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CASE REPORT

"Lack of knowledge is no excuse" HIV positive patient with progressive multifocal leukoencephalopathy. Case report from Kenya

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Abstract

Progressive multifocal leukoencephalopathy (PML) is a severe demyelinating disease that affects the central nervous system, which has high morbidity and mortality and no effective, targeted therapies are available. According to the data from developing countries, it affects about 3 to 5% patients who are HIV positive. We present a case of a 27-year-old patient, who got infected with the HIV virus from his mother. The patient had poor compliance to the therapy since its initiation. Due to poor compliance and immunological and virological failure of the first line ARVs, the patient developed PML. Despite confirmed diagnosis of PML and change of the regimen to the second line ARVs, due to progression of the condition, he sought care of an unknown physician, who prescribed therapy with azathioprine 150 mg twice daily, which the patient used for more than 2 weeks. Despite immediate virological suppression, the condition significantly worsened, until the patient developed paraparesis, postural tremor, head tremor, severe dysarthria; he was not able to walk, eat or express himself.

The major roadblocks to diagnosis of PML include poor access to health care in general, as well as poor knowledge of the rare condition among the health care professionals. Therapy with azathioprine has been proved to be associated with the development of PML.

Thus, in resource limited settings, there is an urgent need for improved access to health care and imaging and laboratory diagnostic means, which would decrease the economic and social burden of severe conditions, such as PML.

INTRODUCTION

Progressive multifocal leukoencephalopathy (PML) is a severe demyelinating disease that affects the central nervous system, which has high morbidity and mortality and no effective, targeted therapies are available. It is caused by human JC polyomavirus (known as JCV), which was first isolated and characterized, the name "JC" being derived from the initials of the patient with PML. (White & Khalili 2011). PML primarily affects individuals with chronically and severely suppressed immune system, i.e. individuals infected with HIV virus, individuals with haematological

malignancies and individuals on immunosuppressive therapy.

JCV is ubiquitous in the human population and at least 50% of the population is seropositive for JC virus. (Adang & Berger 2015). According to the data from developing countries, it affects about 3 to 5% patients who are HIV positive. (Ferenczy *et al.* 2012). PML is considered an AIDS-defining disease and despite the availability of HAART, it is still considered a major neurological complication of the HIV infection.

PML has been also associated with the use of various immunosuppressive drugs.

In general, prognosis of PML still remains dismal. HIV+ patients with PML still face poor outcomes, with ~50% of them dying within 2 years from the disease onset. (Pavlovic *et al.* 2015).

CASE REPORT

A 27-year-old male regularly attended a primary health clinic providing comprehensive care for HIV positive clients in the suburbs of Nairobi. At the age of 11 years, he was diagnosed as HIV positive; the transmission of HIV virus in his case was concluded as vertical from his mother. According to the patient's report, he was then initiated on the first line ARV (antiretroviral) therapy with zidovudine, lamivudine and nevirapine as well as on prophylaxis with sulfamethoxazole-trimethoprim (SMZ-TMP). From the initiation of the therapy, the adherence of the patient had been poor, yet according to the patient he developed no significant complications of the underlying disease. At the age of 25 years, for the first time, he sought care at our clinic due to oral thrush. At that time, he reported that he had defaulted from the ARVs and SMZ-TMP 3 years ago. He expressed his wish to start the therapy again as he was aware of possible consequences of his unmanaged condition. In October 2013, based on the respective national guidelines, he was re-initiated on zidovudine, lamivudine, nevirapine and SMZ-TMP with CD4 count 11 cells/μl and viral load of 206,450 copies/ml. Since the re-initiation of the ARVs, despite intense counselling, the patient's adherence to the therapy had been poor with frequent short-term discontinuations of the therapy. The CD4 count and viral load were fluctuating in the range from 9 to 124 cells/μl and 23,209 to 104,748 copies/ μl, respectively. Due to poor adherence and refusal of the second line ARV therapy, despite probable virological failure, the patient continued with the above mentioned regimen with no clinical signs and symptoms of the underlying disease.

