

A CASE OF PROGRESSIVE MULTIFOCAL LEUCOENCEPHALOPATHY AND CEREBRAL TOXOPLASMOSIS IN AN HIV-INFECTED PATIENT

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Abstract. *Progressive multifocal leukoencephalopathy (PML) is an opportunistic infection of the central nervous system (CNS) caused by the reactivation of John Cunningham polyomavirus (JCV). Most often, this disease is observed in patients with severe immune suppression, such as those with AIDS. Cerebral toxoplasmosis results from the reactivation of a latent infection with Toxoplasma gondii, an intracellular parasite. This parasitosis is relatively rare in the United States, while in some regions of Europe the seropositive population is over 90%. Similarly, to PML, cerebral toxoplasmosis develops in stages of advanced immune deficiency. Both of these opportunistic infections of the central nervous system can cause severe neurological symptoms, and their simultaneous presentation can represent a diagnostic and therapeutic problem. We present a case of a 59-year-old patient with a newly diagnosed HIV infection with manifestations of epilepsy and progressive cognitive impairment. The patient was diagnosed initially with cerebral toxoplasmosis and subsequently with progressive multifocal leukoencephalopathy.*

Key words: cerebral toxoplasmosis, progressive multifocal leukoencephalopathy, AIDS, immune deficiency, survival

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INTRODUCTION

Progressive multifocal leukoencephalopathy (PML) is an infection occurring as a severe demyelinating process of the CNS. It is caused by John Cunningham polyomavirus (JCV), which is a DNA virus of the genus Polyoma. It is mostly observed in severely immunosuppressed patients, such as those with AIDS. Severe immune deficiency is common, but not prerequisite for the development of PML, although CD4 counts of the patients are usu-

ally below 100/μl at the time of disease presentation. Overall, 4-6% of the patients infected with HIV develop progressive multifocal encephalopathy. In the era before the introduction of highly active antiretroviral therapy (HAART), the prognosis for patients with PML was poor. The median interval between the onset of the first neurological symptoms and the fatal outcome was 3 to 6 months. Survivors beyond 1 year were usually those among whom PML was the first AIDS-defining disease. According to a Spanish study, 30% of patients died within 2 years after the disease

onset despite HAART. According to an Italian study, patients receiving HAART had an average survival of 245 days and those without therapy 66 days.

Cerebral toxoplasmosis results from the reactivation of a latent infection with *Toxoplasma gondii*, an intracellular parasite. This parasitosis is relatively rare in the United States, while in some regions of Europe the seropositive population is over 90%. Similarly, cerebral toxoplasmosis develops with severe immune deficiency.

CASE PRESENTATION

We present a case of a 59-year-old patient who tested positive for HIV in November 2018. The patient's complaints dated back to September 2018, while during his stay in Nigeria he developed a generalized tonic-clonic seizure with loss of consciousness. An MRI was performed, and a brain abscess was diagnosed, then he was transported to Bulgaria, where he was admitted to a neurosurgery department. After establishing his HIV status, he was transferred to the Department for Acquired Immunodeficiency of the Specialized Hospital for Active Treatment of Infectious and Parasitic Diseases in Sofia. Upon admission to the department, the patient was conscious, contact, sometimes inadequate, afebrile. No deviations in the somatic status were observed. From the examination of the neurological status there was no evidence of meningeal irritation, brisk bilaterally symmetrical tendon reflexes; no pathological reflexes and automaticity of the lips were found. During the initial hospitalization of the patient in the Department for AIDS, there were laboratory data of anemia (haemoglobin level was 87 g/l), without significant deviations in the other parameters of the blood count and biochemistry. The supratentorial CT scan of the right parietotemporal area showed a hypodense area with perifocal edema as well as small hypodense foci to the left in the basal nuclei area and the external capsule. After an intravenous application of contrast agent, the described edematous area on the right parietal side was visualized as an oval lesion with dimensions of 30/27 mm and peripheral contrast (Fig. 1). The patient had extremely severe immune deficiency with CD4+ T-cell values of 2 cells/ μ L (reference values are between 400 and 1600 cells/ μ L); CD8+ T-cells – 165 cells/ μ L (reference values are between 200 and 1100 cells/ μ L); and high HIV viral load (VL) – 1,236,452 c/ μ L. An ELISA test was performed for detection of IgG antibodies against *Toxoplasma gondii* which was positive. Due to the specific characteristics of the lesions described, which were indicative of cerebral toxoplasmosis and the positive serology, exactly this opportunistic parasitosis was considered and the cor-

responding treatment with clindamycin (3 x 600 mg i.v.) was carried out. In November 2018 antiretroviral therapy with abacavir/lamivudine (600/300 mg x 1 tab./d.) and dolutegravir (50 mg x 1 tab./d.) was also initiated. Antiepileptic therapy with depakine (500 mg p.o.) was also given. The patient was discharged in the end of February 2019 in satisfactory general condition. Since mid-March 2019, the patient suffered generalized tonic-clonic seizures again. An MRI was performed which revealed reduction in the lesions diagnosed as cerebral toxoplasmosis. Tevaleptin (300 mg p.o.) was added to the antiepileptic therapy. The next hospitalization of the patient in the department was in July 2019, due to persistent changes of consciousness presenting as confusion at times. The patient's immunological and virological results at this time were as following: CD4+ T-cells – 146/ μ L; CD8+ T-cells – 729/ μ L; VL < 50 c/ μ L (undetectable). During this hospitalization, a lumbar puncture was performed and the examination of CSF showed slightly increased values of protein (0,76 g/l) without other abnormalities. The cerebrospinal fluid was examined for JCV and the PCR test was positive – 2.36×10^3 copies/ml. Control magnetic resonance imaging was performed and it revealed significant reduction of the dimensions of the lesions characteristic of cerebral toxoplasmosis as well as the demyelinating changes in the white matter of the brain (Fig. 2).

