CASE REPORT

Medycyna Ogólna i Nauki o Zdrowiu 2026, Tom 32, Nr 2, 167–170
www.monz.pl

Meningovascular syphilis of the central nervous system in an HIV-infected patient – case report

Kiła meningonaczyniowa ośrodkowego układu nerwowego u pacjenta zakażonego wirusem HIV – opis przypadku

Klaudia Płudowska[1,C-E] ✉, **Danuta Borowska**[1,A,C-D], **Mieszko Czaplinski**[1,B-D], **Olaf Pokrzykowski**[1,A,D,F], **Julia Strzelec**[1,B,D,F]

[1] *Department of Infectious Diseases, Medical University, Gdańsk, Poland*
A – Research concept and design, B – Collection and/or assembly of data, C – Data analysis and interpretation, D – Writing the article, E – Critical revision of the article, F – Final approval of the article

Płudowska K, Borowska D, Czaplinski M, Pokrzykowski O, Strzelec J. Meningovascular syphilis of the central nervous system in an HIV-infected patient – a case report. Med Og Nauk Zdr. 2026;32(2):167–170. doi:10.26444/monz/220989

Abstract

Introduction. Syphilis, caused by the spirochete Treponema pallidum, despite its declining incidence, still represents a significant concern for public health. The report presents the case of a 42-year-old man with concurrent tertiary syphilis, manifesting as neurosyphilis, and human immunodeficiency virus (HIV) infection. The patient was admitted to the department due to qualitative disturbances of consciousness; alcohol-related encephalopathy was initially suspected in the preliminary diagnostic process. Routine laboratory and toxicology tests showed no significant abnormalities and did not indicate the presence of infectious factors. Brain imaging findings were non-specific, and the initial cerebrospinal fluid examination also did not allow for a definitive diagnosis.

Results. Extended serological testing revealed HIV infection, which facilitated the diagnosis of late-stage syphilis. The patient was treated with intravenous crystalline penicillin and antiretroviral therapy was initiated. This case demonstrates that the diagnosis of neurosyphilis in HIV-infected individuals remains a significant diagnostic challenge, as standard serological tests, including VDRL, may yield false-negative or inconsistent results.

Conclusion. The case highlights the need for comprehensive diagnostic evaluation and a high degree of clinical vigilance, particularly in patients with a complex medical history, neuropsychiatric symptoms, and co-existing suspicion of immunodeficiency.

Key words

HIV, sexually transmitted infections, central nervous system syphilis

Abbreviations

HIV – Human Immunodeficiency Virus; **STI** – Sexually Transmitted Infection; **CDC** – Centre for Disease Control; **MSM** – Men having Sex with Men; **HBV** – Hepatitis B Virus; **HCV** – Hepatitis C Virus; **CT** – Computer Tomography; **ECG** – Electrocardiography; **MRI** – Magnetic Resonance Imaging; **CSF** – Cerebrospinal Fluid; **CNS** – Central Nervous System; **CMV** – Cytomegalovirus; **EBV** – Epstein-Barr Virus; **HSV-1** – Herpes Simplex Virus 1; **HSV-2** – Herpes Simplex Virus 2; **HHV-6** – Human Herpesvirus 6; **HPV** – Human Papillomavirus; **VZV** – Varicella-Zoster Virus; **IgG** – Immunoglobulins G; **TPHA** – Treponema Pallidum Haemagglutination Assay; **VDRL** – Venereal Disease Research Laboratory; **ART** – Anti-Retroviral Therapy; **RNA** – Ribonucleic Acid

Streszczenie

Wprowadzenie. Kiła, wywoływana przez krętka *Treponema pallidum*, mimo zmniejszenia zapadalności na tę chorobę, nadal stanowi istotne zagrożenie dla zdrowia publicznego. W artykule przedstawiono przypadek 42-letniego mężczyzny z jednoczesną kiłą trzeciorzędową, manifestującą się jako kiła centralnego układu nerwowego, oraz zespołem upośledzonej odporności spowodowanej wirusem HIV. Pacjent został przyjęty na oddział z powodu jakościowych zaburzeń świadomości, przy czym diagnostykę wstępną przeprowadzono pod kątem encefalopatii alkoholowej. Podstawowe badania laboratoryjne oraz toksykologiczne nie wykazywały istotnych odchyleń od normy i nie wskazywały na obecność czynników infekcyjnych. Wyniki badań obrazowych mózgu były nieswoiste, a początkowe badania płynu mózgowo-rdzeniowego również nie pozwalały postawić rozpoznania.

