Case Report

Navigating through the clinical course of a patient with newly diagnosed acquired immunodeficiency syndrome - "from 3 to 1 in 2 weeks" - case report

Punam Bhende[1], Jyoti Mannari[2], Ramesh Chaudhary[3], Rishikesh Wagh[3], Naman Patel[3], Vrajesh Parikh[3], Rahul Talavia[3], Mehul Rathod[4], Mansi Patel[4]

From [1]Associate Professor, [2]Professor, [3]Junior Resident, [4]Senior Resident, Department of Medicine, Pramukhswami Medical College, Bhaikaka University, Anand, Gujarat, India

ABSTRACT

We present the case of a 39-year-old male, newly diagnosed with acquired immunodeficiency syndrome, after being evaluated for fever, chronic diarrhea, significant weight loss, and referred with altered sensorium. Initially, the CD4 count was 1, and the human immunodeficiency virus viral load of 28 lakh copies. Screening for other infections led to the diagnosis of syphilis, *Cryptosporidium parvum*, methicillin-resistant *Staphylococcus aureus*, skin and soft-tissue infections, multidrug-resistant organism *Escherichia coli*, and cytomegalovirus over a short period of time. Choosing drugs for prophylaxis and treatment, monitoring, initiation of antiretroviral therapy, and the fear of immune reconstitution inflammatory syndrome made the fortnight challenging. A new symptom, sign, or abnormal laboratory parameter kept the team brainstorming. Support from the team of microbiologists, critical inputs by infectious disease specialists remotely, and the contribution of each member of the treating team made this a case for teamwork and experiential learning.

Key words: Acquired immunodeficiency syndrome, CD4 count, Human immunodeficiency virus, Opportunistic infections

Acquired immunodeficiency syndrome (AIDS) is diagnosed when a person with human immunodeficiency virus (HIV) presents with an AIDS-defining condition (ADC) or has a CD4 count of <200 cells/mm^3 regardless of ADC. The number of people with HIV in India was estimated to be between 21,00,000 and 30,00,000 and the number of deaths due to AIDS was estimated to be between 26,000 and 62,000 [1]. Delays in diagnosis and treatment, side effects of drugs, and coexisting infections make the clinical course stormy and navigating it challenging.

Our case report highlights one such case, and hence, we wish to share it with colleagues and postgraduate students caring for people living with HIV-AIDS.

CASE REPORT

A 39-year-old male, newly diagnosed with AIDS, was referred to us with altered sensorium due to severe hypoglycemia and hyponatremia.

At presentation, the patient was afebrile, emaciated, pale with a blood pressure of 100/70 mmHg, pulse rate of 100/min, and oxygen saturation of 99% on room air. Glasgow Coma Scale (GCS) was E4V1M5, and the blood glucose level was 46 mg/dL, which was corrected with 25% dextrose and improved GCS to 15/15. Table 1 shows the investigations and their results upon admission.

He was admitted to the intensive care unit, started on piperacillin+tazobactum 4.5 g intravenous every 6 hourly, tablet oseltamivir 75 mg twice a day, tablet cotrimoxazole twice a day, and shifted out under our care on 3rd-day. The following section highlights the key problems, reports, and the thought process of the treating team, along with treatment administered day-wise (Table 2).

Over the next few days, the patient improved, remained afebrile, and regained appetite and weight. He was shifted to oral prednisolone at 1 mg/kg/day, which was tapered by 10 mg every 5 days. The cytomegalovirus (CMV) quantitative report revealed a viral load of 45,750 IU/mL and hence injectablegancyclovir was continued for 1 more week. The patient was discharged soon after.

DISCUSSION

Patients newly diagnosed with AIDS are usually admitted under physicians as infectious disease specialists may not be available

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Correspondence to: Punam Bhende, Department of Medicine, Academic Centre, Bhaikaka University, Karamsad, Anand - 388325, Gujarat, India. E-mail: punamvb@charutarhealth.org

