Hashimoto's encephalopathy: a long-lasting remission induced by intravenous immunoglobulins

Hašimoto encefalopatija: dugotrajna remisija indukovanā intravenskim imunoglobulinima

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Abstract

Background. Hashimoto’s encephalopathy (HE) is a rare autoimmune syndrome characterized by various neuropsychiatric manifestations, responsive to steroid treatment and associated with Hashimoto’s thyroiditis. There are only a few reports suggesting that intravenous immunoglobulins (IVIG) might represent an efficacious treatment modality for the severe steroid-resistant HE cases. We presented a patient with HE who developed a complete recovery after the IVIG therapy followed by a long-lasting remission. Case report. We described herein a female patient with the one-year history of autoimmune thyroiditis before the development of neuropsychiatric manifestations. In May 1999, a 38-year-old woman presented at the Institute of Neurology, Clinical Center of Serbia, Belgrade, with the brain-stem syndrome which responded well to steroid treatment. After detailed examinations, the diagnosis of Hashimoto’s encephalopathy was established. In January 2002, the patient received IVIG (0.4 g/kg body weight daily for 5 days). Gradual improvement was noticed and a complete recovery developed over the following weeks. Up to March 2009, during a 7-year follow-up period, remission persisted.

Conclusion. To our best knowledge, this is the first report of a long-lasting remission of Hashimoto’s encephalopathy after IVIG therapy. Therefore, this case further supports administration of IVIG, as a potentially beneficial treatment modality, in severe cases of Hashimoto’s encephalopathy which are completely or partially resistant to steroids.

Key words: thyroiditis, autoimmune; brain diseases; therapeutics; immunoglobulins, intravenous; treatment outcome; remission induction.

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DOI:10.2298/VSP1105452D
Introduction

Hashimoto's encephalopathy (HE) is a progressive and/or relapsing encephalopathy, associated with chronic autoimmune thyroiditis, and responsive to glucocorticoid therapy. It has been reported that plasmapheresis and intravenous immunoglobulins (IVIG) might represent an alternative treatment modality for steroid-resistant HE patients.

We presented here a patient with HE who had developed a complete clinical recovery after the therapy with IVIG. To our best knowledge, this is the first report describing IVIG-induced recovery of HE with a long-lasting (7 years) remission.

Case report

In May 1999, a 38-year old woman, complaining of subacute onset of dysarthria, dysphagia, and paresthesias in the left extremities, was admitted to the Institute of Neurology, Clinical Center of Serbia, Belgrade. She had the one-year history of Hashimoto's thyroiditis which was treated by administration of substitution therapy (100 μg levothyroxine, daily). The medical history was otherwise unremarkable. Neurological examination revealed hypomotility of both palatine vela (bulbar paralysis), hypesthesia, and slight weakness of the left extremities, exaggerated deep tendon reflexes on the left, and diminished plantar response on the left. Apart from thyroid goitre, there was no other abnormality on general physical examination.

Trimodal evoked potentials, electroencephalography (EEG), brain computed tomography, and magnetic resonance imaging (MRI) findings were normal. Cerebrospinal fluid (CSF) examination disclosed the normal protein and glucose level, and normal number of lymphocyte cells; agarose isoelectric focusing with immunofixation did not reveal oligoclonal immunoglobulins. No abnormal findings were revealed regarding the routine blood hematology and biochemistry, infection serology and autoantibody screens, apart from the presence of antimitochondrial antibodies (AMA) in the presented patient, serum concentration of antithyroid peroxidase (TPO) antibodies was elevated, 584 IU/mL (normal, < 60 IU/mL), and antithyroglobulin antibodies were negative.

In June 2001, the patient became irritable and apathetic. After two weeks, dosage of prednisolone was reduced by 10 mg daily, each month for 3 months, then from 20 to 10 mg daily over another six months, with slow tapering thereafter. A gradual improvement was noticed immediately and full neurological recovery occurred within 6 months. The diagnosis of HE was established. The steroid therapy was discontinued after 12 months. At that time, TPO antibody increased to 896 IU/mL. Methylprednisolone (1,000 mg daily) was started. After two weeks, dosage of prednisolone in a daily dosage of 60 mg, with subsequent reducing a dose by 10 mg each 6 weeks. Up to January 2002, pyramidal deficit and ataxic gait gradually subsided, but the patient still complained of frequent, intense, disturbing headaches, irritability, and apathy. The patient also developed partial complex epileptic seizures. EEG disclosed independent sharp waves in theta range, bilaterally in temporal regions, on the mixed alpha-theta background activity. Therapy with carbamazepine was initiated. The steroid therapy was discontinued.

