JIDC | THE JOURNAL OF INFECTION IN DEVELOPING COUNTRIES

Case Report

Uremic syndrome with newly diagnosed HIV infection: reflections on a particular case

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Abstract

Introduction: Diagnosis with Western blot test (WB) may not provide clear results for certain patients, including those who are not infected with human immunodeficiency virus (HIV) but produce non-specific reactions, individuals in the HIV window period (WP), those with acute HIV infection, and advanced acquired immunodeficiency syndrome (AIDS) patients. HIV-positive individuals face an elevated risk of developing kidney disease. HIV peritoneal dialysis patients may be more susceptible to catheter-related infections. This study reports a case of HIV detected during early development of a nephrotic syndrome into uremic syndrome.

Case presentation: A 46-year-old male individual diagnosed with stage 5 chronic kidney disease was admitted to the hospital in preparation for his first renal replacement therapy. During routine check-ups, the patient was identified as having a reactive response to the HIV antigen/antibody test. The rapid detection results exhibited a weak reaction across all manufacturers, while the enzyme-linked immunosorbent assay (ELISA) test (Bio-Rad, Hercules, USA) showed a reactive response. Nonetheless, the third and fourth generation tests did not yield a response, suggesting that the patient's internal concentration of HIV antigen or antibody was relatively low at the time. However, the confirmation test did not provide conclusive results, leading the patient to decline further renal replacement therapy. Two months later, the patient's HIV antigen/antibody levels were measured as 95.23 in the outpatient department of our hospital.

Conclusions: This case underscores the importance of actively exploring various detection strategies to enhance the efficiency of detecting acute phase HIV infection during the testing process.

Key words: uremic syndrome; HIV; hemodialysis; peritoneal dialysis.

J Infect Dev Ctries 2024; 18(9):1453-1457. doi:10.3855/jidc.18860

(Received 09 July 2023 – Accepted 26 December 2023)

Introduction

According to the World Health Organization (WHO), as of 2022, over 37 million people worldwide are living with human immunodeficiency type-1 (HIV-1) infection, representing a significant global health challenge [1]. Currently, the Western blot test (WB) is the primary method for diagnosing HIV infection in China; however, it has limitations. For instance, WB may not provide clear results for certain patients, such as those who are not infected with HIV but produce non-specific reactions, individuals in the HIV window period (WP), those with acute HIV infection, and advanced acquired immunodeficiency syndrome (AIDS) patients. This leads to a certain number of patients with indeterminate HIV antibodies.

The identification and diagnosis of acute HIV infection (AHI) play a crucial role in effectively combating the ongoing HIV epidemic. AHI refers to the initial phase of HIV infection during which individuals exhibit active viral replication; however, the presence of detectable antibodies to the virus is not yet apparent [2]. The transmission rate of HIV is particularly elevated during the early stage of infection [3]. The timely identification of post-transmission infection is of utmost importance, as it not only provides crucial information to the affected individual but also serves as a potential tool to limit the further dissemination of the virus [4]. Notably, advancements in HIV detection technology and the enhancement of reagent sensitivity have contributed to a reduction in the diagnostic WP. Currently, the WP for HIV antibody detection is approximately 3 weeks, while for antigen detection and nucleic acid detection, it is around 2 weeks and 1 week, respectively.

HIV-positive individuals face an elevated risk of developing kidney disease. However, the current guidelines for the prevention and treatment of kidney disease in this specific patient population primarily rely

on studies conducted on the general population. Uremic syndrome (also written as uraemic syndrome), represents an end-stage renal disease necessitating long-term maintenance through hemodialysis or peritoneal dialysis. The syndrome manifests through the accumulation of small-molecule uremic solutes and uremic toxins in the plasma, multifaceted organ dysfunction, and dysbiosis of the gut microbiota [5]. Notably, HIV peritoneal dialysis patients may be more susceptible to catheter-related infections. This study reports a case of HIV detected during early development of a nephrotic syndrome into uremic syndrome.

