Concurrent occurrence of multiple sclerosis and primary CNS lymphoma: a case report

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Abstract

We present the patient with the diagnosis of multiple sclerosis (MS), relapsing-remitting form with long lasting remission. Unexpectedly, this patient presented dramatical clinical deterioration and revealed clinical symptoms such as bradypsychia, cognitive symptoms, central vestibulare syndrome, spastic quadruparesis. Clinical findings suggested secondary progressive MS, but MRI called in question this diagnosis. The MRI appearance suggested, that MS had been complicated by a different brain pathological lesion, and the brain biopsy was indicated. A histological examination confirmed primary CNS lymphoma (PCNSL).
This case exemplifies important aspects of clinical neurology. A re-evaluation of the diagnosis of MS should always be performed in a patient when new symptoms are presented that are unusual or could be due to other pathological processes. MRI offers the highly sensitive way to detect the coexistence of MS and other brain disease. Primary goal of imaging modalities is differential diagnosis betveen demyelinating diseases, such as MS and other brain lesions. Advanced focus demand contrast- enhancing and mass-effect lesions. It is important to realize, that contrast-enhancement and brain edema may be mitigated by treatment with corticosteroids. In some cases a brain biopsy is needed.

INTRODUCTION

Diagnosis of multiple sclerosis (MS) is determined with high probability based on clinical symptoms, course of the disease and para-clinical examination: Magnetic resonance imaging (MRI), cerebro-spinal fluid (CSF) analysis, evoked potential responses and urinary bladder dynamic examination. Presently MRI is the most important para-clinial tool for MS diagnosis. MRI reveals multifocal lesions predominantly in white matter which progress in the space and the time. Typically these abnormalities don't correspond to neurological symptomatology. Pathological MS lesions have increased signal on T2 weighted sequence and FLAIR sequence and occasionally correlate with decreased signal on T1 weight sequence. In the acute, inflammatory phase of MS these lesions may disrupt blood- brain barrier (BBB) leading to contrast enhancement [1,2]. Enhancing lesions are usually imaged as a homogenous or ring like enhancing nodules, very specific is incomplete ring like enhancement. Although MS plaques can be found throughout the brain, either gray or white matter, typical occurrence is in peri-ventricular and juxtacortical white matter. Location in brain stem, cerebellum, and spinal cord (mainly in the cervical region) significantly raises the specificity

CASE REPORT

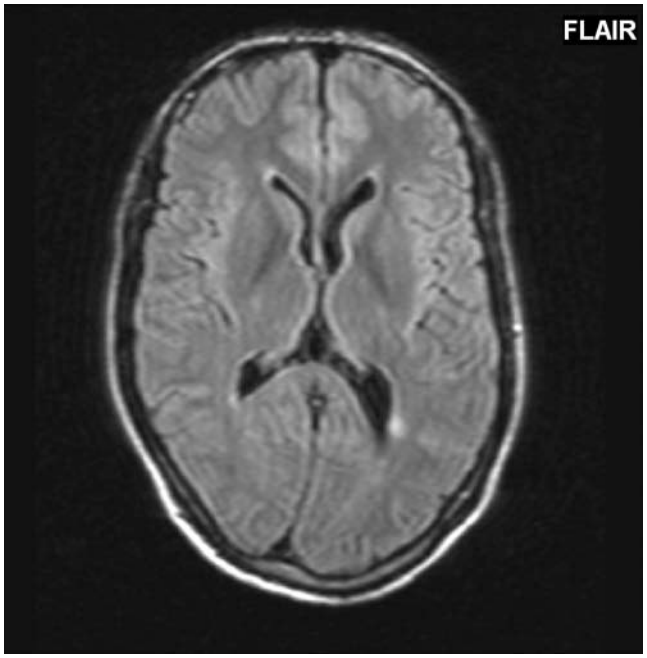

Fig. 1: Transverse FLAIR. Two small supratentorial lesions of increased signal.

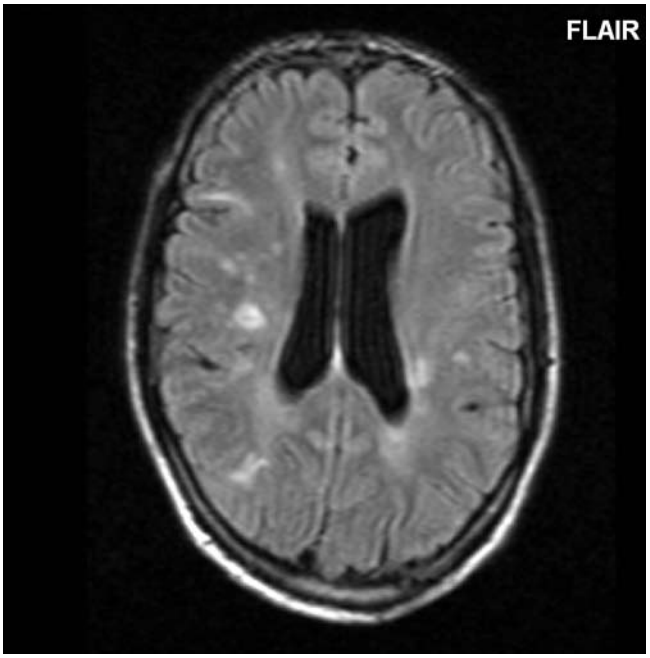

Fig. 2: Transverse FLAIR. Numerous supratentorial hyperintense lesions in the white matter.

for MS diagnosis. Deep gray matter lesions are very unusual.

