

Remission of progressive multifocal leukoencephalopathy in HIV- positive patient after multidisciplinary rehabilitation: a case report

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Abstract

Introduction: One of the most common neurologic disease in Acquired Immunodeficiency Syndrome (AIDS) caused by Human Immunodeficiency Virus (HIV) is represented by progressive multifocal leukoencephalopathy (PML), being caused by John Cunningham (JC) polyoma virus.

Case presentation: We report a case of a 27 years old women, HIV-positive since childhood, under specific antiretroviral therapy with good adherence to it in that period but starting with adolescence adherence to highly active antiretroviral therapy (HAART) decreased. In this context her HIV viral load increased to a 690.000 copies/ml, and CD4 collapsed at 57 cells/mm³. She presented in our clinic with ataxic left hemiparesis, truncal ataxia and left hemi-hypoesthesia. Cerebrospinal fluid (CSF) showed a slightly pleocytosis and polymerase chain reaction performed from CSF diagnosed John Cunningham (JC) virus. Once diagnosis established, we reinitiated HAART, but some neurologic disorders persisted like difficulty of the left upper member, having the modified Rankin scale (mRS) of 5. The patient started a multidisciplinary rehabilitation (MDR) treatment, specifically adapted. It consisted of 4 sessions of neuromotor treatments, 20 sessions of massages, and 12 sessions of occupational therapy. According to MDR, the patient improved the ataxic walking, without support, presenting an improvement mRS of 3.

Conclusions: AIDS patients with PML could require a prolonged MDR treatment for neurological disorders and rehabilitation treatment promptly should be applied when such diagnosis is suspected.

Key words: *progressive multifocal leukoencephalopathy, human immunodeficiency virus, neurological disorder, multidisciplinary rehabilitation,*

Introduction

Known as an opportunistic disorder, progressive multifocal leukoencephalopathy (PML) is usually caused by John Cunningham (JC) polyomavirus. First PML case mentioned in the literature was for a patient with chronic lymphocytic leukemia (1). Nowadays, considering the plethora of different viruses like Human Immunodeficiency Virus (HIV), the PML incidence has raised, AIDS patients accounted for about 85% of PML (2). AIDS represent the late stage of HIV infection which occurs when immune system is damaged by the virus and immunity, expressed by CD4 count, decreased less than 200 cells/mm³.

Generally, the clinical symptomatology of patients with PML is very poor, which will lead to death in approximately 6 months from onset of symptoms. Interestingly, only a rate between 7 till 9% of PML patients showed a higher survival rate, without any etiologic therapy (3,4).

The suspicion of PML arises in AIDS patients with a low CD4 cell count, considering the clinical manifestations such as insidious onset, with focal and behavior deterioration. Symptoms noticed in HIV-positive patients with PML are motor weakness, especially hemiparesis, visual deficits such as hemianopsia, diplopia, mental changes, aphasia, limb apraxia, ataxia and so on (4-6).

Regarding the treatment options, multidisciplinary rehabilitation (MDR) should be positively seen by the physician in PML patients in order to counteract the clinical effects of many brain injury, like stroke, spinal cord injury, respiratory diseases or rheumatologic disorders (7-12). In accordance with the same aim, the National Institutes of Health retrospective study, evaluated HIV-positive patients which were further analysed by the different rehabilitation therapy point of view (13,14). In this regard, although neurological abilities were

improved at the end of this study, some degree of disability still remains and many neurological regressions were reported (15-19).

The area from central nervous system most affected by PML is parieto-occipital white matter. More profound, white matter showed single or multiple lesions without mass effect and magnetic resonance imaging (MRI) sustain the hypointense on T1-weighted images and hyperintense on T2-weighted together with fluid-attenuated inversion recovery (FLAIR) sequences (20).

CSF is usually normal, but sometimes pleocytosis less than 20/ μL can occur and protein levels may be slightly elevated (20).

Because there is no specific anti-JC treatment, some patients have experienced spontaneous improvements with highly active anti-retroviral therapy (HAART) (4-6). HAART is a very potent regimen for HIV-AIDS patient which initially included three classes of medication: protease inhibitors associated with nucleoside reversetranscriptase inhibitory and nonnucleoside reversetranscriptase inhibitors.

Therefore, the dynamics of neural plasticity in HIV-positive patients with PML are still unknown. The present case report describes the positive effect of MDR therapy in a HIV-positive patient with PML.

Case presentation

We report a case of a 27 years old women, diagnosed with HIV at age of 3, with different diseases in her childhood (i.e. extrapulmonary TB, recurrent bacterial pneumonia, recurrent parotiditis, chronic diarrhea, chronic hepatitis B, and oral candidiasis). After her HIV diagnosis, the patient was under specific antiretroviral therapy, with a good adhesion in childhood but with decreased adherence to HAART (i.e. lopinavir/ritonavir in associating with zidovudine/lamivudine) in adolescence.

