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HIV-RELATED PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY: A CASE REPORT

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ABSTRACT

The JC virus is widespread within individuals across the globe. It is usually in a latent form, but if immunity is decreased in a person this virus is reactivated leading to progressive multifocal leukoencephalopathy (PML). This is a rare neurological disease that can occur in cases of uncontrolled HIV/ AIDS. This report aims to highlight the importance of patients with HIV following a strict treatment regime and ensuring that this message is expressed to them by physicians in practice. We specifically report a patient case study in which our patient was non-compliant with his HIV medication, leading to neurological deficits. On admission, our patient presented with left limb paraesthesia, walking difficulties, and temporospatial disorientation. Many investigations and bedside tests were carried out before an MRI confirmed the presence of demyelinating gliotic lesions in the brain, leading to the diagnosis of PML. Due to the nature of PML, despite antiviral treatment, his condition progressively worsened. He presented two months later with further neurological pathologies, specifically a visual field disorder. Despite this disease being rare, the aim of this paper is to place emphasis on the lethality of the condition, therefore shifting a focus on preventing the disease in the first place via patient compliance with HIV medication.

Keywords: HIV, Acquired Immunodeficiency Syndrome, JC Virus, Leukoencephalopathies

Introduction

Progressive Multifocal Leukoencephalopathy (PML) is a rare, neurological disease of the central nervous system (1, 2). It occurs due to the reactivation of the JC virus (JCV), which is a DNA virus of the polyomaviridae family (3).

The biggest cause of reactivation is immunosuppression, mainly due to HIV/ AIDS. This is proven by the increased number of PML cases during the HIV epidemic (4, 5). Reactivation can also be due to haematological diseases or pharmaceutical treatments such as rituximab, efalizumab, and natalizumab (6). Initial contact with the virus usually occurs before 20 years of age and remains latent in the kidneys or bone. It is estimated that around 80% of the world's population has this latent virus (7). Once reactivated, the virus spreads to the central nervous system, specifically the oligodendrocytes leading to the destruction of myelin; making PML a demyelinating disease (8).

The localisation of demyelination in the brain determines the symptoms. It's important to note that in the latent phase, JCV doesn't cause any symptoms. However, once it has progressed to PML pathological changes are present, such as; motor weakness, gait abnormalities, language and vision difficulties, and cognitive disturbances.

HIV-related PML is mainly distinguished by motor changes (9).

MRI scans demonstrate the myelin changes, the lesions are hyperintense on T2 images and hypointense on T1. Commonly, demyelination is viewed as asymmetrical subcortical white matter lesions but sometimes presents as mono-focal and in the grey matter or cerebellum (10). We cannot solely rely on radiological findings for a diagnosis, therefore a CSF sample is taken for viral load investigation. This JVC-PCR in combination with the scans is usually sufficient to form a diagnosis, but in some cases, a brain biopsy may be required (2, 3).

A low viral load in the JVC-PCR and a high CD4 count indicate a favourable prognosis. Unfortunately, mortality rates are still high (around 3-6 months). But it's known that the use of highly active antiretroviral therapy (HAART) improves outcomes (3, 4).

In this article, we present a case of an HIV-positive patient who developed PML.

Case Report

A 36-year-old Caucasian man with an 11-year history of HIV and a diagnosis of chronic hepatitis B presented with progressively worsening left limb paraesthesia, walking difficulties, and temporospatial disorientation, which worsened over a 2-month period. It's important to note that upon presenting the patient claimed that he had discontinued his HIV medication about a year ago and restarted these 3 weeks before arrival to the hospital.

Clinical examination of the patient displayed blood pressure to be 128/74 mmHg, a heart rate of 68 bpm and SpO2 was 98%. Upon observation, he had an altered general state, slight pallor, cervical lymphadenopathies, and white deposits on the surface of his tongue. Patient history also revealed vertigo and significant motor deficits.

On admission, laboratory investigations revealed increased ESR levels, liver enzymes (Table 1), high platelet count, and mild hyperglycaemia. The levels of creatinine were slightly decreased with eGFR>90 and calcium levels had also decreased. Moreover, the patient tested positive for Candida albicans, which provided an explanation for the white deposits seen on the tongue during observations.

Table 1. Liver enzyme levels

ALT	66 U/L
AST	49 U/L
GGT	156 U/L

Due to the known patient history of HIV, it was vital to test for the markers of this virus to give us an idea on the status of this disease, these include the CD4+ and the viral load. The CD4+ levels indicate the strength of immunity, normal levels range from 491-1,734U/L. This patient had extremely decreased levels amounting to 66.0U/L, indicating a weakened immune system. This had decreased since 2019, as seen in Figure 1.

