ELSEVIER

Brain & Development xxx (2017) xxx–xxx

BRAIN & DEVELOPMENT
Official Journal of the Japanese Society of Child Neurology

www.elsevier.com/locate/braindev

Original article

Hashimoto encephalopathy in pediatric patients: Homogeneity in clinical presentation and heterogeneity in antibody titers

Jiwon Lee [a], Hee Joon Yu [b], Jeehun Lee [a,*]

[a] Department of Pediatrics, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea
[b] Department of Pediatrics, Hanllym University Sacred Heart Hospital, Anyang, Republic of Korea

Received 1 May 2017; received in revised form 19 July 2017; accepted 20 July 2017

Abstract

Objective: Hashimoto encephalopathy is an autoimmune encephalopathy characterized by elevated antithyroid antibodies and a favorable response to corticosteroid. This study delineated the clinical characteristics of pediatric Hashimoto encephalopathy and the significance of low antithyroid antibody titers in diagnosis and treatment.

Subjects and methods: Clinical manifestations, antibody titers, and treatment responses were retrospectively reviewed in six consecutive children diagnosed with Hashimoto encephalopathy between August 2008 and July 2016.

Results: Age at diagnosis was 10–17 years. Presenting symptoms were seizures, altered consciousness, behavioral changes, psychosis, tremor, and dystonia. Thyroid function was normal in five patients, and one had hypothyroidism prior to the encephalopathy. Antithyroid antibody titer was increased at presentation in five patients and one week later in the other. Antibody levels were extremely varied (anti-thyroglobulin, 20.5–2318.0 U/ml; anti-thyroid peroxidase, 12.5–2231.0 U/ml; reference range, <60 U/ml) and <180 U/ml in two patients. Electroencephalogram was abnormal in five patients. Brain magnetic resonance imaging was unremarkable. Four patients responded to high-dose corticosteroid and one improved with additional intravenous immunoglobulin. The remaining patient did not respond to both treatments and normalized after plasmapheresis. Autoantibody titers decreased with treatment response in the acute stage. Two patients with low antibody titers showed similar clinical presentations and responses.

Conclusions: The clinical presentations and treatment responses in Hashimoto encephalopathy were similar, irrespective of antithyroid antibody titer. Because the initial antithyroid antibody titers can be normal or mildly-elevated, follow-up testing of antithyroid antibodies is required in patients who are clinically suspect for Hashimoto encephalopathy.

Keywords: Hashimoto encephalopathy; Steroid-responsive encephalopathy associated with autoimmune thyroiditis; Pediatric patients; Antithyroid antibody titer; Steroid treatment

1. Introduction

Hashimoto encephalopathy or steroid-responsive encephalopathy associated with autoimmune thyroiditis is characterized by acute encephalopathy, elevated antithyroid antibodies, and exclusion of other etiologies of encephalopathy, such as infection, tumor, toxic, or metabolic processes [1]. The estimated prevalence is 2.1 per 100,000 [2]. It is relatively rare in the pediatric population, with about 60 cases described to date and an unknown prevalence [3,4]. The pathogenesis and role of increased antithyroid antibody are still unclear. The increase in antithyroid antibody is extremely varied,

* Corresponding author at: Department of Pediatrics, Samsung Medical Center, Sungkyunkwan University School of Medicine, 81, Irwon-Ro, Gangnam-Gu, Seoul 06351 Republic of Korea.
E-mail address: jhlee0101@skku.edu (J. Lee).

http://dx.doi.org/10.1016/j.braindev.2017.07.008
0387-7604/

with median anti-thyroid peroxidase antibody titer at diagnosis of 900 U/ml (range, 0–270,000) and anti-thyroglobulin antibody titer of 179 U/ml (0–36,569) [5].

Several reports highlighted the challenge of diagnosing Hashimoto encephalopathy in adult patients with low serum antithyroid antibody titers [6]. However, information on pediatric patients with low antibody titers is scant [7,8]. The present study delineated the clinical features and laboratory findings of pediatric Hashimoto encephalopathy and the significance of low antithyroid antibody titers in diagnosis and treatment.