Primary CNS lymphoma (PCNSL) represents 3.1% of all primary brain tumors. In absolute majority, this is a non Hodgkin lymphoma from B lymphocytes. The occurrence is slightly prevalent in men. Frequently CNS lymphoma is diagnosed in patients with congenital or acquired immunodeficiency. The most frequent location of PCNSL is cerebral hemispheres, basal ganglia, corpus callosum, and cerebellum. Lesions are typically in contact with cerebrospinal fluid spaces, both ventricular or subarachnoidal. There is usually strong and homogeneous contrast enhancement on MRI [3].

CASE PRESENTATION

27 year old male diagnosed in 2001 with relapsing – remitting form of MS. The first symptom was optic neuritis. At the same time he complained of transient paresthesias in left arm and right calf. MRI finding was very discreet with two supra-tentorial periventricular lesions (Fig.1) and one juxtacortical lesion of increased signal on T2 weighted and FLAIR sequences. By McDonald criteria this appearance was not enough for diagnosis of MS. However, CSF findings indicated increased intrathecal IgG synthesis. Follow up MRI performed in 2003 showed new lesions in the supra-tentorial white matter in periventricular and juxtacortical locations. The McDonald criteria for dissemination in space and time were fulfilled at this timepoint. MRI performed in 2005 revealed mild progression again. Progression of MRI appearence did not correlate with clinical findings. Based on MRI findings the corticosteroid therapy was initiated.

In October 2006 the patient was admitted with generalized epileptic seizure (grand mall) and presented with long-lasting confusional state. Neurological examination was without any focal finding. MRI showed again increase of supratentorial T2W hyperintense lesions in the white matter. There was a new wedge-shaped cortico-subcortical lesion in the right hemisphere (Fig.2) and a small lesion with increased signal on T2 weighted sequence in the cervical spinal cord. The patient kept being treated with corticosteroids.

In four months, the patient was re-admitted to the hospital with epileptic seizures and confusion. The secondary progressive form of MS was considered. Epilepsy may be a consequence of MS in about 7.5% of patients, predominantly during secondary progression [4]. The patient was discharged one week later in improved condition. At that time new MRI wasn't performed.

Three weeks later, the patients' condition rapidly deteriorated after viral infection. Patient became somnolent, and confused. Neurological examination showed bradypsychia, cognitive symptoms, central vestibular syndrome and spastic quadruparesis. These untypical symptoms evoked a new investigation. MRI showed multifocal and confluent high signal lesions on T2 weighted and FLAIR sequences, predominantly located in the right brain hemisphere (Fig. 3). These lesions were accompanied with brain edema and with mass effect (deformation of right lateral ventricle and sub-falcine herniation). Contrast enhanced T1 weighted images showed ring like and geographic enhancement (Fig.4). The CSF analysis revealed syndrom of protein-cytological dissociation. Based on clinical course and MRI finding it was suggested, that the MS had been complicated by other CNS disease. Lymphoma, viral encephalitis,

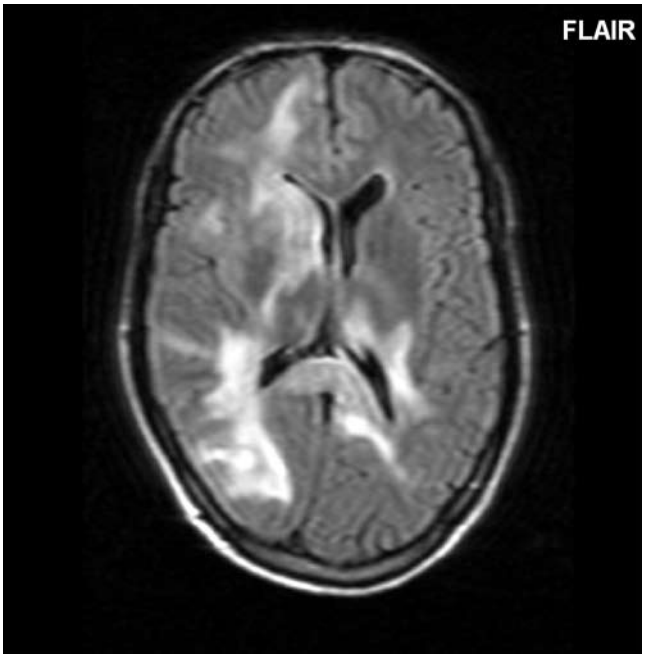

Fig. 3: Transverse FLAIR. Confluent high signal lesions accompanied with edema, predominantly located in the right brain hemisphere.