Case presentation

The case involves a male patient, aged 46 years, presenting with a notable history of hepatitis B virus (HBV) spanning several years. The patient initially sought medical attention at a local clinic over a year ago due to dizziness and was subsequently diagnosed with hypertension. Despite receiving oral Chinese medicine treatment, disease management exhibited suboptimal efficacy. Subsequently, the patient required hospitalization at our institution on four separate occasions for nephrotic syndrome, from April 2020 to December 2022. Over the course of these admissions, the patient's condition progressed from an early stage of nephrotic syndrome to uremic syndrome, representing an end-stage renal disease.

In the final week of November 2022, the patient experienced a loss of appetite, nausea, and vomiting without any apparent cause. The vomit primarily consisted of stomach contents. This abdominal discomfort and distension persisted for approximately one week.

On 4 December 2022, the patient was admitted to our hospital's nephrology department due to multiple comorbidities, including stage 5 chronic kidney disease, stage 5 anemia of chronic kidney disease, an extremely hypertensive crisis, polycystic kidney disease, polycystic liver disease, and hepatitis B antigen carrier status. The patient was admitted for a routine evaluation

Table 1. Routine clinical laboratory indicators.

Test date	Indicator	Result	Reference values
4 December 2022			
	White blood cell count	3.03↓	3.5–9.5*10^9/L
	Neutrophil absolute value	2.42	1.8–6.3*10^9/L
	Lymphocyte absolute value	0.39↓	1.1–3.2*10^9/L
	Hemoglobin	142	130–175 g/L
	Blood platelet count	88↓	125–350*10^9/L
	Creatinine	990↑	35–115 μmol/L
	Uric acid	577 ↑	208–428 μmol/L
	Endogenous creatinine clearance rate	4.47↓	80–120 ml/min
	Blood glucose	11.76↑	3.89–6.11 mmol/L
	Triglyceride	3.6↑	0.56–1.7mmol/L
	Lactic dehydrogenase	253↑	120–250 U/L
	Microalbumin	> 0.15g/L	0–20 mg/L
	Hepatitis B surface antigen	74.77 (positive)↑	(negative): < 0.05; (positive): ≥ 0.05
	Hepatitis B surface Antibody	1 (negative)	(negative): < 10.00; (positive): ≥ 10.00
	Hepatitis B virus e antigen	> 65(positive) ↑	(negative): < 0.70; (positive): ≥ 0.70
	Hepatitis B e antibody	0.4 (negative)	(negative): < 2.00; (positive): ≥ 2.00
	Hepatitis B core antibody	9.11 (positive)↑	(negative): < 5.30; (positive): ≥ 5.30
	Syphilis antibody (Luminescence) method)	0.14 (negative)	(negative): < 1.00; (positive): ≥ 1.00
	Hepatitis C antibody (Luminescence) method)	0.08 (negative)	(negative): < 1.00; (positive): ≥ 1.00
	Nucleic acid testing of SARS-CoV-2	Negative	Negative
5 December 2022			
	HIV antigen/antibody	To be decided	(negative): < 1.00; (positive): ≥ 1.00
7 December 2022			
	HIV Western blot analysis (CDC)	p24	Negative
	HIV highly sensitive nucleic acid testing	5.74E+04	Negative
11 December 2022			
	Absolute lymphocyte count	1067↓	1530–3700/μL
	Helper T cells count CD4+	227↓	404–1612/μL
	Inhibit T cell count CD8+	549	220–1129/μL
	CD4/CD8 ratio	0.41↓	0.71–2.78
	Nucleic acid testing of SARS-CoV-2	Positive	
	ORF1ab	33.6	
	N	31.83	
17 December 2022			
	HIV Western blot analysis (CDC)	gp160 p24	
08 February 2023			
	HIV antigen/antibody	95.23	(negative): < 1.00; (positive) ≥ 1.00

CDC: Centers for Disease Control and Prevention; HIV: human immunodeficiency virus; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2.

