIV negative by antibody-based tests used in National HIV testing programs. However, when his sample was further analyzed by more sophisticated HIV tests, there was the presence of early anti-HIV-1 gp160 antibodies in western blot and HIV-1 RNA in nucleic acid testing. Within 8 days of his HIV-negative result, his clinical condition deteriorated. Later, the patient expired despite the best of clinical efforts at the apex tertiary care center of India. The technical difficulty in confirming HIV diagnosis by antibody-based tests used in National HIV testing programs and thereby noninitiation of antiretrovirals in a case where cell-mediated immunity is already compromised by non-HIV reason could have serious consequences. There is a need to update the existing HIV testing strategies in National HIV testing programs to include the needs of special cases.

Key words: Acute myeloid leukemia, AIDS, human immunodeficiency virus, human immunodeficiency virus diagnosis, human immunodeficiency virus dilemma, human immunodeficiency virus testing

Introduction

The diagnostic window period for detection of human immunodeficiency virus (HIV) after exposure ranges from 23 to 90 days by antibody-based rapid tests and self-tests.[1] People with leukemia undergo repeated blood transfusions and, therefore, have a high chance of blood transfusion-associated HIV transmission during the diagnostic window period. Due to the high demand of blood in leukemia patients, socioeconomic underprivileged individuals could be seeked out for blood which is again at high risk for transmitting HIV, particularly during the diagnostic window period.[2,3] Acute HIV stage among patients with non-HIV immunocompromised status such as acute myeloid leukemia (AML) could be challenging.

Case Report

A peripheral blood sample was received from a 54-year-old male from the medical oncology unit at the National HIV/AIDS testing laboratory for HIV screening. The patient had AML ETO + with 3 + 7 regimen 41 days back with complete remission and minimal residual disease (MRD) negative. ETO (MTG8, RUNX1T1) gene located on chromosome 8 is commonly involved in chromosomal translocation with the AML1 (RUNX1) gene on chromosome 21 in nearly 50% of human AMLs. 7 + 3 regimen consists of getting cytarabine continuously for 7 days, along with short infusions of an anthracycline on each of the first 3 days. The MRD-negative result means that no disease was detected after treatment. The sample was found nonreactive for anti-HIV glycoproteins (gp) 120 and gp41 antibodies in screening test through Combaids RS Advantage kit (the World Health Organization [WHO] 2015 and National AIDS Control Organization, India, [NACO] 2016 approved kits)[4,5] and, therefore, reported as HIV negative. The current WHO as well as NACO testing strategy for HIV diagnosis allows reporting of HIV-negative results at a single antibody-based screening test. HIV testing strategy IIB of National HIV testing guideline is used for diagnosis in symptomatic patients.[6] ELISA/rapid tests, which detect HIV-specific antibodies in blood samples, are used in all HIV testing strategies I, II, and III.[6,7] After 1 week of

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Quick Response Code:

Website: https://journals.lww.com/ijst

DOI: 10.4103/ijstd.ijstd_111_23

How to cite this article: Maurya SP, Sharma A, Jahan F, Gautam H, Das BK. Diagnostic dilemma for human immunodeficiency virus in a fatal case of acute myeloid leukemia. Indian J Sex Transm Dis 2024;45:139-41.

Submitted: 11-Dec-2023 **Revised:** 13-Feb-2024
Accepted: 21-Feb-2024 **Published:** 13-Dec-2024

the first sample, the second blood sample was received at our laboratory and found nonreactive for HIV at a single screening assay as earlier. However, this time, we performed two other HIV immunoassays (Tredro and VoXpress; NACO approved kits) since we had recently reported this patient as HIV negative, but the oncologist had received a report of HIV plasma viral load of 246,054 copies/ml. The second sample was found nonreactive for HIV-specific antibodies in all three immunoassays. We also performed HIV western blot with second sample and here, we found one band for anti-HIV gp160 antibodies. Since HIV confirmation through Western blot requires at least two HIV-specific bands, the sample was reported as HIV indeterminate/inconclusive. The current NACO as well as the WHO guidelines allow screening after 14 days if HIV test results are inconclusive/indeterminate. Due to lack of a confirmatory HIV report, antiretroviral therapy for HIV was not initiated.

