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Case report

Disappearance of white matter lesions on MRI and clinical recovery after initiating antiretroviral therapy in a case of HIV infection presenting as spastic paraparesis

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ABSTRACT

We present a case of a 30-year-old Polish female who presented with increasing for about 2 years spastic paraparesis and urinary incontinence. She denied any risky sexual behaviors, drug abuse, there was no history of surgery or blood transfusions. MRI of the brain showed diffuse, hyperintensive in T2, poorly defined lesions in the white matter. About 3 months later paraparesis increased and control MRI showed progression of previously described lesions. She was then diagnosed with HIV infection. There was a suspicion of progressive multifocal leucoencephalopathy (PML) or vacuolar myelopathy in the course of HIV infection. Antiretroviral treatment was initiated leading, together with rehabilitation, to a progressive improvement of symptoms. Pathological lesions on brain MRI completely disappeared. In conclusion, HIV test should be done in every patient with neurological signs of unknown cause.

1. Introduction

According to the World Health Organization, since the beginning of the epidemic in 1985, almost 70 million people have been infected with HIV (human immunodeficiency virus) worldwide and approximately 35 million people have died of AIDS (acquired immunodeficiency syndrome). According to the Polish National Health Institute – National Institute of Hygiene, since 1985 till the end of November 2013, there have been 17 389 infected individuals in Poland: 3022 have been diagnosed with AIDS and 1237 have died. Disorders of the peripheral and central nervous system develop in over half of the infected individuals [1]. There are two major groups of

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nervous system disorders encountered in HIV-infected patients – primary neurological disorders and opportunistic infections. Progressive multifocal leukoencephalopathy (PML) is an opportunistic infection that is the third most common cause of neurological symptoms in HIV-infected patients, after Toxoplasma encephalitis and HIV-associated neurocognitive disorder (HAND) [2]. Neurological symptoms rarely occur as early signs of AIDS. That is why if a patient is not in a group at risk of HIV infection, diagnosis in this direction is often omitted. It leads to the delay of both diagnosis and introduction of an appropriate treatment of potentially reversible neurological deficits. In Polish literature there are no case reports concerning neurological presentation of HIV infection that is why we decided to present this problem.

2. Case report

A 30-year-old Polish white female was admitted because of increasing for about 2 years spastic paraparesis and urinary incontinence (treated with oxybutynin). She was married, childless, lived in the country, had secondary education and was denying any risky sexual behaviors and drug addiction. There was no history of surgery or blood transfusions. Her problems began in 2008 when erythema on the cheeks occurred, increasing after sunlight. There was a suspicion of rosacea, but skin lesions withdrew without any treatment. In April 2009 she suffered from pain of upper limbs, since September 2009 she has had pain of the right lower limb. In the anamnesis there has been a history of recurrent depressive disorders treated for 2 years with citalopramum and secondary amenorrhea for 6 months. The patient connected all these complaints with severe stress (death of her father, departure abroad). In the laboratory results there has been thrombocytosis and high ESR since 2008. In the examination the presence of tumor-like lesion on the right side of her neck, tonsils enlargement, stomach pain and periodically – liver enlargement, were observed. In March 2010 she was hospitalized in the department of internal diseases where connective tissue diseases were excluded. Because spastic paresis of lower limbs was the main symptom, she was hospitalized in neurological department outside our hospital, with the suspicion of multiple sclerosis, however MRI of the brain and cervical spinal cord did not reveal any abnormalities. As she was admitted to our Department in August 2010 in neurological examination there was spastic paraparesis, more pronounced on the right side, with bilateral Babinski sign, no touch disorders, walk with one-side help. She also complained of memory problems, anxiety and difficulties with concentration.