of nephrotic syndrome, and the test results are summarized in Table 1. The white blood cell count and lymphocytes were slightly below normal levels, while hemoglobin was within the normal range. Additionally, the blood platelet count was reduced. Serum creatinine and uric acid levels were elevated at 990 μmol/L and 577 μmol/L, respectively. The patient's endogenous creatinine clearance rate was only 4.47 mL/min, indicating significant kidney dysfunction. Furthermore, the patient presented with hypertriglyceridemia and hyperglycemia. The urine test result showed microalbumin levels exceeding 0.15 g/L, suggestive of early kidney damage. Hepatitis B surface antigen, hepatitis B virus e antigen, hepatitis B core antibody, and HBV quantification test results were positive, indicating active hepatitis B infection.

On 5 December 2022, the HIV antigen/antibody test results were inconclusive (reactive, but weak) using the biological gold label reagent (Abio, Shanghai, China). The individual had three previous hospitalization HIV tests that were negative. There was no history of sick contacts, recent travel, or high-risk sexual behavior. To confirm the initial findings, we used two different reagents. The first reagent, human immunodeficiency virus antigen antibody diagnostic (enzyme-linked immunosorbent assay, ELISA) kit (Kehua, Shanghai, China), did not react and had a S/CO ratio lower than 1. The second reagent, human immunodeficiency virus antigen and antibody combined assay kit (Abbott, Hangzhou, China), reacted weakly. The third reagent, ELISA kit (Bio-Rad, Hercules, USA) was reactive. As per standard protocol, the sample was sent to a superior laboratory for confirmation. Additional reagents from different manufacturers were used at the confirmation laboratory. The results were as follows. 1) When different batch numbers of the Kehua HIV antigen antibody diagnostic kit were used, the results were consistent with the preliminary screening results, with a S/CO ratio lower than 1. 2) The fourth generation antibody ELISA kit (Wantai, Beijing, China) detection reagent did not react. 3) There was a there was a reactive (weak) result with the Livzon (Zhuhai, China) biological gold label reagent. 4) There was a reactive (weak) luminescence value using chemiluminescence antigen/antibody detection with reagent from Abbott (Hangzhou, China). Based on these findings, we concluded that the individual did not have HIV.

On 7 December 2022, the local Centers for Disease Control and Prevention (CDC) conducted laboratory tests, revealing that WB results displayed P24 bands. The WB results were inconclusive. On the same day, highly sensitive nucleic acid testing for HIV was conducted on plasma samples collected in the clinical laboratory, resulting in the detection of HIV-1 highly sensitive copies at a concentration of 57,400 copies/mL.

On 11 December 2022, the T cell count revealed a CD4+ count of 227/μL and a CD4/CD8 ratio of 0.41. Additionally, nucleic acid testing for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) yielded a positive result. Based on these clinical findings, the patient was diagnosed with HIV infection. The patient was informed about the recommended course of action, which included receiving antiviral therapy and renal replacement therapy. However, the patient declined the proposed treatment.

Subsequently, on 17 December 2022, the CDC verified through laboratory tests that the WB results indicated the presence of P24 and gp160 bands. Furthermore, on 8 February 2023, the HIV antigen/antibody results for the patient were recorded as 95.23 in the outpatient department of our hospital. Upon the patient's third admission, it was determined that he had uremia, an advanced stage of kidney disease, and immediate kidney replacement therapy was recommended. The patient declined and requested discharge. In December 2022, the patient was readmitted for the fourth time to undergo kidney replacement therapy. During routine screenings, a positive response to the HIV antigen/antibody test was observed; however, the confirmatory test results were inconclusive. Despite this, the patient refused further treatment. In May 2023, our laboratory conducted an inquiry at the CDC in an attempt to retrieve the pertinent information associated with the patient under investigation. Regrettably, our efforts to establish contact with the patient were unsuccessful.

