sciendo Acta Marisiensis - Seria Medica / Ahead of Print DOI: 10.2478/amma-2025-0037

CASE REPORT

A case report of a complex case of advanced new HIV infection with CMV meningoencephalitis, *Salmonella* sepsis, and esophageal candidiasis: Diagnostic and therapeutic challenges

Alexandra Ioana Asztalos[1], Tudor Fleseriu[1,2,3], Akos Vince Andrejkovits[1,2,3], Vlad Adrian Pop[1*], Anca-Meda Vasiesiu[1,2]

1. Infectious Diseases Clinic of Targu Mures, Mures County Clinical Hospital, Romania
2. Department of Infectious Diseases, George Emil Palade University of Medicine, Pharmacy, Science, and Technology of Targu Mures, Romania
3. Doctoral School of Medicine, George Emil Palade University of Medicine, Pharmacy, Science, and Technology of Targu Mures, Romania

Introduction: Co-occurrence of multiple systemic diseases, particularly in late presenters, can obscure diagnosis and delay appropriate treatment. This work aims to highlight the complex clinical presentation, diagnostic and treatment challenges of a late presenter with new human immunodeficiency virus infection, complicated by *Salmonella* sepsis, oropharyngeal candidiasis, and Cytomegalovirus meningo-encephalitis, as well as the importance of a comprehensive diagnostic approach in immunocompromised patients with polymorphic symptoms.

Material and Methods: We report the case of a 43-year-old male who presented with systemic symptoms, including fever, wasting syndrome, urinary and neurological complaints. Clinical, microbiological, imaging, and molecular diagnostic tools were used to evaluate the patient. Diagnostic investigations included blood and urine cultures, human immunodeficiency virus and syphilis serology, cerebrospinal fluid analysis via molecular detection tools, and imaging studies.

Results: The patient was diagnosed with Human Immunodeficiency Virus-1 infection, *Salmonella enterica* group B sepsis emerging from a urinary infection, oropharyngeal and esophageal Candidiasis, and cytomegalovirus meningoencephalitis confirmed via polymerase chain reaction testing of cerebrospinal fluid. He was treated with a combination of antibacterial (Ceftriaxone), antifungal (Fluconazole), and antiviral therapy (Ganciclovir/Valganciclovir), alongside supportive care and initiation of antiretroviral therapy. After 29 days of hospitalization, he exhibited notable clinical improvement, including weight gain, neurological recovery, and resolution of oropharyngeal lesions.

Conclusions: This case illustrates the diagnostic and therapeutic complexity of managing patients with advanced Human Immunodeficiency Virus infection and multiple opportunistic complications. The prompt use of diagnostic tools, a multidisciplinary approach, and the staged initiation of antiretroviral therapy were fundamental for achieving favorable outcomes. Early recognition of late presenters remains essential to prevent life-threatening complications.

Keywords: HIV-1, AIDS-related infections, CMV encephalitis, oro-esophageal candidiasis, Salmonella sepsis, late-presenter

Received 30 June 2025 / Accepted 30 July 2025

Introduction

In 2024, UNAIDS (Joint United Nations Programme on HIV/AIDS – acquired immunodeficiency syndrome) reported 39.9 million people were living with HIV (Human Immunodeficiency Virus), and 1.3 million people were diagnosed with new HIV infection in 2023, 630000 people died from AIDS-related illnesses, 30.7 million people were accessing antiretroviral therapy, and 88.4 million people have become infected with HIV since the start of the epidemic. 43.3 million people have died of AIDS-related infections since the beginning of the epidemic. New HIV infections have been reduced by 60% since the peak in 1995 [1].

Since its documented emergence in 1981, the HIV infection has grown into a global pandemic. Four decades later, scientific advancements have resulted in the approval of over 30 antiretroviral agents, and combination therapies have transformed the prognosis from a fatal condition to a chronic and controllable disease in most cases [2].

Opportunistic infections are a significant hallmark of advanced HIV infection, especially when CD4+ T-cell counts fall below certain thresholds.

Cytomegalovirus (CMV) infection is one of the most incriminated AIDS-related illnesses that affects people with HIV infection, especially those with low CD4+ counts. In people with advanced HIV, especially those with CD4+ counts below 50 cells/mm^3, CMV may reactivate and cause serious end-organ disease [3].

The most common manifestation is CMV retinitis, which can present with visual floaters, blurred vision, and visual field defects that may lead to blindness if untreated. The retina often displays necrotic areas with hemorrhage, described as the classic “pizza pie” appearance [4].