In her laboratory results at the time of presentation in our Department:

Basic laboratory panel showed high ESR (↑91, 81 mm/h), CRP – normal, in morphology: WBC = 9.28, 6.94, RBC = 3.78, 3.89, HGB = 9.6, 10, MCV = 77.6, 80.5, PLT = ↑573, ↑659. There was anemia of chronic diseases: iron: ↓15 μg/dl (normal level: 50–170); transferrin: ↓106 mg/dl (normal level: 250–380); ferritin: ↑581 ng/ml (normal level = 10–291). In urinary sediment: leukocytes-countless, bacteria-multiple; in urine culture: doubtful result, mixed bacteria. Vit. B12 level was normal, there was no pathology of coagulation; liver, and kidney function tests were normal. In the CSF: cytosis-12 cells/μl, protein = 60 mg/dl, glucose = 53 mg/dl, oligoclonal bands were negative.

Autoimmune lab tests showed polyclonal gammapathy (immunoglobulins IgA, IgG, IgM – increased), C3 and C4 – normal, Ab against *Borrelia burgdorferi* – negative in the blood and in the CSF, RF, ANA, ANCA – negative, beta-2-microglobulin = ↑6.5 mg/l (normal level 0.7–1.8), Ca125, CA 15–3, CA 19–9, CEA, AFP – normal, the Wassermann test – negative, CMV IgM – negative, IgG – positive, EBV IgM – negative, IgG – positive, HSV IgM – negative, IgG – positive.

Neurophysiological examinations. Visual evoked potentials revealed prolonged to 120–124 ms latency of P100 bilaterally, in EMG there were features of neurogenic process in distal parts of the limbs.

Radiological results. In the X-ray of the chest pleural effusion on the right side was noticed (it disappeared in the control X-ray), ultrasonography of abdomen and gynecologic ultrasonography were normal, in neck ultrasonography there were multiple augmented (to 15 mm) lymph nodes on both sides. On MRI of the cervical, thoracic, lumbo-sacral region of the spinal cord and spinal cone – there was no pathology, whereas MRI of the brain showed diffuse, hyperintensive in T2, poorly defined lesions in semioval center, paraventricularly, at the back of the trunks of the lateral ventricles, without contrast enhancement, an atrophical enlargement of cerebral ventricles and cortico-subcortical atrophy (Fig. 1).

About 3 months later paresis of lower limbs increased, she needed walker aid and control MRI of the brain showed progression of previously described lesions (Fig. 2). Antibodies against HIV1/HIV2 were present, confirmatory test (Western blot) was positive, sgp120, gp 41, p31 were present. There was a suspicion of PML or vacuolar myelopathy in the course of HIV infection.

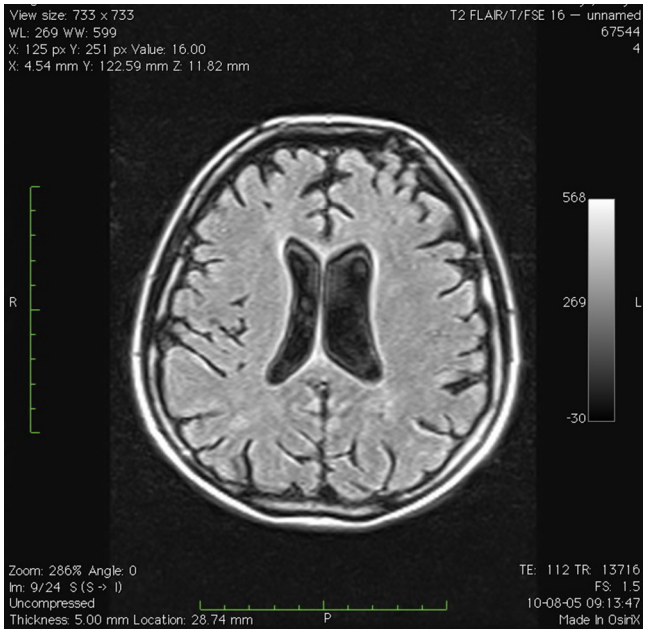

Fig. 1 – MRI of the brain (FLAIR weighted image): diffuse, hyperintensive, poorly defined lesions in semioval center, paraventricularly, at the back of the trunks of the lateral ventricles, without contrast enhancement, an atrophical enlargement of cerebral ventricles.