Table 1: Investigations and results at admission

Investigation	Results
Magnetic resonance imaging brain	No abnormality detected
Contrast-enhanced computed tomography abdomen	Fatty liver
High-resolution computed tomography chest	Few bilateral ground glass opacities in subpleural distribution
Serum sodium	130 mEq/L
Hemoglobin	9 g/dL
Total leucocyte count	2,600/μL
Platelet count	33,900/μL
Liver function tests	Normal except serum albumin 1.2 g/dL
Serum creatinine	0.67 mg/dL
Erythrocyte sedimentation rate	98 mm/1st h

everywhere. Despite highly active-antiretroviral therapy, in resource-limited settings, mortality occurs due to advanced immunodeficiency soon after starting therapy [2]. In 2022, India reported an estimated 39.6 thousand annual AIDS-related deaths. Increasing the CD4 threshold for treatment initiation over time lowered the risk of mortality [3]. Lower CD4 counts at presentation are associated with higher mortality. Mean CD4 counts were 176.04±163.49 cells/μL in newly diagnosed patients presenting to a teaching hospital in Eastern India [4]. The median CD4 count among late presenters was 134 cells/μL (interquartile range 72.25–219) in a South Indian cohort [5]. Profile of newly diagnosed patients with HIV infection in North Easter Romania revealed that 43.11% of cases had a CD4 level between 1 and 199 cells/μL. Our patient had a CD4 count of 1 cells/μL, which is very unusual.

At a CD4 count of 1, the patient is vulnerable to multiple opportunistic infections (OI). Ghate *et al*. analyzed the incidence

Table 2: Clinical course from Day 3 to Day 15

Day	Problem	Reports	Thoughts and discussion	Investigation	Treatment
3	Diarrhea, fever, hypoglycemia, and hyponatremia. Skin lesions on legs? Pyoderma gangrenosum (cleaned and dressed, and pus was sent for culture)	Absolute CD4 count – 1, PCR HIV quantitative (viral load) – 28,12,750 IU/mL	Hypoglycemia is? Sepsis-related? Drug-induced (cotrimoxazole) hyponatremia is hypovolemic hyponatremia due to fluid losses through diarrhea	Cultures repeated, HbsAg, HCV antibody, and sputum sample sent for Gram stain, AFB, and culture	OI prophylaxis (Cotrimoxazole+ trimethoprim, fluconazole, azithromycin), antibiotics, intravenous hydration. ART center reference and visit
4	Diarrhea, fever, hypoglycemia	Pus culture from skin lesions grows MRSA, and VDRL is positive. Cryptococcal antigen negative	Stool routine and microscopy will not pick up parasites. A stool sample was sent for modified acid-fast staining for parasites (Kinyouns cold ZN stain). Non-treponemal tests can be false positives. Treponemal test (RPR) sent	Tuberculin test, fundus for retinitis	Clindamycin added. ART started-TLD
5	Diarrhea, hypoglycemia. The grade of fever reduces	Modified acid-fast staining of stool shows oocytes of *Cryptosporidium parvum*. RPR is positive with a tire of 1:8, and TPHA is positive with a titer of>1:80. Leukopenia persists	Treatment indicated for *Cryptosporidium parvum* infection as ART will take time to have effect and diarrhea very probably is due to *Cryptosporidium parvum* infection. Nitazoxanide is drug of choice. Leukopenia – infection-related/sepsis-related? Drug-induced (cotrimoxazole). Should bone marrow aspiration be considered to look for infiltrative conditions/ lymphoma?	IgG and IgM toxoplasma, IgM CMV is non-reactive, and IgG CMV is reactive (>250 AU/mL)	2.4 million units of benzathine penicillin were administered, and nitazoxanide was added.
6	Diarrhea and hypoglycemia. Irrelevant talking and drowsiness. Grade of fever reduces further	Serum sodium 122 mmoL/L. Sputum culture grows multidrug-resistant *Escherichia coli*, tuberculin tests – negative, gene expert CBNAAT (sputum) – negative, IgG and IgG toxoplasma are non-reactive, IgG CMV	Tuberculin test is false negative due to anergy. Should INH prophylaxis be given? Can markers such as CRP and IL6 help in predicting IRIS? Is the altered sensorium due to hyponatremia? CNS infection. Should a LP be done? Why is there hyponatremia? SIADH? Why? Is SIADH due to drugs? (cotrimoxazole)	CRP, IL6	Meropenem added. Hypertonic saline has no response to normal saline.

(*Contd*...)