Less frequently, CMV can affect the central nervous system, causing encephalitis. Diagnosis is confirmed by detecting CMV DNA inside the cerebrospinal fluid (CSF)

* Correspondence to: Vlad Adrian Pop
E-mail: popvlad424@gmail.com

using polymerase chain reaction (PCR), often via multiplex panels. Treatment includes intravenous ganciclovir or oral valganciclovir, with therapy continued until sustained immune recovery is achieved, commonly defined as CD4+ counts above 100 cells/mm³ for at least three months on antiretroviral therapy (ART). Maintenance therapy can be discontinued when the CD4+ count is greater than 100–150 cells/mm³ [5].

Another opportunistic condition that affects immunocompromised populations is the invasive *Salmonella* infection. *Non-typhoidal Salmonella* (NTS), particularly *Salmonella enterica* serovars such as *Typhimurium* and *Enteritidis*, are a well-recognized cause of invasive bacterial disease, especially in individuals with advanced HIV infection. In immunocompetent hosts, NTS typically causes self-limiting gastroenteritis. However, in patients with HIV, especially those with CD4+ counts below 200 cells/mm³, the infection can disseminate hematogenously, resulting in bacteremia, sepsis, and recurrent bloodstream infections [6,7]. These patients often present with fever, chills, abdominal pain, and diarrhea, though in some cases, gastrointestinal symptoms may be absent [6,7]. Diagnosis is made via positive blood cultures, and stool cultures may also reveal the pathogen. Invasive disease with *Salmonella* is considered an AIDS-defining condition by the CDC [8]. Treatment involves third-generation cephalosporins (e.g., ceftriaxone) or fluoroquinolones, with therapy generally lasting 10–14 days or longer in severe or recurrent cases. Long-term secondary prophylaxis may be considered in patients with repeated infections and persistently low CD4+ counts. Early initiation of antiretroviral therapy is vital for reducing the risk of recurrence and improving long-term outcomes [6,7].

Much like *Salmonella* bacteremia and sepsis, Candidiasis of the bronchi, trachea, or lungs, and esophageal Candidiasis are also well-recognized AIDS-related conditions. Esophageal Candidiasis is one of the most common AIDS-defining opportunistic infections, particularly in individuals with CD4+ T-cell counts below 200 cells/mm³. Caused predominantly by Candida albicans, the infection may follow or coexist with oral thrush but can also occur independently [9]. The clinical picture typically consists of odynophagia (painful swallowing), dysphagia, and retrosternal discomfort. Since esophageal involvement cannot be diagnosed solely through an oral examination, upper GI endoscopy is the diagnostic gold standard, revealing characteristic white plaques and pseudomembranes on the mucosa [10].

Fluconazole is the recommended first-line treatment due to its efficacy, oral absorption, and tolerability. Intravenous antifungals, such as amphotericin B or echinocandins, are reserved for severe cases or when oral therapy is not possible. In most cases, the choice of antifungal therapy, including the type, dosage, and treatment duration, is determined by clinicians based on factors such as age, overall health, immune function, site of infection, and disease severity [10,11].

Current guidelines do not recommend routine long-term suppressive therapy after an initial episode, as recurrence rates are relatively low. Still, they may be considered in patients with persistent severe immunosuppression or repeated infections. The advent of effective antiretroviral therapy (ART) has significantly reduced the incidence and severity of esophageal Candidiasis in this population group [12].

Case Presentation

In this paper, we present the case of a 43-year-old male patient with no significant past medical history who was admitted to the Emergency Department of Târgu Mureș, Romania, reporting generalized fatigue, unintentional weight loss of approximately 18 kg over the past three months, dysuria, increased urinary frequency, urinary incontinence, fever, chills, dysphagia, and wasting syndrome. He reported two recent episodes of urinary tract infection, for which he had received oral antibiotic treatment: ciprofloxacin for 14 days and levofloxacin for 3 days.

Initial laboratory tests performed in the emergency department revealed anemia, lymphopenia, and neutrophilia (Table 1). The patient was transferred to the Infectious Diseases Clinic I for further evaluation and specialized treatment, but initially refused hospitalization. Four days later, as the symptoms persisted, he returned, and this time, he went directly to the Infectious Diseases Clinic, where he agreed to be admitted.

Upon admission, the clinical examination revealed a poor general condition. The patient appeared asthenic and cachectic, with a face that was expressionless and pale skin exhibiting decreased turgor. The oropharyngeal mucosa was entirely covered with whiteish deposits. Bilateral, painless, mobile cervical and inguinal lymphadenopathies (~1 cm) were noted; cardiac and respiratory exams were unremarkable, with no hepatosplenomegaly. The renal areas were non-tender, and Giordano's sign was negative bilaterally. On the neurological exam, he exhibited dysmetria on finger-to-nose testing, unsteady gait, and a positive Romberg sign, without signs of meningeal irritation or focal neurological deficits.