Discussion

This case involves a uremic patient who initially refused peritoneal dialysis during his third hospitalization. However, upon his fourth admission, the patient consented to receive the treatment. Notably, after a routine hospital examination revealed a positive response to an HIV antigen/antibody test, the patient again refused peritoneal dialysis. HIV can exist in peritoneal dialysis materials, causing virus transmission; so, consumables need to be properly handled. The question remains whether routine pre-peritoneal dialysis surgery and peritoneal dialysis would have increased the risk of others contracting HIV if the patient had been admitted a few days earlier and had undergone HIV antigen/antibody testing, effectively bypassing the window period for HIV screening.

Chronic kidney disease (CKD) is a frequent complication of HIV infection [6]. But cases of HIV infection during the development of chronic kidney disease are rare. As of 5 December 2022, HIV antigen/antibody test results were inconclusive. Subsequent WB experiments revealed a progressive pattern of HIV infection. On 7 December 2022, HIV-1 copies were detected at a high concentration of 57,400 copies/mL. During the emergence of coronavirus disease 2019 (COVID-19) in China, the patient tested positive for COVID-19 on 11 December 2022, and a decrease in CD4+ was also observed. This result might be attributed to either COVID-19 or HIV infection [7]. On 8 February 2023, HIV antigen/antibody test results for the patient in our hospital's outpatient department were 95.23. Unfortunately, the CDC did not pursue further outcomes for the patient.

The results of the rapid case detection test indicated a weak reaction across all manufacturers. While the ELISA Bio-Rad test was reactive, the third and fourth generations did not respond, suggesting that at this time, the patient's internal antigen or antibody concentration was very low. This finding was consistent with the HIV screening test results and indicated that the patient was in the phase of antigen-antibody transformation, also known as the acute late stage. During this stage, the patient's immune system was activated, and the amount of antigen and virus in the body was present in large quantities. However, due to the downward trend and insufficient production of antibodies, various reagents showed weak or no response due to sexual heterogeneity and sensitivity issues [8].

Various detection methods may have varying windows of detection due to the differences in detection markers and periods. The same method may be subject to the immunogenicity of the virus and individual immunity, leading to variations in factors such as the strength of response. Therefore, the diagnosis of HIV acute stage samples is of great significance for controlling HIV transmission. Previous studies have shown that more than 50% of HIV transmissions occur during the acute early stage of HIV infection [9].

In our case, even though HIV was promptly diagnosed, there are three noteworthy points for discussion. Firstly, the patient was hospitalized just beyond the window for HIV testing. If he had been admitted a few days earlier and undergone HIV antigen/antibody testing, would it have been possible to successfully avoid the HIV screening window? Secondly, the rapid method used had a positive reaction, but the ELISA reagents from two manufacturers did not respond. In theory, ELISA is more sensitive than the gold standard method, yet the opposite phenomenon occurred in our case, which is rare in daily detection work. Finally, the initial screening unit used rapid screening first and then performed a fourth-generation ELISA retest, leading to a positive diagnosis. If the case had followed the routine screening laboratory test process of first-generation ELISA screening, it is possible that the detection would have been missed.

Conclusions

Based on our results, it is advisable for the detection point to stockpile two distinct manufacturers' rapid detection reagents and for the screening laboratory to retain at least two types of reagents with distinct detection principles. Additionally, we should actively explore various detection strategies in different scenarios to maximize the efficiency of detecting acutely infected individuals. For instance, would it be safer to conduct HIV screening the day prior to dialysis surgery in the case of special patients, such as peritoneal dialysis patients? Furthermore, when dealing with high-volume testing, we should opt for highly sensitive reagents to prevent any possible missed detections, favoring chemiluminescence or nucleic acid mixed detection methods. Although the CDC's screening laboratory does not conduct extensive testing, as most individuals tested are at high risk, we must remain vigilant and utilize at least two distinct reagents for screening to prevent missing any potential acute phase infections.

Authors' contributions

XW and DW designed the study and wrote the first version of the manuscript; TL and YG reviewed the paper; YG supervised the study. All authors read, provided feedback, and approved the final manuscript.

Funding

This work was supported by Fuyang City Health Committee scientific research project of 2021 (NO. FY2021-054).

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Conflict of interests: No conflict of interests is declared.