Wyniki. Pogłębiona diagnostyka serologiczna ujawniła zakażenie wirusem HIV, co ułatwiło rozpoznanie kiły w fazie późnej. Pacjenta poddano leczeniu dożylną penicyliną krystaliczną oraz wdrożono terapię antyretrowirusową. Przypadek ten pokazuje, że rozpoznanie kiły układu nerwowego u osób zakażonych HIV nadal pozostaje istotnym wyzwaniem diagnostycznym, ponieważ standardowe testy serologiczne, w tym VDRL, mogą dawać wyniki fałszywie ujemne lub niespójne.

Wnioski. Podkreśla to konieczność kompleksowej diagnostyki oraz zachowania wysokiej czujności klinicznej, szczególnie u pacjentów z wywiadem wskazującym na obciążenie, objawami neuropsychiatrycznymi i współistniejącym podejrzeniem niedoboru odporności.

Słowa kluczowe

HIV, choroby przenoszone drogą płciową, kiła układu nerwowego

✉ Address for correspondence: Klaudia Płudowska, Department of Infectious Diseases, Medical University of Gdańsk, 80-210 Gdańsk, Poland
E-mail: klaudia.pludowska@gumed.edu.pl

Received: 21.09.2026; accepted: 22.04.2026; first published: 01.06.2026

INTRODUCTION

Syphilis, caused by the spirochete Treponema pallidum, due to its ever-increasing incidence, continues to pose a potential threat to public health. The case is presented of a 42-year-old male with HIV co-infection and tertiary syphilis manifesting as neurosyphilis. Initially, alcoholic encephalopathy was suspected. Neuroimaging findings were non-specific, and preliminary laboratory investigations did not confirm the presence of common infectious etiologies. It was only upon cerebrospinal fluid examination and extended serological testing that HIV infection and late-stage syphilis were diagnosed.

The patient was treated with intravenous crystalline penicillin, and a four-drug antiretroviral regimen was initiated, which led to the resolution of neurological symptoms as well as to the improvement in overall condition.

This case underscores the diagnostic challenges associated with neurosyphilis in individuals with HIV infection, as standard serological assays, including the VDRL test, may yield false-negative or incongruent results. It highlights the necessity for comprehensive diagnostic evaluation and heightened clinical vigilance, particularly in high-risk populations. The importance is emphasized of early detection and prevention of sexually transmitted infections, which remain burdened by substantial social stigma and limited public health awareness. Regular screening, patient education, as well as open clinician–patient communication, may significantly reduce the incidence of late-stage complications of syphilis and improve outcomes in cases of HIV co-infection.

CASE REPORT

Background. Although the incidence of syphilis has significantly decreased, a resurgence in cases has been witnessed in recent years [1], highlighting its continued relevance. In 2023, the Polish Institute of Hygiene reported 2,988 cases, including 102 diagnosed at the tertiary stage [2], while in 2022, the CDC reported over 200,000 cases in the United States [1] Populations at higher risk include men who have sex with men (MSM), individuals who use intravenous drugs, and those with HIV; moreover, those already infected with HIV are at greater risk of contracting syphilis and developing later, more advanced stages of this ailment [1, 3]

Syphilis is caused by the spirochete *Treponema pallidum*, which is sexually transmitted from an infected individual. It typically presents with a painless ulcer, known as a chancre, which often goes unnoticed and untreated. If left untreated, the chancre heals spontaneously, and the infection enters a latent phase, followed by the secondary stage characterized by a maculopapular rash, mucosal ulcerations, and lymphadenopathy. In the absence of treatment, the infection can remain latent for several years before progressing to tertiary syphilis, which may involve gummatous lesions and neurological complications.