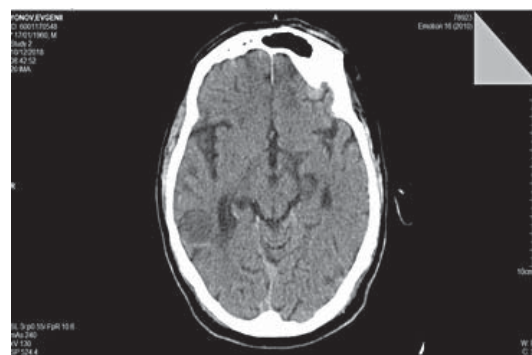


Fig. 1. First MRI – before treatment

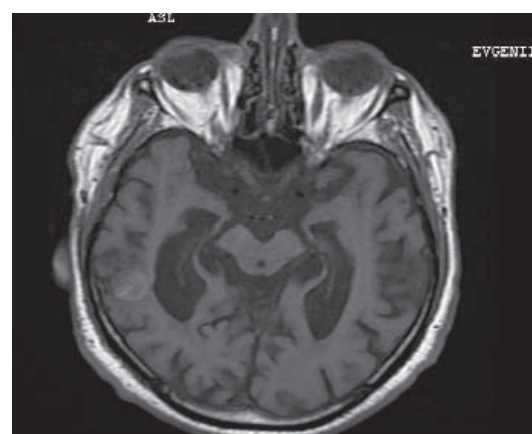


Fig. 2. MRI at the 3rd year of the treatment

The examination of the somatic status of the patient revealed no abnormalities. However, intermittent partial epileptic seizures continued regardless of triple antiepileptic therapy (depakine – 500 mg p.o., levetiracetam – 500 mg p.o. and tevaleptin – 300 mg p.o.), as well as the cognitive disorders.

As of August 2021, the patient's antiretroviral therapy was changed due to inability to achieve undetectable viral load levels and unsatisfactory immune response (CD4 – 220/ μ L; CD8 – 1281/ μ L; VL < 73 c/ μ L (detectable). The patient's current HAART regimen is emtricitabine/tenofovir alafenamide/bictegravir (200/25/50 mg x 1 tab./d.) and the most recent immunological and virological results are as following – CD4 – 361/ μ L; CD8 – 1201/ μ L; VL < 20 c/ μ L (undetectable).

DISCUSSION

The presented case is of particular interest due to the overlapping of two AIDS-defining opportunistic infections with severe neurological symptoms. Although cases in Europe have been reduced by almost 1/4 as a result of the combined antiretroviral therapy, cerebral toxoplasmosis remains one of the most important neurological opportunistic infections among HIV-infected patients in many regions of the world. The clinical manifestations of the disease depend upon the localization of the lesions. The main manifestations include focal neurological symptoms – paresis, speech disorders or sensory disorders. Epileptic seizures in the absence of other symptoms could be the leading initial presentation, which was the case with our patient. The patient's satisfactory response to clindamycin therapy (since there was not another therapy for toxoplasmosis available in Bulgaria), in parallel with the antiretroviral and symptomatic therapy, did not direct us towards searching for another reason for the neurological symptoms during the patient's first hospitalization. During the subsequent hospitalization due to deepening of the patient's cognitive impairment, we purposefully searched for an additional cause of the neurological deficit, since the control MRI imaging showed a significant reduction of the cerebral toxoplasmosis lesions. CSF was tested for JCV by means of PCR and specific genomic sequences of the same virus were demonstrated, confirming a second neurological opportunistic infection. This explained the patient's persistent cognitive impairment. PML is a disease with a poor prognosis, especially in combination with another opportunistic infection affecting

the CNS, as in the presented case of cerebral toxoplasmosis. Modern antiretroviral therapy provides the possibility of immune recovery and longer patient survival by means of achieving high concentration of the antiretroviral drugs in the CNS. As it could be seen in our case, the patient had a good immunological response and optimal viral suppression, despite his advanced age and severe initial immune deficiency.

The supratentorial CT scan of the right parietotemporal area showed a hypodense area with perifocal edema as well as small hypodense foci to the left in the basal nuclei area and the external capsule. After an intravenous application of contrast agent, the described edematous area on the right parietal side was visualized as an oval lesion with dimensions of 30/27 mm and peripheral contrast.

The control MRI revealed significant reduction of the dimensions of the lesions characteristic of cerebral toxoplasmosis as well as the demyelinating changes in the white matter of the brain.

Ethical approval and written informed consent:

Written informed consent was obtained from the patient for publication of this case report and the accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal upon request.

Author contribution: NY described the case and prepared the present manuscript. NY, DS and RG were involved in the diagnosis establishment and treatment of the patient. IR and NT performed the parasitological tests. MN performed the immunological tests. IA performed the virological tests. All authors read and approved the final manuscript.

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ERRATUM

Поради допусната техническа грешка в сп. Acta Medica Bulgarica бр. 4/2022 г. DOI номерата на част от статиите са дублирани с тези на други статии от 2021 г.

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