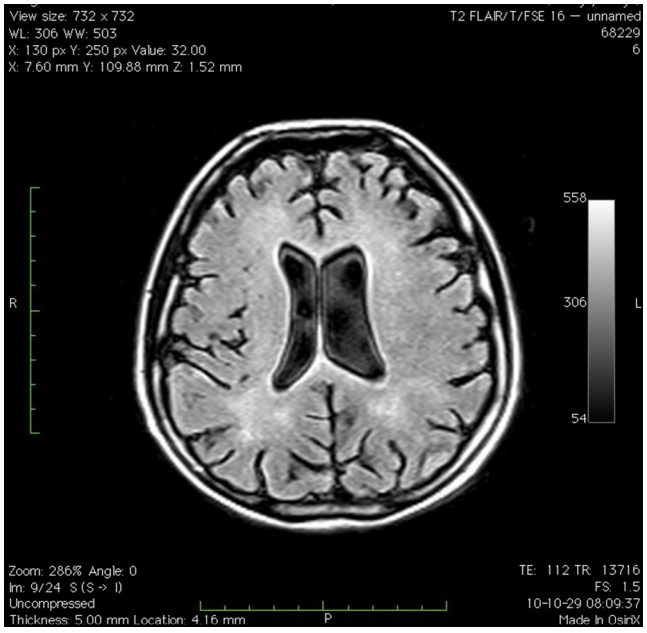

Fig. 2 – MRI of the brain (FLAIR weighted image), 3 months later: progression of previously described lesions.

Antiretroviral treatment was then initiated, according to ARV scheme: lamivudine, tenofovir, darunavir, ritonavir. Then due to increase in the number of HIV RNA copies in serum (84 copies per ml) the pharmacotherapy was intensified with introduction of maraviroc. The treatment regimen together with rehabilitation lead to progressive improvement of symptoms: paraparesis decreased and the patient was able to walk with nordic-walking sticks. The MRI of the brain conducted about 10 months later normalized and pathological paraventricular lesions completely disappeared (Fig. 3). Along with treatment continuation, neurological status of the patient recovered and finally she does not use any walking aids.

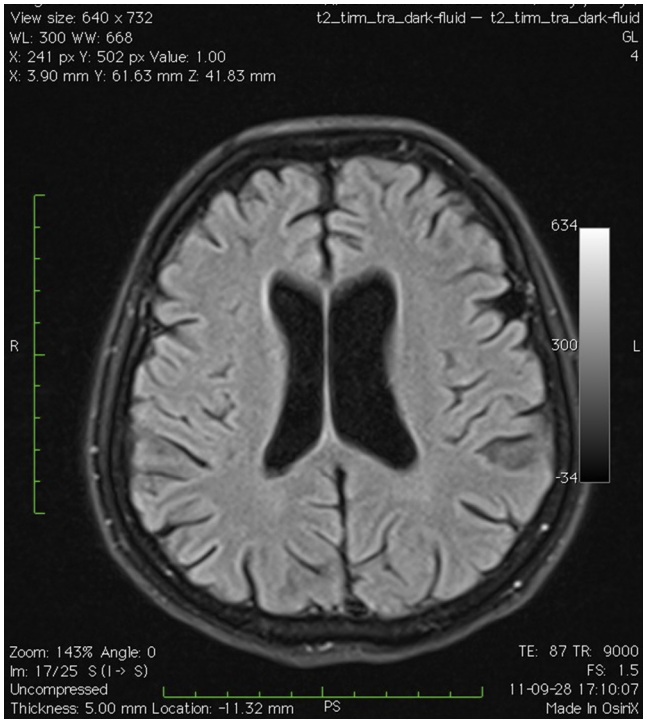

Fig. 3 – Control MRI of the brain (FLAIR weighted image), 1 year later: disappearance of previously described lesions.