Upon admission, blood cultures, urine cultures, pharyngeal swabs, tongue swabs, HIV-1 and 2 antibody tests, HCV antibody tests, and *Treponema pallidum* haemagglutination assay (TPHA) tests were collected.

The results revealed the presence of *group B Salmonella* in both urine and blood cultures, as well as positive HIV-1 antibodies and a positive TPHA. Mild hepatocellular injury was also noted. Antibacterial, antiretroviral, antifungal, symptomatic, and hepatoprotective treatments, as well as rehydration therapy, were initiated.

During hospitalization, the patient developed mild neck stiffness and persistent dysmetria on finger-to-nose testing, with bilateral brisk deep tendon reflexes and intentional tremor, more pronounced on the left. Cranial CT showed a chronic parietal lesion on the right but no acute pathology.

Table 1. Laboratory results during hospitalization

Test / Date	Admission	Day 6	Day 14	Day 21	Day 28	Day 60
RBC (10^3/µL)	3.49	3.55	3.28	-	3.34	4.16
Hematocrit (%)	28.9	31.0	27.8	-	30.3	40.1
Hemoglobin (g/dL)	9.90	10.3	9.40	-	10.1	13.4
Lymphocytes %	12.2	12.8	20.0	-	17.5	15.9
Lymphocytes # (10^3/µL)	0.53	0.45	0.80	-	0.35	1.16
Monocytes # (10^3/µL)	0.40	0.22	0.31	-	0.06	0.39
Monocytes %	9.20	6.30	7.80	-	2.80	5.40
Neutrophils # (10^3/µL)	3.40	2.87	2.80	-	1.43	5.63
Neutrophils %	78.10	80.8	69.9	-	71.0	77.1
Leucocytes (10^3/µL)	4.35	3.54	4.00	-	2.01	7.30
Platelet (10^3/µL)	341.0	164.0	268.00	-	364.0	383.0
BUN (mg/dL)	47.08	77.0	21.0	47.0	37.0	51.0
Creatinine (mg/dL)	1.02	1.01	0.69	0.92	0.66	0.77
K (mmol/L)	4.08	5.16	4.41	-	4.46	4.67
Na (mmol/L)	135.0	145.0	136.0	-	140.0	139.0
CRP (mg/dL)	-	-	3.33	1.01	0.10	-
Fibrinogen (mg/dL)	-	533.0	-	384.00	-	-
ESR (mm/1h)	-	130.0	-	-	110.0	-
INR	-	1.03	-	-	0.94	-
ALT (U/L)	19.0	33.0	42.0	-	43.0	31.0
AST (U/L)	29.0	56.0	44.0	-	34.0	21.0
Total bilirubin (mg/dL)	0.39	0.5	-	-	-	-
Serum glucose (mg/dL)	121.0	119.0	87.0	100.0	-	87.0

The fundoscopic examination was within normal limits. A lumbar puncture was performed, and PCR panel testing for meningitis/encephalitis was positive for cytomegalovirus (CMV) (Table 2); TPHA from the cerebrospinal fluid (CSF) was negative. Antiviral therapy was initiated with IV ganciclovir 250 mg twice daily for 14 days, followed by oral valganciclovir 450 mg twice daily.

On the following days, the patient reported intercostal pain. Thoraco-abdominopelvic CT revealed suspected urinary bladder fistulae, diverticula, and possible small renal abscesses. Nephrology and urology consults were obtained, but no evidence of acute inflammation was found; imaging follow-up was recommended.

On hospital day 23, the patient developed multiple soft, yellow stools. Testing for *Clostridioides difficile* A and B toxins, as well as stool cultures, were negative; however, the *Helicobacter pylori* antigen test was positive.

After 29 days of hospitalization in Infectious Diseases Clinic I, the patient was discharged in clinically improved condition: afebrile, conscious, oriented in time and space, with a weight gain of 11 kg. Oral examination showed resolution of the previous whitish deposits. Neurological evaluation revealed only mild horizontal nystagmus and slight dysmetria on finger-to-nose testing. Gait was stable, the Romberg test was negative, and no signs of meningeal irritation were present.