The unique feature of our case was the complete clinical recovery again. Neurological examination showed mild spastic left hemiparesis and hemihypesthesia, and ataxic gait. The patient was oriented, but her verbal responses were slow. EEG showed asynchronous slowed background rhythm with intermittent bitemporal theta slow waves. Carotid Doppler studies, brain MRI scans, and MRI angiography were normal. TPO antibody increased to 896 IU/mL. Methylprednisolone (1,000 mg daily) in intravenous infusion was administered for 5 days, followed by oral prednisolone in a daily dosage of 60 mg, with subsequent reducing a dose by 10 mg each 6 weeks. Up to January 2002, pyramidal deficit and ataxic gait gradually subsided, but the patient still complained of frequent, intense, disturbing headaches, irritability, and apathy. The patient also developed partial complex epileptic seizures. EEG disclosed independent sharp waves in theta range, bilaterally in temporal regions, on the mixed alpha-theta background activity. Therapy with carbamazepine was initiated. The steroid therapy was discontinued.

The patient underwent a course of IVIG (400 mg/kg body weight, daily, for 5 days). Her clinical status began to improve three days after IVIG therapy and in the following weeks, headache, seizures and personality changes gradually disappeared.

Up to March 2009, during a 7-year follow-up period, the patient did not experience any neuropsychiatric symptom, and regular neurological examinations disclosed consistently normal finding. Concerning anti-TPO antibodies, their level was found to be repeatedly elevated in sera, with values ranging from 200–890 IU/mL, while the titer of AMA fluctuated from 1:40 to 1:160.

Discussion

We presented a case of HE in a 48-year-old woman with the history of thyroid disease, whose clinical presentation was in accordance with previous descriptions of two types of HE presentations: vasculitic (stroke-like episodes) and diffuse progressive (with cognitive impairment, seizures, psychiatric symptoms and altered consciousness). Non-specific EEG abnormalities, which occur frequently in HE, were detected. However, neither CSF abnormalities nor brain MRI lesions, which have been described in about half of the cases with HE, were found.

In the presented patient, serum concentration of anti-TPO antibodies was consistently elevated throughout the disease course. This serological abnormality is recorded in all patients with HE. Antithyroid antibodies have been also found in CSF from patients with HE but not in all the tested. Up to now, their role in the pathogenesis of HE has not been fully elucidated yet.

The unique feature of our case was the complete clinical recovery after the IVIG therapy which lasted within a 7-year follow-up period. According to our best knowledge, until now, only a few patients with HE have been treated with IVIG. In two patients, no effect was observed, and in one of them ataxia was partly reduced. Recently, Jacob and

Rojabally \(^6\) reported a case with initial steroid-responsive HE, which became steroid-resistant and then responded well to IVIG. Similarly, the patient was only initially steroid-responsive. Two years after the first steroid-responsive neurological episode, new neuropsychiatric features occurred. Steroids induced an incomplete remission, and severe behavioral changes persisted. However, the patient responded dramatically well to the consequently applied IVIG therapy. This treatment was followed by gradual disappearance of behavioral changes. The patient remained well during a 7-year follow-up period.

The reason for administration of IVIG in autoimmune diseases is based on their diverse mechanisms of action that include: reticuloendothelial cell blockage, complement inhibition, idiotype/antiidiotype antibodies, and modulation of cytokine production \(^9\). Additionally, IVIG may also prove useful in the treatment of these diseases due to Fas-mediated tissue destruction. Thus, it was shown that thyrocytes from HE glands expressed large amounts of Fas on their surface \(^11\). It is presumed that the Fas/FasL pathway is important for the progression of HT, most likely by the induction of apoptosis at the site of inflammation. Therefore, it might be assumed that apoptotic mechanisms involved in initiation of thyreoiditis could also result in the progression of encephalopathy in genetically susceptible host.

Patients with HE may have a wide variety of autoantibodies including antineuronal, antinuclear antibodies, AMA, those directed against cytoskeletons and liver membrane, which may be serological markers of polyclonal B-cell activation. Antibodies against amino terminal of alpha-enolase have been suggested to be a diagnostic marker for HE \(^12\). However, there is no evidence that these antibodies could have any pathogenic role in HE. In the presented patient we detected AMA without any evidence consistent with primary biliary cirrhosis (PBC). Patients with HT are considered as population at high risk for PBC, but up to now, only one case of HE associated with PBC was reported \(^13\).

**Conclusion**

Our report further supports a notion that therapy with IVIG should be considered in patients with HE, completely or partially resistant to steroids. Additionally, beneficial effect of this treatment would corroborate the immunopathological basis of this disease whose precise mechanisms remain to be elucidated.

**Acknowledgements**

This study was supported by grants from the Ministry of Education and Science, Republic of Serbia (projects no. 175031 and 175065).

**REFERENCES**


**Received on December 1, 2009. Accepted on March 18, 2010.**