In June 2015, the laboratory analysis results were as follows: CD4 count 9 cells/μl and viral load was 433 copies/ml and the patient reported excellent adherence for the past one month. However, at the beginning of September 2015, he entered the clinic with dizziness, dysarthria, ataxia, poor concentration and reduced dexterity persisting for one week. Based on a viral load result of 13,206 copies/μl, done in September 2015, and following intense counselling, he was immediately switched to the second line ARV therapy with tenofovir, lamivudine, atazanavir/ritonavir. He was also referred for a CT scan of the brain, which, due to low socioeconomic status, came 3 weeks after the onset of the symptoms.

The CT scan showed a single, ill-defined, hypoattenuating, non-enhancing lesion in the right cerebellar hemisphere measuring approximately 2.5 (AP) × 2 cm (T) × 1.5 cm (CC). With a working diagnosis of progressive multifocal leukoencephalopathy, the patient was referred for a MRI of the brain. However, again due to financial constraints, the MRI was done only in October 2015 and showed three demyelinating lesions – two in the cerebellum and one around the posterior ventricle, but confirmed the diagnosis of PML. Due to financial constraints, no other procedures, which would support the diagnosis of PML, were performed.

At that time the patient sought care from another clinician, whose diagnosis was unknown, however the patient was prescribed with azathioprine 150 mg twice daily and deflazocort 12 mg twice daily, which the patient took for 16 days. Since September 2015, the condition of the patient gradually worsened. In October 2015, he again entered our clinic with diplopia, severe ataxia, postural tremor and severely impaired dexterity. He began with physiotherapy, had excellent adherence to the second line ARVs and viral load level was at that time 297 copies/ml. In December 2015, the condition of the patient significantly worsened; gradually, he developed paraparesis, postural tremor, head tremor, severe dysarthria; he was not able to walk, eat or express himself. Currently, he continues with the second line ARV therapy with complete virological suppression and physiotherapy with no improvement of his condition.

DISCUSSION

Our patient and his family – he lived only with his mother and two siblings, who were HIV negative – had low socioeconomic status. Despite the low socioeconomic status, the patient studied Law at one of the national universities in Kenya and had only three months to graduation.

He suffered from stigmatisation in the family, where only his mother knew about his status and no one else was allowed to get to know about it, and low self-esteem. He was not able to engage in close friendships with his peers or have a relationship with a girl.

Among the factors significantly contributing to the development of the PML included also stigmatization caused by improper disclosure of his status when he was 18 years old, defaulting from the treatment (for 3 years) and refusal of the timely initiation of the second line ARVs. The patient was provided with intense counselling services and was well aware of possible outcomes of his condition including virological failure of the

first line. Despite all the possible interventions, he was reluctant about taking the second line ARV therapy (Duque *et al.* 2010).

The fact, that he sought care from another physician, who for an unknown reason prescribed therapy with azathioprine for 16 days, may have influenced the progression of the disease as well. Therapy with azathioprine has proven to be associated with the development of PML (Arkema *et al.* 2012).

PML is a devastating disease, which in the case of our patient led to severe disability as well as loss of economic potential of the patient (Tan *et al.* 2009; Engsig *et al.* 2009).

CONCLUSION

There is a lack of data concerning PML from the low resource countries, including Kenya. The major roadblocks to diagnosis of PML include poor access to health care in general, as well as poor knowledge of the rare condition among the health care professionals (Santos *et al.* 2013).

Contributing factors to the development of progressive multifocal leukoencephalopathy include not only unknown HIV-positive disease status, antiretroviral drug resistance, poor drug compliance and recreational drug abuse; but also low socioeconomic status, poor access to quality health care, laboratory and imaging diagnostic methods and generally low knowledge level concerning this rare condition among the healthcare professionals in low income settings (Cinque *et al.* 2009).

We believe that low socioeconomic status of an HIV positive patient increases the probability of the development of PML due to the above mentioned facts, thus leading to higher morbidity and mortality (Bowen *et al.* 2016).

The presented case clearly demonstrates the need for a timely switch to the second line ARV therapy in settings where testing of resistance to the first line ARVs is not available as well as the need for prompt diagnosis of the etiology of neurological symptoms associated with probable HIV-related diseases (Bowen *et al.* 2016). Although, introduction of HAART has led to decrease in the incidence of progressive multifocal leukoencephalopathy, in low income settings this condition still has a huge and devastating social and economic impact on the patient and family, as well as society.

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