One month after discharge, the patient returned to the Infectious Diseases Clinic I in Târgu Mureș for clinical and immunological reassessment, which showed an improvement in terms of both virological control and immunologic restoration (Table 3). At home, the patient continued his treatment with Valganciclovir 900 mg once

Table 2 - PCR syndromic test meningitis/encephalitis

Pathogen	Results Day 14	Results Day 60
Escherichia coli K1	Not detected	Not detected
Haemophilus influenzae	Not detected	Not detected
Listeria monocytogenes	Not detected	Not detected
Neisseria meningitidis (encapsulated)	Not detected	Not detected
Streptococcus agalactiae	Not detected	Not detected
Streptococcus pneumoniae	Not detected	Not detected
Streptococcus pyogenes	Not detected	Not detected
Cytomegalovirus (CMV)	Present	Not detected
Mycoplasma pneumoniae	Not detected	Not detected
Herpes Simplex Virus 1	Not detected	Not detected
Herpes Simplex Virus 2	Not detected	Not detected
Human Herpes Virus 6	Not detected	Not detected
Enterovirus	Not detected	Not detected
Human parechovirus	Not detected	Not detected
Cryptococcus gattii/Cryptococcus neoformans	Not detected	Not detected
Varicella-zoster virus	Not detected	Not detected

*QIAstat-Dx® Meningitis/Encephalitis (ME) Panel

Table 3 – Virological decrease and immunological restoration

Test / Date	Day 8	Day 60
CD3+T lymphocyte %	86.56	80.07
CD3+T lymphocyte #	156.00	932.00
CD4+T lymphocyte %	9.83	13.52
CD4+T lymphocyte #	18.00	157.00
CD8+T lymphocyte %	74.11	63.86
CD8+T lymphocyte #	133.00	743.00
CD45+T lymphocyte #	180.00	1163.00
CD4+/CD8+	0.13	0.21
Viral load ARN HIV-1 (copies/mL)	152508	Undetectable

daily, antiretroviral therapy with Doravirine-Lamivudine-Tenofovir-Disoproxil once daily, and PCP (Pneumocystis jirovecii pneumonia) prophylaxis with Trimethoprim/Sulfamethoxazole 480 mg twice daily.

Discussion

This case highlights the complex clinical presentation and management of a young male immunocompromised patient newly diagnosed with HIV. The patient's medical history, without known comorbidities, presents with nonspecific symptoms, including fatigue, significant unintentional weight loss, fever, and urinary symptoms, which raises the suspicion of an underlying immunodeficiency, illustrating the diagnostic challenges often encountered in late presenters.

The work conducted by Susan Profeta *et al.* highlights that nontyphoidal *Salmonella* infections, as in the case we reported, are a significant and often early complication in patients with AIDS, with an unusually high rate of bacteremia (71%) compared to the general population [13]. This concerning trend is further supported by Uche *et al* in a newer systematic review, documenting that non-typhoidal *Salmonella* accounted for up to 39% of community-acquired bloodstream infections in subSaharan Africa [14]. The findings reflect the role of cell-mediated immunity (CMI) in controlling *Salmonella* infections, which is the most important target in HIV infection and is severely affected in AIDS [15].

One of the earliest and most common infections seen in HIV patients is esophageal Candidiasis, reflecting a severe T-cell dysfunction and remaining an essential opportunistic infection in those with advanced HIV, especially when CD4+ counts fall below 100 cells/μL [16]. As described in our study, the patient initially presented with multiple white lesions on the oropharyngeal mucosa, accompanied by wasting syndrome. These findings could have raised the suspicion of an advanced immunodeficiency even before the detection of specific HIV-1 antibodies, viral loads, and total CD4+ counts.

In the study conducted by Melissa Reimer-McAtee and her team, CMV encephalitis was significantly more common in HIV-infected patients than in HIV-negative individuals (27.8% vs. 3.3%), underscoring its role as a significant opportunistic pathogen in advanced immunosuppression [17]. Despite this, CMV PCR was performed in less than half of HIV-positive cases, suggesting it is often underdiagnosed. Neuroimaging in CMV cases frequently showed T2/FLAIR hyperintensities and leptomeningeal enhancement, which, in the context of low CD4+ counts and altered mental status, should raise clinical suspicion. Delayed initiation of antiviral therapy was common, which may have contributed to the higher one-year mortality seen in the HIV-infected group (31.3%). Early recognition and testing for CMV are key factors in HIV-associated encephalitis to ensure prompt treatment and improve outcomes [17].

Conclusions

The case we presented highlights the diagnostic and therapeutic complexity encountered in patients presenting with advanced, untreated HIV infection and multiple simultaneous opportunistic infections. The combination of CMV meningoencephalitis, *Salmonella* sepsis, and esophageal candidiasis reflects the profound immunosuppression and high risk of life-threatening complications in this group of patients.