In evolution her HIV viral load increased to a 690.000 copies/ml, and CD4 collapsed at 57 cells/mm³. At clinical and neurologic examination, the patient was awake but drowsy and oriented to time, place, and person. In this context she was hospitalized conscious, having coordination normal on the right side, whereas some ataxia was recorded on the left, with cerebellar dysarthria, diplopia at distance, ataxic left hemiparesis, truncal ataxia, and left hemihypoesthesia. The patient was further bedridden. Cerebrospinal fluid (CSF) examination evidenced a slightly pleocytosis (10 cells/mm³),

with no other changes. Polymerase chain reaction (PCR) performed from CSF evidenced presence of JC virus. Other etiology like Toxoplasma, Cryptococcus, Mycobacterium tuberculosis, gram positive or negative bacteria and fungi were excluded by specific CSF examination.

Cranio-cerebral MRI examination performed before and after administration of intravenous contrast showed confluent areas of hyperintense signal T2-FLAIR/hypointense T1, without restriction of diffusion, or contrast enhanced, symmetric in the periventricular white matter with subcortical bilateral extension. Lesions with the same characteristics were described in the cerebellar hemispheres, with a greater extension in the left cerebellar hemisphere. It also showed an inactive communicating hydrocephalus, probably induced by the aqueductal stenosis caused by the adherences (Figure 1). In this case clinical manifestation, biological and imaging changes sustained the PML diagnosis.

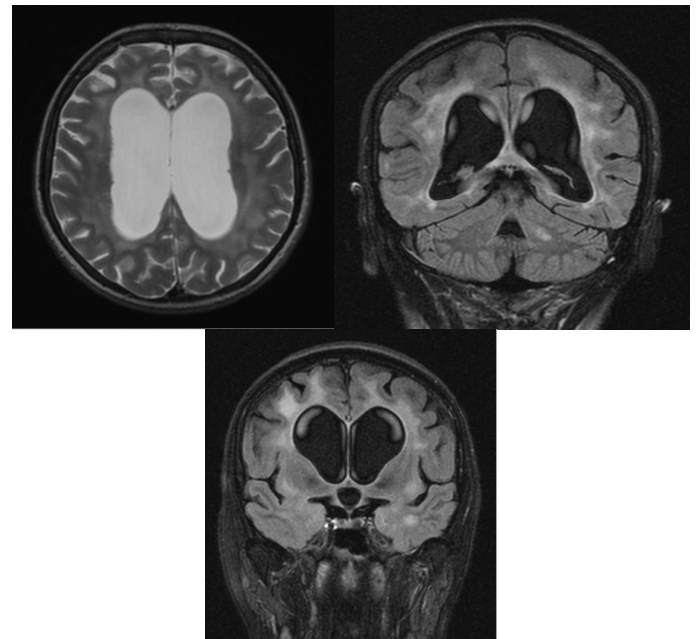


Fig. 1. Confluent areas of hyperintense signal T2-FLAIR/hypointense T1, without restriction of diffusion, symmetric in the periventricular white matter with subcortical bilateral extension.

After the established diagnosis, a symptomatic treatment was introduced and further reinitiated HAART (i.e. darunavir/ritonavir, raltegravir, associated with zidovudine/ziagen), but some neurologic disorders persisted like orthostatism and walking with great difficulty, supporting by another person, coordination and balance disorders, showing partial recovery in speech disorders and using with

difficulty the left upper member. The degree of disability was measured using the modified Rankin scale (mRS) in which after 5-years of follow-up, the patient presented a mRS of 3 (moderate disability; requires some help, but able to walk unassisted-according with mRS) from initially 5 (severe disability; requires constant nursing care and attention, bedridden, incontinent, according to mRS). The mRS present a score from 0 to 6 in which 0 are patients with no symptoms and 6 were dead persons (20).

In this context, the patient started a MDR treatment according to a neurologist and specialist in balneo-rehabilitation. The treatment was applied 5 years, 4 days/week, specifically adapted having the aims: muscle-ligament trophicization, recovery of the coordination of the left upper member function in order to increase muscle strength. Moreover, the program also included 4 sessions of neuromotor treatments, 20 sessions of massages, and 12 sessions of occupational therapy. The program ensures the more passive mobilization of the fingers, increasing the patient's ability in grasping in a functional position, according to special guiding techniques.

A control cerebral MRI was performed after 4 years which shows the sequelae of the lesions previously described, the same hydrocephalus, but with an evident cortical atrophy (Figure 2). Images correlated with the physical improvement but also with the cognitive decline and behavior disturbances. The patient has been also showed an increased CD4 to 430/ mmc and became undetectable 7 months after HAART resumption.