After 8 days of the second sample, the patient reported Grade-4 neutropenia, Grade-4 thrombocytopenia, Grade-3 anemia, and Grade-3 febrile neutropenia. Intravenous antibiotics: cefoperazone/sulbactam and amikacin with antifungal voriconazole were started. In view of cytopenias, granulocyte colony-stimulating factor was started and single donor platelet and packed red blood cells were given. High-resolution computed tomography (HRCT) thorax was done which was Suggestive (s/o) centrilobular nodules in the right lung. Fever was persistent so Gram-positive coverage – teicoplanin was added, amikacin changed to meropenem, and voriconazole to amphotericin B. Despite the upgrade of antibiotics/antifungal, fever was persistent and the patient clinically deteriorated requiring oxygen support. Antibiotics were upscaled to piperacillin/tazobactam and polymyxin B. Absolute neutrophil count did not recover so granulocytes were given. The patient developed hypoxia and hypercarbia so he was put on noninvasive ventilation. A repeat HRCT thorax was done which depicted pulmonary hemorrhage. Intravenous dexamethasone was started along with single-donor platelet support. His sensorium deteriorated so he was electively intubated and put on mechanical ventilation. Noncontrast computed tomography head was done to rule out (r/o) intracranial bleeding, which was s/o subarachnoid hemorrhage. The patient deteriorated further, shock worsened, and the ventilatory requirement went high. He developed cardiac arrest. Cardiopulmonary resuscitation was given with advanced cardiovascular life support protocol but could not be revived and was declared expired.

Discussion

The technical difficulty in confirming HIV diagnosis and thereby noninitiation of antiretrovirals in cases where cell-mediated immunity is already compromised by AML or other non-HIV reasons could have serious consequences. Microbial infections such as HIV are not rare among cancer patients.[8,9] HIV depletes CD4+ cells (helper T-cells and monocytes/macrophages) which in turn affects the frequency and function of other immune cells. All blood donors are treated as per existing national guidelines at our center. Screening for HIV at blood banks involves just one test of high sensitivity (4th generation p24 antigen plus HIV specific antibody test), which usually detects HIV after 18 days of exposure.[1,6] HIV-specific antibodies-based tests (anti-gp120/gp41) usually detect HIV after 23 days of exposure.[1] Antibodies against HIV gp160 often allow for early HIV diagnosis and it was the only detectable HIV-specific antibody in our Western blot. Gp160 is a precursor protein which is folded and processed into gp120 (HIV fusion protein) and gp41 (HIV transmembrane protein). NAT usually detects HIV after 10 days of exposure, however, not currently used for adult HIV diagnosis in NACO HIV testing strategies.[1,6,7] NAT could help in the confirmation of HIV infection when the results of antibody-based HIV diagnostic tests are inconclusive. In Fiebig acute HIV Stage I–II, an individual has antibody-negative but RNA-positive test results. There is a need to update existing strategies in National HIV testing programs to include the needs of special cases. About 0.6/10,000 US/Canadian populations are exposed to HIV through blood during the window period. In India, there is no publicly available scientific data on individuals exposed to HIV through blood during the window period. However, as per media reports, NACO in an RTI has said that around 1342 people across India contracted HIV infection due to blood transfusion in 2018–2019.[10]

Acknowledgment

We are thankful to the Department of Health Research, Ministry of Health and Family Welfare, Government of India, for providing fellowship in HIV/AIDS to Dr. Shesh Prakash Maurya under the DHR-HRD scheme.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

The authors are grateful to the National AIDS Control Organisation, India, for technical support (Mr. Ashutosh Sharma) and the Department of Health Research (DHR) for fellowship on HIV/AIDS research (Dr. Shesh Prakash Maurya).

Conflicts of interest

There are no conflicts of interest.

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