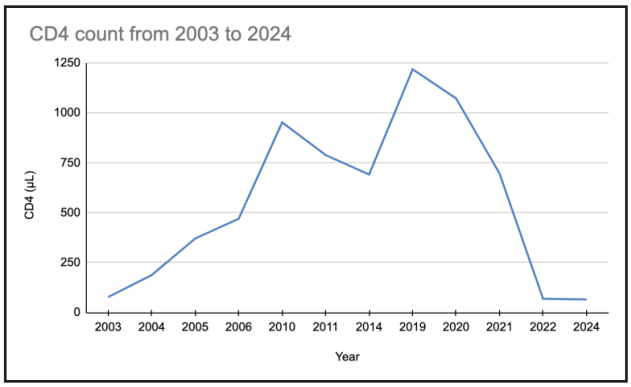

Figure 1. Line graph showing the changes in CD4 levels from 2003 to 2024.

Additionally, testing for the viral load is crucial to indicate the levels of HIV virus in the blood. The main goal of HIV treatment is to reduce the HIV viral load to an 'undetectable' level in the blood, this essentially means it is too low to be counted. Figure 2 demonstrates the changes of HIV RNA over time in the patient, illustrating 112 copies/ml in 2024.

Further investigations were required before forming a diagnosis. This included a chest CT scan which signalled paraseptal emphysema changes bilaterally and an abdominal echography displaying an enlarged, homogenic liver and a gallbladder that was increased in size with double septate. A neurological exam was also indicated due to the presenting complaints. The patient was cooperative and had partial spatial awareness.

Furthermore, this exam highlighted his left-sided hemiparesis and ataxia.

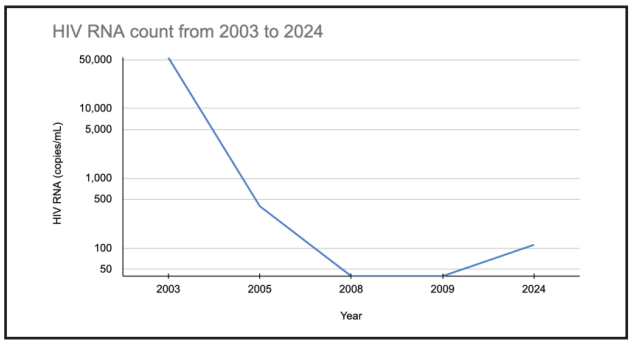

Figure 2. Line graph showing the changes in HIV RNA levels from 2003 to 2024.

An MRI scan (Figure 3) was performed due to the pathologies displayed in the neurological examination. Conclusions from the report demonstrate the presence of supratentorial demyelinating gliotic lesions due to the vast number of foci in the T2/FLAIR hypersignal located in the hemispheric white matter. It also showed irregular thickening of up to 9mm of the left frontal sinus mucosa, ethmoid cells, and floor of the bilateral maxillary sinus; this indicated sinusitis. Bilateral mastoiditis was also revealed largely due to the T2 hyperintense material occupying several mastoid cells bilaterally. Finally, nasopharyngeal adenoid proliferation which extended into the nasopharyngeal space led to the conclusion of nasopharyngeal adenoid microcystic hyperplasia.

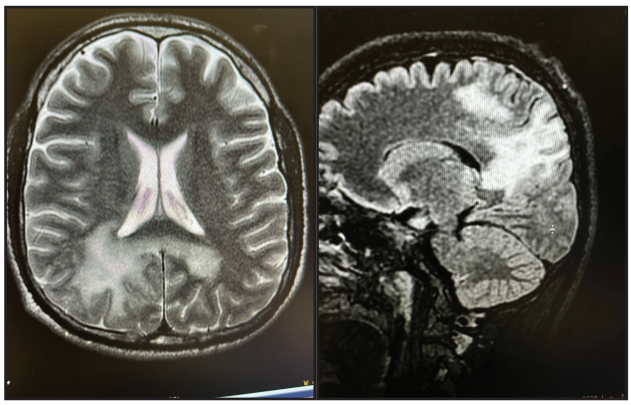

Figure 3. Cranio-cerebral MRI scans with contrast. Transverse and sagittal planes are shown.

