PROGRESSIVE ENCEPHALOMYELITIS WITH RIGIDITY AND MYOCLONUS: A CASE REPORT

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ABSTRACT

Introduction: Progressive encephalomyelitis with rigidity and myoclonus (PERM) is a rare disorder presenting as the rigidity of limbs and trunk, muscle spasms, brainstem signs and life-threatening hyperekplexia.

Methods & Material: We report a 38-year-old woman, previously healthy with a rapid form of PERM developed over seven months.

Results: To the State Hospital of Neurology in Skopje has referred a 38-year-old woman, previously healthy for the subacute onset of severe and progressive gait disturbance associated with painful muscular rigidity and spasms of the trunk and lower limbs. Additionally, unstable posture followed by involuntary movement of the right leg appeared. Symptoms appeared four months before hospitalization with a blurred vision of the left half of the eye field and few seizures described like a generalized tonic-clonic seizure (GTCS), but without urination and biting of the tongue. Electroencephalography (EEG) showed theta-delta dysrhythmia, the evoked potentials were normal, except somatosensory evoked potential (SEP) of n. tibialis with mildly prolonged latency. Manganese was slightly higher at 1.3 μg/L (reference 0.3-1.1μg/L), glutamate decarboxylase (GAD) antibodies were 33.6 IU/mL (reference <10 IU/mL), and she was also positive to HuD and Ri (paraneoplastic) antibodies. Symptoms were partially responsive to baclofen, corticosteroids, and levetiracetam. The patient so far has received three cycles of intravenous immunoglobulin (IVIg), and recently a series of three plasmapheresis, but without a marked therapeutic effect.

Conclusions: The three cycles of IVIg and the three plasmapheresis did not provide a satisfactory therapeutic effect. Her condition on the neurological plane is getting worse. These factors contribute to a very unfavorable prognosis for her. The presence of the above antibodies may be responsible for the progressive character of this rare disease.

Keywords: PERM, GAD antibodies, IVIg

INTRODUCTION

Progressive encephalomyelitis with rigidity and myoclonus (PERM) is a rare variant of the stiff-person syndrome (SPS) characterized by a variable expression of brainstem signs, myoclonus, stiffness, rigidity, muscle spasms, autonomic dysfunction, and hyperekplexia [1]. Symptoms can be explained by the disruption of the inhibitory glycinergic synaptic transmission, which is prominent in the spinal cord and brainstem [2]. Subsequent studies established PERM as an autoimmune disorder, most frequently associated with antibodies against glutamic acid decarboxylase (GAD) [3]. Classical PERM affects women two to three times more often than men. Several classifications have been proposed for SPS according to the severity or distribution of the stiffness, related neurological findings, and association with neoplasia [4]. In most patients, disease progression occurs subacutely over weeks and, the duration of illness ranges from weeks to years, often with various episodes of exacerbation and remission [5].

METHODS & MATERIAL

We report a 38-year-old woman, previously healthy with a rapid form of PERM developed over seven months.

RESULTS

To the State Hospital of Neurology in Skopje has referred a 38-year-old woman, for the subacute onset of severe and progressive gait disturbance associated with painful muscular rigidity and spasms of the trunk and lower limbs. Additionally, unstable posture followed by involuntary movement of the right leg appeared. After a short period, there was also an involuntary movement of the left leg with propagation to myoclonic limb jerks with hyperekplexia. Symptoms appeared four months before hospitalization with a blurred vision of the left half of the eye field, and few seizures described like a generalized tonic-clonic seizure (GTCS), but without urination and biting of the tongue. At that time, a first neurological examination was unremarkable except for left hemianopsia. Electroencephalography (EEG) showed theta-delta dysrhythmia, the evoked potentials were normal, except somatosensory evoked potential (SEP) of n. tibialis with mildly prolonged latency. Chest x-ray, thyroid and stomach sonography were normal. Furthermore, the magnetic resonance of the brain showed the following pathological findings: spondylarticular changes on the cervical-thoracic segment. Easily reduced cervical lordosis and thoracic kyphosis were also noticed. At level, C5-C6 herniation, dorzocentric stumps with complete obliteration of the front subarachnoid space with mild compression on the medulla spinalis were presented. Tumor and bone markers were all in referent levels. Anti-Aquaporin 4-IgA and IgM, Yo and NMDA receptors antibodies (IgG, IgA, IgM), IgM viral markers, anti-dsDNA, c-ANCA, ANA, cuprum, ceruloplasmin were negative. Cerebrospinal fluid (CSF) was negative for Brucella. Neuropsychological testing did not show any deflection. Manganese was slightly higher at 1.3μg/L (reference 0.3-1.1μg/L), glutamate decarboxylase (GAD) antibodies were 33.6 IU/mL (reference <10 IU/mL), and she was also positive to HuD and Ri (paraneoplastic) antibodies. Symptoms were partially responsive to baclofen, corticosteroids, and levetiracetam. The patient so far has received three cycles of intravenous immunoglobulin (IVIg), and recently a series of three plasmapheresis, but without a marked therapeutic effect.

DISCUSSION

Progressive encephalomyelitis with rigidity (PERM) was initially described in 1976 as a subacute disorder characterized by muscular rigidity, stimulus-sensitive spasms, brainstem dysfunction and the pathological finding of perivascular lymphocyte cuffing and neuronal loss in the brainstem and spinal cord with relative sparing of the cortex. Some authors regarded this as a more aggressive variant of the stiff-person syndrome [2]. A major breakthrough in our understanding of the pathogenesis of PERM occurred in 1988 when an association between anti-GAD antibodies and PERM was first reported by Solimena et al. 26-GAD is the rate-limiting step in the decarboxylation of L-glutamate to Ωaminobutyric acid (GABA) [6]. PERM is a very challenging diagnosis. Electromyography (EMG) and antibodies in serum and cerebrospinal fluid (CSF) could help to confirm the diagnosis. Initial clinical presentation can be very unspecific and uncommon, and this case is no exception. Common differential diagnoses of PERM syndrome are stiff person syndrome, paraneoplastic Stiff-person syndrome (SPS) [7]. The differential diagnosis of a patient who has muscle rigidity and "jerking" in the ICU includes tetanus, status dystonicus (dystonic storm), status spasticus due to SMS, serotonergic syndrome, neuroleptic malignant syndrome, etc. A thorough evaluation is necessary to identify the cause early to prevent

morbidity and mortality [8]. Concerning immunotherapy, plasmaphereses, intravenous immunoglobulin (IVIg), corticosteroids and rituximab have been reported to be successful in individual cases, although the efficacy of these agents has not been established [9]. Besides, some reports have demonstrated the efficacy of long-term basement azathioprine treatment for SPS spectrum disorders [10]. However, PERM remains an expanding clinical entity that is constantly being enriched with new symptoms and antibodies. The findings indicate that PERM is all of which affect the brainstem, spinal cord, and other CNS regions. These mechanisms might include humoral responses inducing pathogenic antibodies to cell surface antigens causing neuronal surface antibody syndrome, as well as antibodies to intracellular antigens [11]. Future directions in the management of this condition may emerge as we better understand the role if any, that these antibodies play in the emergence of symptoms. This could lead to the development of targeted therapies that minimize systemic side effects [12].

CONCLUSION

The three cycles of IVIg and the three plasmapheresis did not provide a satisfactory therapeutic effect. Her condition on the neurological plane is getting worse. These factors contribute to a very unfavorable prognosis for her. The presence of the above antibodies may be responsible for the progressive character of this rare disease.

DECLARATION OF INTEREST

Authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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