

# Hashimoto Encephalopathy: Advanced Review of Clinical and Scientific Aspects

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## Introduction

Hashimoto encephalopathy (HE), also known as Steroid-Responsive Encephalopathy associated with Autoimmune Thyroiditis (SREAT), appears to be a form of encephalopathy that develops against the background of an increased level of antibodies; complications such as brain tumors, stroke or infection of the central nervous system have not been observed. Although the incidence of HE is relatively low, there have been reports of patient deaths and the development of status epilepticus as a result of the given pathology. This makes the earliest possible start of therapy critical issue, especially since the overwhelming majority of patients respond positively to corticosteroid therapy.

However, diagnosis of HE is difficult due to its non-specific clinical features and a wide range of symptoms, including alterations in behavior, delusions, and hallucinations-exclusion of encephalopathies associated with cognitive impairments, autoimmune encephalitis, prion disease, as well as other neurological pathologies is required before a diagnosis can be made.

In this regard, further HE studies and the identification of new specific diagnostic criteria for this disease remain a relevant direction in modern medicine.

The purpose of this article is to provide an integrated, synthesized overview of the current state of knowledge and outline the scope of the topic. Specifically, this review focuses on the definitions, pathogenesis and treatment of HE. We also review the currently available therapies and approaches to treat HE as well as the scientific and clinical data that support their effectiveness.

Due to the infancy of research in this area, the reasons for the relationship between thyroid dysfunction and autoimmune encephalitis remain unclear. Further analysis is required to support the hypothesis that a high level of serum anti-TPO (anti-thyroid peroxidase) antibodies increases the chances of suffering from neuropsychiatric symptoms. Clinical studies with novel therapeutics, antibodies, and different signal transduction inhibitors demonstrate

their clinical activity in various autoimmune encephalitides, however, it remains unclear how to successfully integrate novel agents either alone or in combination with steroids into the overall schema for HE.

## Hashimoto encephalopathy epidemiology

At present, Hashimoto encephalopathy (HE) is defined as a syndrome of encephalopathy and high serum anti-thyroid antibody concentrations that reacts to glucocorticoid therapy. The first case of HE was described in 1966 and was associated with hallucinations, tremors, exaltation, altered mental status and elevated antibody levels against the thyroid gland. In this case, the diagnosis of HE was confirmed after establishing the Hashimoto autoimmune thyroiditis diagnosis based on the thyroid biopsy results. As of 2017, more than 200 cases of HE have been reported. In most cases, patients respond well to therapy but serious clinical manifestations such as status epilepticus and three fatal outcomes have been reported [1].

It is necessary to mention that some specialists will not consider HE to be an independent nosological unit until definitive evidence is obtained that antibodies against thyroid antigens really do cause encephalitis [2].

Chong JY et al. analyzed articles in the MEDLINE database published before June 2002 and identified 85 patients with encephalopathy and high level of anti-thyroid antibodies in their blood serum; at the onset of disease, the average patient age was 44 years old (with a range from 9 to 78 years old) [3]. Clinical features of patients with HE is presented in Table 1.

According to the latest estimates, the frequency of HE is 2.1/100,000, with predominance in women in the 5<sup>th</sup> to 6<sup>th</sup> decades of life. The reported sex ratio for this disease is 4.1 in favor of women, and HE is less common in children than in adults [1].

Within the pediatric population, the average age of disease onset is 14 years; it should also be noted that the majority of pediatric patients are female. About 30 HE cases in children and adolescents were

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