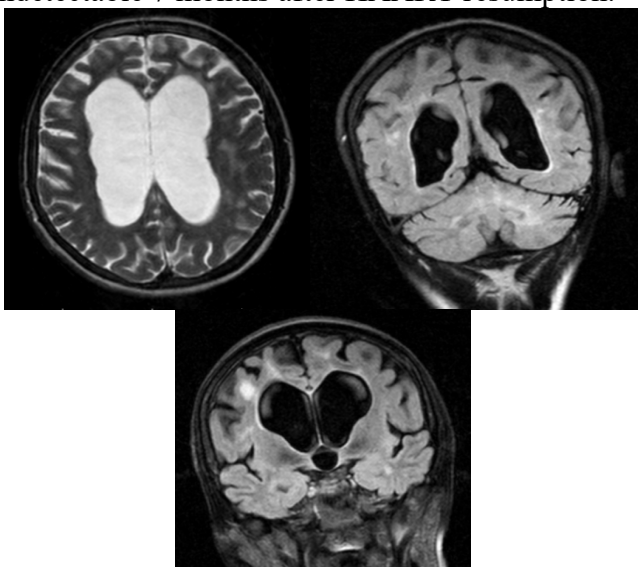


Fig. 2. MRI imaging of diffusion coronal sequence. The sequelae of the lesions previously described, presenting an evident cortical atrophy.

The patient improved the ataxic walking, performing short distance walking, without support, with an improved mRS of 3, without any severe sequelae.

Discussion

Worldwide epidemiology and morbidity by different infectious diseases changed over the last years. In some diseases like boutoneuse fever, shigella or salmonella, evolution is related with environmental factors (21-24), in other diseases evolution is related with outbreaks that can appear in absence of vaccination (25–28). In other diseases like TB or HIV evolution and mortality changed over the years according with early or late diagnosis and also with availability and adherence of specific treatment (29-34).

If, at the onset of the HIV pandemic, both physicians and patients were concerned only with prolonged survival, as this was achieved through complex treatment and specialized care, new clinical and therapeutic challenges are emerging for these patients. Currently, the medical approach of HIV-positive patients has changed. The care only by the infectious doctor has been switched to multidisciplinary approach, according with health problems of these patients. In our case neurologic and balneo-rehabilitation support were essential for treatment strategy.

PML showed to be a disease of a white matter cause by JC virus in which diagnosis can be made by using brain imaging investigation and even biopsy (35,36). Although there is no anti-JC treatment until present, in HIV positive patients have been showed an improvement along HAART. In HIV, before HAART survival for PML at one year was only 10%, but in the last years survival is at least 50% (20,37,38). The new biologic therapy (i.e. rituximab, efalizumab or natalizumab), for chronic diseases like rheumatoid arthritis, psoriasis, multiple sclerosis or Crohn's disease contribute to appearance of PML in other diseases, non-HIV related (39). Although survival increased, long term neurological sequelae in PML patients were not very well known. As long as PML is not a curable disease, by an specific treatment, persistence of immune restoration is essential for survival of these patients. Many patients from literature achieving this goal maintain this status and no reactivation or relapses were noticed (40, 41).

In developing rehabilitation strategies for PML in HIV-positive patients, both caregivers and professionals must take into consideration their

external support (42). The attitude and rehabilitation program should be constructed similar with those for patients with cancer, or multiple sclerosis (43,44).

Our study sustain the introduction of MDR program in HIV-positive patients, especially when is complicated by neurological disorders such as PML. At the end of the treatment, our patient showed better performances at left upper member, despite the ataxic left hemiparesis deficits. We can further admit that clinical PML symptoms were ameliorated by physical rehabilitation, although the treatment was applied after few months of symptoms appearance. The increased activation could be recorded by neurological abilities or hydro-kinotherapy (7), along with climatic factors among the effects of balneal cures which influence the quality of life of patients (8, 11), admitting the idea of the consultants' professionalism and experience in the management of changes specific to health systems (9).

In this context, we only can assume that MDR might be used by routine in the practice of HIV-positive patients like in different other disability disorders. Although the number of patients remains limited, physical exercises have been showed to contribute an improving aerobic capacity, along with immune restoration in HIV patients (45,46).

Therefore, in patients with HIV and PML the role of physical rehabilitation could play an important role in achieving their health along with integration in their communities.

Conclusions

Although our study showed that MDR treatment can be highly encouraging in HIV-positive patient with PML, additional studies are demanded in order to achieve this aim. Therefore, larger studies should be acquired in order to identify potential candidates for achieving rehabilitation outcome.

Author contributions.

The authors contributed equally to the work.

Declaration of conflict of interests.

There is no conflict of interest for any of the authors regarding this paper.

Informed consent.

An informed consent was obtained from the patient presented in this case report

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