In addition to a brain MRI, a lumbar MRI was carried out. The results of this revealed left L4-L5 radicular compressive disc protrusion and L3 vertical haemangioma. Once the results of the MRI alongside the clinical and biological data were collated, another neurological exam took place. This narrowed down the differential diagnosis to HIV encephalopathy, stroke sequelae, and the main diagnosis of HIV infection stage C2 alongside immuno-virological failure due to denial of antiretroviral therapy. In view of this diagnosis, the patient was started on antiretroviral therapy in an attempt to manage his condition with dolutegravir and doravirine/lamivudine/tenofovir disoproxil. As supplemental therapy several other medications were prescribed, including; B1 and B6 vitamins, dexamethasone, anxiolytic, statin, acetylsalicylic acid, alpha lipoic acid, and trimethroprim/sulfamethoxazole as PCP prophylaxis. These medications stabilised the patient and he was therefore discharged.

2 months later, the patient returned to the hospital with complaints of a progressively worsening condition. Specifically, he complained of a left-sided visual field disorder which had been accentuated in recent weeks. Similarly to the first visit, lab tests, and neurological tests were undertaken. The results of these were similar to the first presentation. This is with the exception of the CD4+ levels which had now decreased and HIV RNA which was now undetectable.

The visual field disorder suggested that there had been a decrease in the neurological function and therefore the team decided to perform an MRI scan (Figure 4). As expected from the presentation, the demyelization had become more extensive in the bilateral supratentorial hemispheric white matter. An ophthalmology consultation was also recommended whereby the fundus examination on both eyes was normal, but the vision had diminished.

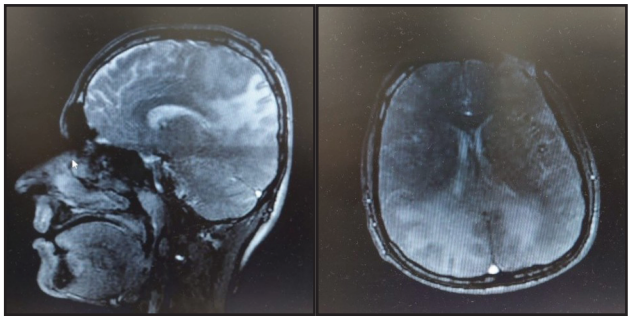

Figure 4. Cranio-cerebral MRI with contrast, sagittal, and transverse planes are shown.

A neurological examination showed key aspects of progressive multifocal leukoencephalopathy. This, alongside the aspect of the MRI brain scans, indicated that despite previous interventions, his condition was worsening. Medrol, Pantoprazole, and Milgamma were also given with the goal of reversing the vitamin B1 deficiency, which may have been an additional cause of the neuropathy.

Upon discharge, he was recommended to continue with the antiretroviral therapy according to a strictly prescribed schedule. Other measures that were advised for the patient to implement included; smoking cessation, dietary modifications such as avoiding animal fats and consuming more calcium and potassium-rich foods, attending regular neurological consultations for clinical re-evaluation, and ensuring all vaccinations were up to date due to the critical immunocompromised state.

Discussions

PML is one of the most challenging complications to manage in patients with HIV/AIDS. This case report focuses on the issues of being non-compliant with antiretroviral treatment and its dire consequences, specifically PML.

Our patient's history of stopping antiretroviral medications on his own accord, followed by a severe drop in CD4+ count increased the risk for opportunistic infections.

His initial clinical presentation was consistent with the neurological manifestations typically seen in PML. It was the combination of these clinical symptoms, the radiological images, and the laboratory findings (most importantly, the detection of JC virus DNA in cerebrospinal fluid via PCR) that confirmed the diagnosis of PML.

The patient's decreased CD4+ count and initially detectable HIV viral load highlights the immunosuppression that allowed the JC virus to take over. The following reduction of HIV viral load to undetectable levels after restarting the antiretroviral therapy is indicative of the benefit of HIV management and healing of the immune system. However, the ongoing decline in CD 4+ count suggests that the antiretrovirals may not always be enough to stop the progression of PML, especially if it was stopped and then taken again after a time of immune depletion.

The prevention of PML in the first place is crucial due to poor prognosis, and lack of treatment options once it takes over. Treating it is further complicated when patients have a history of poor medication adherence. It is found that even if these patients continue antiretroviral therapy after a period of non-compliance, the damage caused by the JC virus is often extensive and irreversible. Moreover, Highly Active Antiretroviral Therapy (HAART) can be given, but it is unlikely to result in full recovery. The difficulty in achieving 100% compliance in previously non-adherent patients adds more complexity to the treatment.

In conclusion, more measures should be taken to prevent HIV opportunistic infections. There is a great need for citizens' education to ensure compliance with HIV medications, thereby preventing consequences such as PML. The healthcare system and the government must put their efforts into preventing it and improving outcomes by educating people about safe sex practices, regular check-ups, launching campaigns, and providing psychological support to infected individuals.

Declaration of patient consent:

The patient provided informed consent for the publication of this case report.

Disclosure:

The authors report no conflicts of interest in this work.

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