2. Patients and methods

This study included six consecutive pediatric patients diagnosed with Hashimoto encephalopathy at two tertiary university hospitals between August 2008 and July 2016. Three patients were reported previously [9]. The diagnosis of Hashimoto encephalopathy was established clinically based on symptoms of encephalopathy and elevated serum antithyroid antibodies (anti-thyroglobulin antibody, anti-thyroid peroxidase antibody, and anti-thyroid stimulating hormone receptor antibody). Patients with other causes of neurologic abnormalities, such as infectious encephalitis, presence of tumor, and other autoimmune encephalitis, were excluded. Clinical manifestations, laboratory findings, results of brain imaging, electroencephalogram (EEG), treatments, and responsiveness to treatment were reviewed retrospectively. A low titer was defined as <3 times of the normal reference value. Only one patient underwent the autoimmune encephalitis panel testing (Advanced Neural Technologies, Seoul, Korea) available since 2013 in South Korea; the cerebrospinal fluid (CSF) was tested for the following antibodies associated with autoimmune encephalitis: anti-N-methyl-D-aspartate receptor, anti-leucine-rich glioma inactivated 1, anti-contactin-associated protein like 2, α-amino-3-hydroxy-5-methylisoxazole-4-propionic acid receptor, gamma-aminobutyric acid-B receptor, anti-Hu, anti-Yo, anti-Ri, anti-Ma2/Ta, anti-CV2/CRMP5, anti-amphiphysin, anti-recoverin, anti-SOX1, and anti-Titin. Serologic markers of other autoimmune disorders including antinuclear antibody, anti-double stranded DNA antibody, rheumatoid factor, and complement were evaluated in three patients. This study was approved by the institutional review board of the Samsung Seoul Hospital (IRB number SMC 2015-05-023).

3. Results

3.1. Clinical characteristics

Five females and one male were diagnosed with Hashimoto encephalopathy at a mean age of 14.1 ± 3.2 (range 10–17.6) years. Various neurologic symptoms were present and impaired consciousness (drowsiness, confusion, or disorientation) was the main feature in all patients (Table 1). Behavioral changes and psychiatric symptoms including aggression, severe irritability, hallucinations, insomnia, or agitation were prominent and disabling in all patients. Four patients had seizures. Seizure semiology varied, with presentations including generalized tonic clonic seizure, automotor seizure, psychic aura, and somatosensory aura. Confusion or altered consciousness became apparent after the seizure developed. In three patients, the seizure was easily controlled with a single antiepileptic medication. The other one patient (patient 1) was transferred with unexplained status epilepticus and was diagnosed with Hashimoto encephalopathy on hospital day 18. Two patients showed abnormal movement, with dystonic posturing and hand tremor.

3.2. Laboratory findings

At the time of symptom onset, anti-thyroglobulin antibody was elevated in five patients and anti-thyroid peroxidase antibody was simultaneously increased in two patients (Table 2). The anti-thyroglobulin antibody titer ranged from 20.5 to 2318.0 U/ml, as did the anti-thyroid peroxidase antibody titer (12.5–2231.0 U/ml).

Table 1
Clinical characteristics and laboratory findings.

Total patients	$n = 6$
Female: male	5:1
Age at diagnosis, years (range)	14.1 ± 3.2 (10–17.6)
Duration of admission, days (range)	38.0 ± 31.6 (9–86)
Response to treatment, days (range)	6.3 ± 4.5 (1–14)
Relapse, *n* (%)	1 (16.7)
Neurologic symptoms, n (%)	
Seizures	4 (66.7)
Alternation of consciousness	6 (100)
Behavioral changes	5 (83.3)
Psychosis	4 (66.7)
Abnormal movements	2 (33.3)
Transient amnesia	1 (16.7)
Thyroid function, n (%)	
Euthyroid, subclinical hypothyroid	5 (83.3)
Hypothyroid	1 (16.7)
Elevated antithyroid antibodies initially, n (%)	
Anti-thyroglobulin antibody	5 (83.3)
Anti-thyroid peroxidase antibody	2 (33.3)
Anti-TSH receptor antibody	1 (16.7)
Treatment to encephalopathy, n (%)	
Corticosteroid	6 (100)
Immunoglobulin	3 (50)
Plasmapheresis	1 (16.7)

Data are *n* (%) values or mean ± standard deviation except where indicated otherwise.
TSH: thyroid-stimulating hormone, MRI: magnetic resonance imaging.

Please cite this article in press as: Lee J et al. Hashimoto encephalopathy in pediatric patients: Homogeneity in clinical presentation and heterogeneity in antibody titers. Brain Dev (2017), http://dx.doi.org/10.1016/j.braindev.2017.07.008