3. Discussion

HIV positive patients present initially with neurological symptoms in about 10–20% and about 40–60% of these patients develop neurological manifestation in the course of the disease [3,4]. Brain disease that is caused by HIV itself includes HAND syndrome that, according to neuropsychological testing, can be divided into three categories: asymptomatic neurocognitive disorder, mild neurocognitive disorder (MND) and HIV-associated dementia (HAD). Brain MRI in HAND syndrome may show leukoencephalopathy and generalized cerebral atrophy [5]. Our patient presented problems with memory and concentration but otherwise did not have any other problems with cognition. Poor performance in two or more domains on neuropsychological or mental status testing in a patient who does not report or demonstrate cognitive decline is classified as asymptomatic neurocognitive impairment [5].

Diseases that are caused by infectious, autoimmune and neoplasmatic processes secondary to immunodeficiency in the course of HIV infection include progressive multifocal leucoencephalopathy (PML), toxoplasmosis, CNS lymphoma, fungal infections (e.g. cryptococcal meningitis), tuberculous meningitis, cerebrovascular diseases, neurocysticercosis and cytomegalovirus encephalitis. Because of clinical picture and the results of additional studies (blood, CSF, brain MRI) the most probable (but not confirmed) diagnosis seems to be PML.

PML is an infection of oligodendrocytes caused by an endogenous reactivation of the JC-virus (John Cunningham virus – from the first identified patient), a human polyomavirus belonging to papovaviridae family. This reactivation takes place during states of immunosuppression including AIDS, neoplasms, leukemia, in transplant recipients and also in patients receiving HAART (in the period of immune recovery) and monoclonal antibodies such as natalizumab (used in the treatment of multiple sclerosis and Crohn's disease) [6], rituximab (used in lupus) [7] and efalizumab (used for the treatment of psoriasis) [8–10]. PML is characterized by the presence of widespread demyelinative lesions of the CNS [11]. Neuroimaging studies in PML reveal typically bilateral, asymmetrically distributed, confluent, predominantly subcortical white matter lesions, located close to the gray-white matter junction and in the periventricular region. They show high signal intensity on T2 weighted imaging and low signal intensity on T1 weighted imaging [12]. In our patient such diffuse lesions were observed in semioval center, paraventricularly and at the back of the trunks of the lateral ventricles; there was also hydrocephalus ex vacuo and

cortico-subcortical atrophy. Vacuolar myelopathy, that could have been also taken under consideration in differential diagnosis, is characterized by the presence of MRI changes in the spinal cord–atrophy or intrinsic cord signal abnormalities: T2-hyperintensive symmetric nonenhancing areas, that may be confined to the posterior columns, especially the gracile tracts, or may be diffuse; they result from extensive vacuolation [13]. In our case, there were no pathologies in the spinal cord and the lesions in the brain were suggestive of leukoencephalopathy, particularly of PML.

Clinically PML can manifest as almost any neurological symptom as it may localize in any part of the brain. PML is characterized by an insidious onset and steady progression of symptoms, like in a described case. Weakness, paresis, apathy, ataxia, dysarthria and confusion are reported more frequently than others [14]. In our patient paraparesis with urinary incontinence was the leading symptom but she also complained of cognition problems.

In the described case we did not establish the etiological factor of brain lesions in the course of HIV infection. It may be called a probable PML because there were clinical and imaging features of the disease but neither CSF examination as to the presence of JCV DNA nor histopathology with demonstration of JCV DNA/protein were done [15]. In HIV infection antiretroviral therapy is the principal approach in case of PML and neurological and radiological improvement in our patient after 10 months of antiretroviral treatment duration could confirm the suspicion of the disease [16].

We should always remember about the possibility of HIV infection – our patient has not been diagnosed until 2 years of symptoms onset although she had been hospitalized previously in internal diseases departments. In conclusion, a HIV test should be done in every patient with neurological signs of unknown cause. It can enable effective treatment when HIV infection is diagnosed.

Conflict of interest

None declared.

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None declared.

Ethics

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; Uniform Requirements for manuscripts submitted to Biomedical journals.

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