Early suspicion based on clinical features, such as wasting syndrome, oropharyngeal candidiasis, and neurological signs, was essential for guiding a targeted diagnostic workup. The use of a multiplex PCR panel enabled the timely identification of CMV in the CSF, and the patient benefited from a multidisciplinary approach involving sequential antimicrobial and antiretroviral therapy.

This study demonstrates the importance of comprehensive evaluation, rapid microbiological diagnostics, and carefully timed ART initiation in managing complex AIDS-related presentations. An optimal management of co-infections at an early stage significantly contributes to a better prognosis, and it improves survival and quality of life in patients with newly diagnosed advanced HIV infection.

Authors' contribution

AIA, A-MV: Conceptualization;
AVA, VAP: Formal analysis;
AIA, VAP: Investigation;
A-MV, TF, AVA : Methodology;
A-MV: Validation;
AIA Writing – original draft;
AIA Writing – review & editing)

Conflict of interest

None to declare.

Institutional Review Board Statement

Ethical approval was not required for this descriptive case report; however, written informed consent was obtained from the patient.

Funding

No external funding was received.

References

1. Unaids. Fact sheet 2024 - Latest global and regional HIV statistics on the status of the AIDS epidemic. 2024.
2. Menéndez-Arias L, Delgado R. Update and latest advances in antiretroviral therapy. Trends Pharmacol Sci. 2022 Jan;43(1):16–29.
3. Stewart M. Optimal management of cytomegalovirus retinitis in patients with AIDS. Clinical Ophthalmology. 2010 Apr;285.
4. Zhang J, Kamoi K, Zong Y, Yang M, Zou Y, Miyagaki M, et al. Cytomegalovirus Retinitis: Clinical Manifestations, Diagnosis and Treatment. Viruses. 2024 Sep 7;16(9):1427.
5. - Panel on Guidelines for the Prevention N, of Opportunistic Infections in Adults T, With HIV A. Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents With HIV Cytomegalovirus Disease.
6. Gordon MA. Salmonella infections in immunocompromised adults. Journal of Infection. 2008 Jun;56(6):413–22.
7. Feasey NA, Dougan G, Kingsley RA, Heyderman RS, Gordon MA. Invasive non-typhoidal salmonella disease: an emerging and neglected tropical disease in Africa. Lancet. 2012 Jun 30;379(9835):2489–99.
8. CDC. Appendix A. 2008. AIDS-Defining Conditions.
9. Panel on Guidelines for the Prevention N, of Opportunistic Infections in Adults T, with HIV A. Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents With HIV Candidiasis (Mucocutaneous).
10. Mohamed AA, Lu X liang, Mounmin FA. Diagnosis and Treatment of Esophageal Candidiasis: Current Updates. Can J Gastroenterol Hepatol. 2019 Oct 20;2019:1–6.
11. CDC. Fungal Diseases. 2024. Treatment of Candidiasis.
12. Pappas PG, Kauffman CA, Andes DR, Clancy CJ, Marr KA, Ostrosky-Zeichner L, et al. Clinical Practice Guideline for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America. Clinical Infectious Diseases. 2016 Feb 15;62(4):e1–50.
13. Profeta S, Forrester C, Eng RH, Liu R, Johnson E, Palinkas R, et al. Salmonella infections in patients with acquired immunodeficiency syndrome. Arch Intern Med. 1985 Apr;145(4):670–2.
14. Uche IV, MacLennan CA, Saul A. A Systematic Review of the Incidence, Risk Factors and Case Fatality Rates of Invasive Nontyphoidal Salmonella (iNTS) Disease in Africa (1966 to 2014). PLoS Negl Trop Dis. 2017 Jan 5;11(1):e0005118.
15. Gordon MA, Graham SM, Walsh AL, Wilson L, Phiri A, Molyneux E, et al. Epidemics of Invasive *Salmonella enterica* Serovar Enteritidis and *S. enterica* Serovar Typhimurium Infection Associated with Multidrug Resistance among Adults and Children in Malawi. Clinical Infectious Diseases. 2008 Apr;46(7):963–9.
16. Laranjeira MR, Gomes JQ, Ferreira AR, Ramalheira S. Unveiling Esophageal Candidiasis. Cureus. 2025 Feb 16;
17. Reimer-Mcatee M, Ramirez D, Mcatee C, Granillo A, Hasbun R. Encephalitis in HIV-infected adults in the antiretroviral therapy era. J Neurol. 2023 Aug 28;270(8):3914–33.