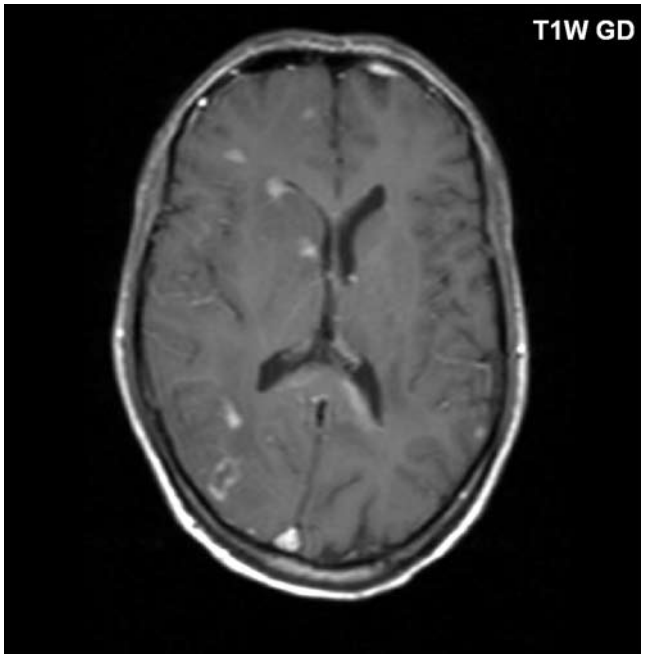

Fig. 4: Transverse T1WI after contrast administration: Ring like and geographic enhancement of pathological lesions in the right hemisphere.

acute disseminated encephalomyelitis (ADEM), and malignant form of MS have been considered.

Stereotactic brain biopsy was performed. Histological examination showed large cell B-cell centroblastic non Hodgkin Lymphoma. Computed tomography (CT) of thorax, abdomen, and pelvis didn't reveal other lesions.

DISCUSSION

Neither clinical picture nor paraclinical test is specific for demyelinating diseases such as MS. MRI is the most important paraclinical tool for MS diagnostics. In 2001 Mc Donald *et al*. recommended diagnostic criteria for MS,[5] in 2005, the Mc Donald criteria were revised. In 2006, new criteria were proposed [6]. New criteria offer a higher sensitivity 72% (2005 Mc Donald, 60%) without compromising specificity – 87%((2005 Mc Donald, 88%). By new criteria the first MRI of the reported patient performed in 2001 already fulfilled criteria for diagnosing MS. Nevertheless, MRI differential diagnosis of white matter lesions remains extensive, because these quantitative guidelines lack qualitative parameters of lesions. Seeing rapid clinical course and in MRI increased signal within the white matter on T2 weighted sequence we must include into the differential diagnosis: Margburg´s disease clinically characterized by a severe clinical course, often with large tumor-like demyelinating plaques. Disseminated encephalomyelitis (DEM) which is often associated with a viral infection or a vaccination. Most of the lesions on MRI are very large, near symmetrical, and enhance with gadolinium [7]. Viral encephalitis, clinical picture and MR finding in viral encephalitis usually resemble ADEM. MR imaging is very non-specific [8]. Vasculitis represents a heterogeneous group of inflammatory diseases such as primary CNS vasculitis, SLE and polyarteritis nodosa. Vasculitis affects blood vessel wall resulting in multiple arterial stenoses and occlusions [9]. All these CNS afflictions can be present without focal, clinical findings.

Differential diagnosis may be difficult in mass-like contrast enhancing MS lesions. Then MRI may mimic another expansive lesions such as abscess, metastasis or primary brain tumor. Often the brain biopsy is needed [10].

In available literature there are three cases describing concurrent occurrence of MS and PCNSL [11–13]. The question is posed whether MS may play the role such as one of the etiological factor of PCNSL. Firstly, Bernard *et al*. [14] postulated the possibility of an epidemiological association between MS and PCNSL. This hypothesis would be supported by the fact that a large number of patients with PCNSL experienced prior 'autoimmune' disease of systemic or neurological site or underwent therapy with corticosteroids or immunosuppressive agents [3]. Both entities have common risk factors and often history of autoimmune diseases [15]. On the other hand the MS cases with a concomitant PCNSL are rare and there is no increased association between them. We suggest that this concurrent occurrence is rather coincidental.

This case exemplifies importance of MRI in re-evaluation of the diagnosis of MS. Clinical findings suggested secondary progressive MS, but MRI appearance called in question this diagnosis. Very supposedly, the concomitant treatment with corticosteroids might

have mitigated PCNSL manifestation in both, clinical symptoms and MR imaging, for some time. This case is also important from the point of view of MRI differential diagnosis of white matter lesions.

Acknowledgments

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