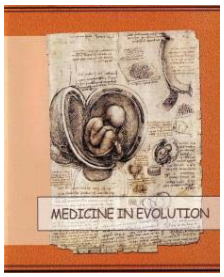
Progressive multifocal leukoencephalopathy (PML). A case report and review of literature.



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Abstract

Progressive multifocal leukoencephalopathy (PML) is a disease that produces neural demyelination in the central nervous system caused by reactivation of a DNA virus that remains dormant in immunocompetent individuals, known as John Cunningham virus (JCV) occasioned by a prior HIV infection with immunosuppression.

We present the case of a 21 years old HIV positive individual with diffuse muscular weakness, dysarthria and severe ataxia and impossibility of maintaining neck and head upward position. Magnetic resonance imagery revealed in the white substance of bilateral cerebellar hemispheres and brainstem extensive T1 hypointense and T2/FLAIR hyperintense lesions, accompanied by discrete water restriction diffusion of water restriction and insignificant contrast substance outlet. Thus, a PML diagnosis was established on radioimagistic grounds.

Keywords: progressive multifocal leukoencephalopathy, brain, magnetic resonance, immunosupression

INTRODUCTION

Progressive multifocal leukoencephalopathy (PML) is a demyelinating disease of the central nervous system caused by reactivation of John Cunningham virus (JCV) - DNA virus, genus Polyomaviridae, Papovaviridae family – in severe immunosuppressed individuals, characterized by typical histopathological and non-radiological changes (1). This is associated with both the both HIV virus types 1 and 2 (3.4). Thus, HIV infection is responsible for approximately 85 % of the cases and the prevalence in the population is of 4 to 5 % (5,6,7). It is one of the pathologies that define the status of AIDS in immunocompromised patients. This pathology has been confirmed also in correlation with the treatment with monoclonal antibodies, however in a much lower percentage (8). Below the age of ten years the vast majority of the population is already infected by John Cunningham virus (JC), but manifests extremely rare (5). Those who develop the disease are more likely to submit a deficient immune system, such as those infected with HIV/AIDS, patients diagnosed with leukemia or Hodkin lymphoma but also those who receive immunosuppressive medication (8).Overall mortality rate raises to 30-50% in the first months of the diagnosis, but fluctuates proportionally with the evolution of disease and indicated treatment. Survivors may experience some neurological sequelae. No correlation has been conclusive between JCV structure and its neurovirulence (9). Symptoms are variable with each case, among we are mentioning the following: loss of coordination and memory, aphasia, visual disturbances, personality disorders and muscular hypotonia in the limbs. Paraclinical examinations contributing in the disease diagnosis are: computer tomography, nuclear magnetic resonance, documenting the presence of the JC virus in cerebrospinal fluid, electroencephalogram and, in selected cases when benefits are above risks, cerebral biopsy (10,11). Upon the date of elaborating this article no significantly effective treatment has been shown yet. Thus, the only way to alleviate or to halt the progression of the disease consists in maintaining a favorable immune status. Imaging of CNS changes represent an important argument in supporting a PML diagnosis, especially if it remains presumptive in the absence of brain biopsy or JCV identification through CSF - PCR techniques. Nuclear magnetic resonance remains the gold standard because it succeeds in detecting brain damage even during early stages; meanwhile CT examination may reveal normal findings proving useful only in established cases, with obvious clinical symptoms. The advantage of MRI over CT is to use a selection of parameters for visualization and detection of lesions (12).

CASE REPORT

We present the case of a 21-years-old patient diagnosed with HIV infection two years prior to hospital presentation on the occasion of a prolonged febrile syndrome. Objective examination revealed no neck pains, however, without being able to keep a sitting position, difficulties in maintaining a head position, also unable to walk more than a few steps accompanied by diffuse muscular atrophy, dysarthria and severe ataxia. The CD4+ lymphocytes count is 196/mmc.

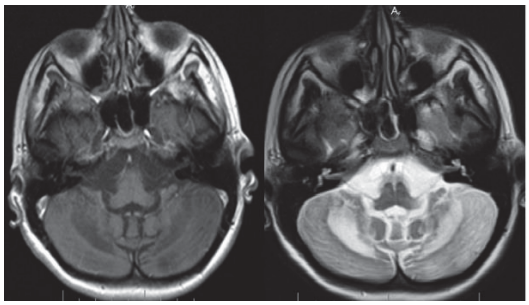

Figure 1. Lesions in hyposignal on T1 and hypersignal on T2 sequences at the level of bilateral cerebellar hemispheres