Syphilis of the central nervous system manifests in a variety of neurological symptoms, including headaches, dementia, increased aggressiveness, seizures, paresis, and psychosis. [4, 5] In some cases, unusual psychiatric presentations, such as Capgras syndrome, have been reported as a first sign of syphilis of the central nervous system [6]. Diagnosis at all stages remains a significant challenge, although penicillin remains the cornerstone of treatment, with a single dose often sufficient in the early stages. The primary difficulty lies in the timely diagnosis of the disease.

CASE REPORT

A 42-year-old man was admitted to the Neurology department due to qualitative disturbance of consciousness. He was found in his apartment, dehydrated and disoriented, with visible bottles of alcohol present. He had last contacted his family a week earlier, during which he appeared incoherent and intoxicated. His history was notable for alcohol dependence syndrome and psychoactive substance abuse; no information on other chronic medical conditions was available.

Upon admission to the Neurology Department, the patient was conscious and able to engage in verbal communication, but he was disoriented regarding time and place. neurological examination revealed no overt paresis, and meningeal signs were absent; however, bilateral positive Babinski signs were observed.

Laboratory tests did not confirm the suspicion of alcohol or psychoactive substance abuse, and results for thyroid function, ammonia poisoning, and other basic biochemical markers were normal. Notably, thrombocytopenia was observed (99,000, which decreased to 57,000 the following day). No other abnormalities were found in the basic laboratory tests.

Negative blood cultures and the presence of HBV and HCV infection markers were recorded. Imaging studies, including computed tomography (CT) of the head, as well as abdominal, pelvic, and thoracic scans, along with echocardiography, Holter ECG, and Doppler ultrasound of cervical and vertebral vessels, were all normal. Brain magnetic resonance imaging (MRI) revealed multiple small, diffuse hyperintense lesions on T2-weighted sequences, some with restricted diffusion, likely corresponding to changes from toxic-metabolic disorders, possibly alcohol-related, with overlapping early diffuse thromboembolic changes. Given the unclear radiological findings, a lumbar puncture was performed.

The clinical presentation and diagnostic interview raised the suspicion of alcohol-related Wernicke›s encephalopathy. Intravenous vitamin B1 supplementation was initiated, but there were no changes in the patient›s neurological condition.

On the fourth day of hospitalization, cerebrospinal fluid (CSF) analysis results were received: appearance clear, glucose 60 mg/dL, proteins 214 mg/dL, chlorides 120 mmol/L, RBCs: 1000 cell count /μL, WBCs cell count 9/μL with lymphocytic predominance, albumin 1116 mg/L, IgG 548 mg/L. No antibodies against *B. burgdorferi* (IgM/IgG) were detected. Tests for common central nervous system (CNS) pathogens, including CMV, EBV, HSV1, HSV2, HHV-6, HPEV, VZV, E. coli, H. influenzae, L. monocytogenes, N. meningitidis, S. agalactiae, S. pneumoniae, C. neoformans, and B. burgdorferi, were all negative. The CSF was also examined for oligoclonal bands and revealed a diagnostically insignificant IgG type 4 titer. Electrophoresis revealed the presence of M protein. The VDRL test in the CSF was negative, as was the test for toxoplasmosis.

The pivotal moment in the diagnostic process occurred when the patient tested positive for HIV infection, prompting his transfer to the Infectious Disease Clinic at the University Centre for Maritime and Tropical Medicine. At discharge from the neurology ward, the patient was conscious and oriented to time and place, although his answers to questions remained illogical. Concomitant Wernicke encephalopathy and HIV encephalopathy were considered in the differential diagnosis.

Upon admission to the Infectious Disease Clinic, the patient was in a generally stable condition but remained disoriented with no significant physical examination findings.

A re-evaluation of syphilis serology confirmed the diagnosis: qualitative TPHA and quantitative VDRL were both positive, with a titer of 1:8. The proteinogram indicated the presence of a gamma fraction and an additional band. Based on these findings, the diagnosis of meningovascular syphilis was made, and the patient was started on intravenous crystalline penicillin, 5 million units four times daily, for a total of 26 days. CSF analysis performed on the eighth day of therapy showed: appearance clear, glucose 60 mg/dL, protein 190 mg/dL, chlorides 127 mmol/L, cell count 3/μL.