Table 2: (*Continued*)

Day	Problem	Reports	Thoughts and discussion	Investigation	Treatment
7	Diarrhea, hypoglycemia, and hyponatremia. Fever increases in grade and frequency, tachypnea and hypoxia develop	Is the fever due to infection? Or IRIS? Why hypoxia? Is it Pneumocystis Jirovecii (PCP)? Is It CMV pneumonitis? Or something else? HRCT done, should we treat as probable PCP and increase dose of Co-trimoxazole? If we do, will it worsen the SIADH, hypoglycemia, and leukopenia? Considering that these were caused by Co-trimoxazole. Should we add primaquine as the patient is already on clindamycin, and both together are the second-line treatment for PCJ	Chest X-ray shows bilateral non-homogenous opacities, and HRCT shows increased GGOs compared to the previous HRCT	CMV Quantitative report, HRCT	Dose of Co-trimoxazole was increased to a therapeutic dose for the treatment of PCP, and injectable steroids were added. IV hydration with normal saline.
8	Hypoxia persists, and fever continues. Hyponatremia corrected	CMV quantitative report- 9,50,500 IU/mL	Now that CMV is positive, should we reduce the dose of cotrimoxazole? Will sputum for GMS stain help guide the decision?	Sputum for GMS stain	IV Ganciclovir added
9	Hypoxia persists and fever continues	Blood cultures- no growth. IL6 levels are normal. PCT – 0.14 ng/mL DCT/ICT - negative	Waiting for response to ganciclovir seems prudent	Routine investigations	continued as before
10	Hypoxia persists, but oxygen requirement is lesser. Fever continues	GMS stain- negative for PCP	Should the cotrimoxazole dose be reduced to a prophylactic dose?	Routine investigations	continued as before
11	Fever grade and frequency reduce, the patient becomes afebrile and reports an increase in appetite and a sense of wellbeing. Minimal oxygen requirement			Routine investigations	continued as before, steroid dose reduced
12	Tachycardia has not settled despite clinical improvement. Minimal oxygen requirement and tolerates intermittent oxygen	Tachycardia has not settled in spite of clinical improvement. Is there any other reason? Can it be inappropriate sinus tachycardia. Discussion with patient reveals that he has had tachycardia for as long as he can remember. Will ivabradine help? Investigations: CD4 count, PCR HIV quantitative (viral load), CMV quantitative report		Continued as before	Reports revealed a CD4 count of 3 cells/cmm and PCR HIV quantitative (viral load) was undetectable

PCR: Polymerase chain reaction, HIV: Human immunodeficiency virus, HCV: Hepatitis C virus, AFB: Acid-fast bacilli, ART: antiretroviral therapy, MRSA: Methicillin-resistant *Staphylococcus aureus*, VDRL: Venereal disease research laboratory, TPHA: Treponema pallidum hemagglutination, CMV: Cytomegalovirus, RPR: Rapid plasma regain, IgG: Immunoglobulin G, IgM: Immunoglobulin M, CBNAAT: Cartridge based nucleic acid amplification test, CNS: Central nervous system, SIADH: Syndrome of inappropriate antidiuretic hormone secretion, HRCT: High-resolution computed tomography, GGOs: Ground-glass opacity, PCT: Procalcitonin, DCT/ICT: Direct and indirect coombs test

of OIs in HIV-infected individuals in Pune according to the stage of immunosuppression and observed that the median CD4 counts around the time of developing tuberculosis, herpes zoster, oral candidiasis, and cryptococcal meningitis were 114.0/mm^3, 207/mm^3, 113/mm^3, and 71/mm^3, respectively [6]. Another study in a tertiary care center in South India in a smaller group revealed that in patients with AIDS-defining illnesses such as CMV esophagitis, central nervous system vasculitis, progressive multifocal leukoencephalopathy, and cryptococcal meningitis, the mean CD4 count was <100 cells/microliter [7]. Our patient, however, had no clinical evidence of pulmonary or extrapulmonary tuberculosis. Sputum for acid-fast bacilli and gene experts were negative. However, these can be false negatives as the sensitivity of these tests in this group is low, as people with AIDS often release fewer bacilli in their sputum [8]. Tuberculin skin test was also negative, but a loss of sensitivity to this can be attributed to anergy [9].

Cryptococcal meningitis is the most common presentation accounting for 70–90% of cryptococcal disease, globally accounting for 15% of all AIDS-related deaths [10]. A study in Mumbai reported cryptococcal antigen positivity of 3.6% among those with CD4 <100 cells/cmm in the treatment-naive group [11]. This underscores the 2022 World Health Organization guidance of screening people living with HIV presenting with CD4 <100 cells/cmm for cryptococcal antigen before initiating or reinitiating antiretroviral therapy (ART). Kadam *et al*. found a high prevalence of cryptococcal antigenemia (8%) among asymptomatic patients with a CD4 count <100 cells/cmm [12]. Our patient surprisingly tested negative for cryptococcal antigen.