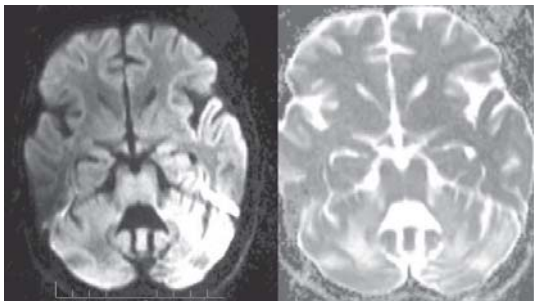

Figure 2. Diffusion sequences in the patient diagnosed with progressive multifocal leukoencephalopathy

Thus, an interdisciplinary medical committee agreed the perform a nuclear magnetic resonance cerebral examination that revealed T1 hypointense and T2/FLAIR hyperintense extensive lesioned areas, accompanied by discrete diffusion of water restriction, with insignificant outlet for the contrast substance. These lesions are highlighted at white substance level of bilateral cerebellar hemispheres as well as the brainstem level. Lesion areas located at the level of bilateral cerebellar hemispheres are part of the criteria for the diagnosis of HIV related PML.

DISCUSSIONS

Reiterating, imaging of CNS changes represent an important argument in supporting PML diagnosis, especially if it has presumptive value in the absence of brain biopsy nor of JCV detection through CSF - PCR techniques. Nuclear magnetic resonance imaging investigation represents the gold standard in such cases, because it succeeds in highlighting the brain tissue damage during earliest stages, in spite of a normal aspect on computer tomography, the latter being useful only in cases where lesions are already established when conspicuous clinical symptoms are already present.

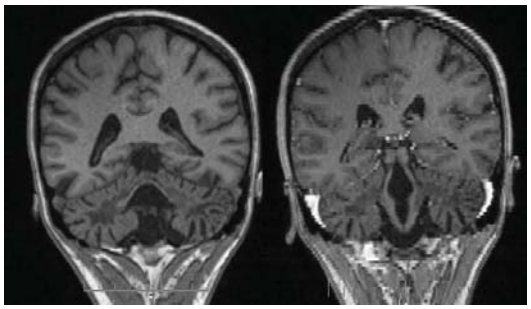

Figure 3. Lesions in T1 sequences in the coronal plane before (left) and after administration (right) of the contrast substance

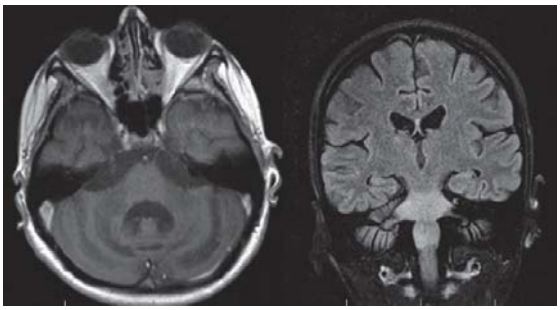

Figure 4. Axial T1 sequence with contrast substance and FLAIR sequence in the coronal plane for the presented case

The advantage of MRI versus CT is the ability of using additional selection of parameters for visualization and detection of lesions (12). In this pathology nuclear magnetic resonance reveals a multifocal, asymmetric periventricular involvement, but also at the subcortical level. However, gadolinium MRI does not have any mass effect or enhancement, but it useful in assessing the U fibers involved mainly in the region of parieto-occipital tissue. Furthermore, it may reveal corpus calosum body involvement in some cases (13-29). In T1 sequences, involved regions are usually in hyposignal while T2 sequences are in hypersignal. The presence of enhancing lesions to certain patients implies a favorable evolution in time.

Lesions, usually, shows peripheral diffusion restriction (13-29). On MRI spectroscopy sequences the decrease of N-Acetyl-aspartate and lactates may be noticed, with concomitant rise of choline and lipids, thus guiding the diagnosis in favor of progressive multifocal leukoencephalopathy (13-29).

CONCLUSIONS

Immunocompromised patients presenting neurological complications in the late stage of the PML disease may have a precise diagnosis through cooperation between doctors. Therefore, in case of health damage admixed with biological constants modification, the attending physician may take in account the indication for further imaging investigations, in selected cases the most reliable being magnetic resonance that would reveal lesions which can support the diagnosis, preferably, without any subsequent risky and difficult cerebral biopsy, just as in the case we have presented, when, through interdisciplinary management a quick, comprehensive diagnosis was feasible without any further biopsy procedure.

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Ethical issues

We have received the ethical board consent within our institution for clinical data acquisition, clinical study publication of and this article.

Conflict of interests

The authors declare no conflict of interest of any kind

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