In connection with the detection and confirmation of HIV infection, following the recommendations of the Polish AIDS Scientific Society, the patient was initiated on four-drug antiretroviral therapy (ART) consisting of darunavir, emtricitabine, tenofovir alafenamide, and cobicistat (commercially available as Symtuza), along with cotrimoxazole in a prophylactic dose to prevent toxoplasmosis and pneumocystis pneumonia. Initial HIV RNA viremia was 86,000 copies/mL, with a CD4+ count of 172 cells/μL (14%). The patient was classified as clinical category B3 for HIV infection. In the first 24 hours of ART, the patient experienced a moderate Jarisch-Herxheimer reaction, with a peak fever of 38.4°C. However, over the course of therapy, gradual improvement was noted in verbal communication and both allo- and autopsychic orientation. Due to the low initial VDRL titer (1:8), no follow-up testing was conducted after completion of therapy.

After one month of hospitalization, a sudden deterioration in the patient's condition was observed, characterized by a significant increase in inflammatory markers and a worsening of consciousness disturbances. Neurological examination revealed spastic tetraparesis with bilateral Babinski signs, foot tremor, and scanned speech. Positive meningeal signs were also present. Diagnostic testing was expanded to include an onconeural profile to rule out paraneoplastic syndrome. However, the results of the panel were negative, and microbiological blood and urine cultures were also unremarkable. Given the lack of new findings on CT head scans, empirical antibiotic therapy with meropenem (2g once daily for three days) and a single dose of dexamethasone (8mg) were administered. This resulted in a gradual and significant improvement in the patient's clinical condition.

At the end of the second month of hospitalization, follow-up tests showed HIV RNA viremia of 165,000 copies/mL, and CD4+ count increased to 244 cells/μL (15%). A repeat brain MRI revealed several small foci of high signal intensity in the white matter of both hemispheres on T2-weighted and FLAIR images, two of which showed diffusion restriction. Compared to the previous MRI, there was clear regression in the number and size of the lesions.

The patient was discharged after three months of hospitalization, in a state of partial allopsychic orientation. He had amnesia covering the two-month period prior to treatment initiation, but focal neurological symptoms were absent. He exhibited some vision and hearing disturbances and was referred for ongoing antiretroviral therapy, prophylactic antibiotic therapy with cotrimoxazole, and neurological rehabilitation.

DISCUSSION AND CONCLUSIONS

Syphilis, known as the 'great imitator' due to its broad, non-specific symptoms, can present significant diagnostic challenges, as demonstrated in this case. Bacterial culture is impractical for diagnosis because of the slow growth of *T. pallidum*, while non-treponemal tests (e.g., VDRL, RPR) are traditionally used as screening tools and treponemal tests (e.g., TPHA, FTA-ABS) as confirmatory assays. In cases where immunocompromised status is suspected, recent CDC guidelines recommend departure from the traditional testing approach and prioritization of treponemal assays as screening tests [7]. This may be particularly relevant in patients with concomitant HIV infection and neurosyphilis, in whom CSF-VDRL may be negative despite active disease [8]. Such a phenomenon was observed in the presented patient, whose initial VDRL result was negative at the beginning of hospitalization, before the initiation of antiretroviral therapy. Moreover, the relationship between VDRL titers and CD4+ cell count has been reported to be weak or non-significant [9], and false-positive VDRL results have also been described in patients living with HIV [10]. It should also be noted that the principal role of non-treponemal tests lies not only in initial diagnosis, but also in monitoring disease activity and response to treatment, as a decline in antibody titers may indicate therapeutic success.

Syphilis of the central nervous system can manifest in various forms, including aseptic meningitis, tabetic form, general paralysis or meningovascular form [11]. This form of tertiary syphilis often manifests itself as an ischemic stroke incident in relatively young patients [11–13]; in such patients, caution should be exercised to include syphilis in the differential diagnosis, particularly in HIV-positive individuals, since immunosuppression can obscure earlier syphilitic manifestations.

Acknowledgements

The authors express their sincere gratitude to Professor Tomasz Smiatacz and Dr. Marcin Dręczewski for their assistance in data collection and for inspiring us, as young researchers, to further explore this fascinating clinical case. This study would not have been possible without the support of the Department of Infectious Diseases at the Clinical Centre of the Medical University in Gdańsk, Poland.

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