CMV infection, another OI prevalent in AIDS, can present with a wide range of clinical manifestations, the common being retinitis, colitis, encephalitis, polyradiculopathy, esophagitis, pneumonia, etc. While adrenalitis and oral ulcers are less common. Chakraborty *et al*. revealed that detectable CMV-DNA in the plasma by polymerase chain reaction (PCR) could independently predict death among AIDS subjects [13]. Our patient had a CMV viral load of 9,50,500 IU/mL on PCR and had no evidence of retinitis, but developed pneumonia which did not respond to anti-Pneumocystis Jirovecii (PCJ) treatment but responded to gancyclovir. His sputum also tested negative for Gomori methenamine silver stain for PCJ which supports the diagnosis of CMV pneumonia. This highlights the need for careful evaluation and consideration of CMV pneumonitis in such patients treated for other pulmonary infections and not responding to it. Similar cases are reported in the literature [14].

Infection with cryptosporidium is one of the major causes of diarrhea in patients with AIDS, and our patient tested positive for *Cryptosporidium parvum* and responded to treatment with nitazoxanide. If undiagnosed, it can lead to severe disease and increase morbidity and mortality, high degree of suspicion and choice of the appropriate test for detecting the parasite in stool needs to be stressed as it cannot be detected by conventional tests. A systematic review and meta-analysis by Ahmadpour *et al*. highlight the need for preventive measures and education, the need for clinicians to pick up early symptoms of cryptosporidiosis to initiate treatment early, and for prophylactic anti-parasite therapy in patients with CD4 counts below 200 cells/cmm [15].

The incidence of syphilis has been rising due to increased transmission in HIV patients and syphilis itself facilitates HIV infection in many ways [16]. Mahmud *et al*. found that HIV and syphilis co-infection is quite prevalent in men who have sex with men in the Asia Pacific region [17]. Our patient tested positive for venereal disease research laboratory, and since non-treponemal tests can be false positive in HIV, rapid plasma reagin, a treponemal test was carried out, which was positive in view of which penicillin was administered.

Besides the above, our patient had skin and soft-tissue infection due to methicillin-resistant *Staphylococcus aureus,* and sputum culture grew *Escherichia coli,* which was multidrug resistant. Infections with drug-resistant organisms are not unusual in AIDS, but add to the medicine burden, drug interaction, and side effects, which need to be kept in mind and checked at every stage.

Hyponatremia, hypoglycemia, and leukopenia that were persistent during the initial course of illness were found to be multifactorial (related to primary illness, OIs, secondary sepsis, drug-induced, syndrome of inappropriate antidiuretic hormone secretion) and could be managed with diligent and step-by-step workup and treatment. Tachycardia persisted and was labeled inappropriate sinus tachycardia after ruling out other causes and treated with ivabradine to which it responded. We decided to send the CD4 count and viral load at the end of 15 days, which was 3 cells/cmm and undetected, respectively. Suppression of this degree is expected with dolutegravir-based ART.

Immune reconstitution syndrome is a dreaded complication in HIV disease after initiation of ART and can manifest in myriad ways and can occur anytime from the first few weeks to many months. An observational cohort study in South India on the epidemiology of immune reconstitution inflammatory syndrome (IRIS) reported an incidence rate of 51.3/100 person-years and noted that one-third (31.4%) experienced at least 1 IRIS event, at a median of 27 days since ART initiation. At the time of writing this case report, our patient is in his 5th week on ART and has not shown evidence of IRIS as yet.

CONCLUSION

The initial clinical course of AIDS can be navigated to lead to favorable patient outcomes with diligent workup and management, initiation of ART at the earliest except contraindicated, supportive microbiology department, and valuable inputs from infectious disease colleagues. Clinicians need to remember that these patients mostly have multiple infections and complications simultaneously. Drug interactions and side effects should be kept in mind, and a high degree of suspicion should be kept for OIs and IRIS. Finally, the patient teaches us what books do not, and postgraduate students should be encouraged to participate in the care of and discussion about such patient in teaching hospital setup.

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