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Hashimoto's encephalopathy presenting with unusual clinical findings in pediatric population: revision of the diagnostic criteria

Pediyatrik popülasyonda alışılmamış klinik bulgularla bulunan Hashimoto ensefalopatisi: tanı kriterlerinin gözden geçirilmesi

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ABSTRACT

Aim: Hashimoto's encephalopathy is a rare progressive and relapsing disease of presumed autoimmune origin associated with high titers of thyroid antibodies. Also named steroid-responsive encephalopathy, the disease can be cured with early treatment. Hashimoto's encephalopathy may occur with various clinical manifestations, but it often presents with symptoms such as seizures, confusion, hallucination, sleep abnormalities, and behavioural problems. Patients are mostly euthyroid or mildly hypothyroid. Hashimoto encephalopathy is a controversial diagnosis for misdiagnosis and overdiagnosis because of the high prevalence of thyroid antibodies in the population. Therefore, this diagnosis requires strict criteria that can highly indicate the diagnosis. We aimed to present the diagnosis and treatment processes from unusual symptoms of patients who are considered to have Hashimoto's encephalopathy with very strict criteria.

Materials and Methods: Here we present five pediatric patients diagnosed with Hashimoto's encephalopathy between 2013 and 2023. The clinical signs and symptoms, laboratory findings, treatment options and response to treatment were obtained from patient records retrospectively.

Results: On admission, patients had striking behavioural changes such as hallucinations, insomnia, purposeless laughing as well as signs of encephalopathy such as status epilepticus and confusion; neurological sequelae; history of surgery, and fever. All patients had high levels of thyroid antibodies and they responded perfectly to steroid treatment in a short period of time.

Conclusion: Hashimoto's encephalopathy should be considered in all patients presenting with encephalopathy in the pediatric age group. These patients may have unusual and clinical manifestations.

Keywords: Hashimoto's encephalopathy, thyroid antibodies, neuropsychiatric symptoms

ÖZ

Amaç: *Hashimoto ensefalopatisi, yüksek antikor titrelerinde tiroid antikorları ile ilişkili varsayılan otoimmün kökenli, nadir görülen, ilerleyici ve tekrarlayan bir hastalıktır. Steroide duyarlı ensefalopati olarak da adlandırılan bu hastalık, erken tedavi ile tedavi edilebilir.*

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Hashimoto ensefalopatisi çeşitli klinik belirtilerle ortaya çıkabilir, ancak çoğu zaman nöbetler, konfüzyon, halüsinasyon, uyku anormallikleri ve davranış sorunları gibi semptomlarla da kendini gösterir. Hastaların birçoğu ötiroid veya hafif hipotiroiddir. Genel popülasyonda tiroid antikorlarının yüksek görülme oranları nedeniyle Hashimoto ensefalopatisi tanısı tartışmalıdır. Bu nedenle, oldukça katı kriterler ile tanı koymak uygun olacaktır. Bu çalışmada, bu kriterler ile saptadığımız Hashimoto ensefalopatili olgularımızdan olağandışı prezente olanların tanı ve tedavi süreçlerini sunmayı amaçladık.

Yöntem: *Bu çalışmada, 2013 ile 2023 yılları arasında Hashimoto ensefalopatisi tanısı konan beş pediatrik hasta dikkate alındı. Klinik belirti ve bulguları, laboratuvar bulguları, tedavi seçenekleri ve tedaviye yanıtları retrospektif olarak hasta kayıtlarından elde edildi.*

Bulgular: *Hastaların başvurularında halüsinasyonlar, uykusuzluk, amaçsız gülme gibi çarpıcı davranış değişikliklerinin yanı sıra status epileptikus ve konfüzyon gibi ensefalopati bulgular gözlemlendi. Tüm hastalarda yüksek tiroid antikorları seviyeleri gözlemlendi ve steroid tedavisine hastalardan kısa sürede çok iyi yanıt alındığı görüldü.*

Sonuç: *Ensefalopati ile başvuran pediatrik yaş grubundaki tüm hastalarda Hashimoto ensefalopatisi düşünülmelidir. Bu hastalarda alışılmadık, olağandışı ve klinik belirtileri olabilir.*

Anahtar Sözcükler: *Hashimoto ensefalopatisi, tiroid antikorları, nöropsikiyatrik semptomlar.*

INTRODUCTION

Hashimoto's encephalopathy is an autoimmune disease with a wide range of neurological symptoms that often respond to steroid therapy. It usually presents with paralysis, seizures, psychiatric and behavioral changes, lack of coordination, and coma. Some studies have classified the disease into two subgroups: 1. Vasculitic type with stroke-like episodes 2. Diffuse progressive type with deterioration of mental functions (1, 2). Electroencephalography (EEG) and cranial imaging findings aren't specific to the condition (1, 3, 4). Although the pathophysiology hasn't been completely elucidated, it's presumed to be originated from autoimmune mechanisms (3). Thyroperoxidase antibodies (TPOAb) are high, whereas patients can be euthyroid, hypothyroid, or rarely hyperthyroid. The disorder is mostly seen in adults, but it can also present in childhood. According to most studies, diagnosis can be made with the following criteria: 1) Presence of neurological clinical manifestations after ruling out other causes of encephalopathy, 2) Presence of increased thyroid antibodies, 3) Significant clinical improvement after treatment with immunomodulators (1-4). However, we developed more strict criteria to make a more accurate diagnosis which are: 1) Encephalopathy with seizures, myoclonus, hallucinations, or stroke-like episodes, 2) At least one positive thyroid antibodies, 3) Imaging findings in favor of thyroiditis, 4) Absence of other neuronal antibodies in serum and cerebrospinal fluid (CSF), 5) Reasonable exclusion of alternative causes (toxic, metabolic, neoplastic), 6) Normal or non-specific changes on brain magnetic resonance imaging (MRI), 7) Complete or near-complete return to the baseline neurologic status with steroid treatment. Herein after we present five cases of Hashimoto's encephalopathy diagnosed according to these strict criteria and responded promptly to systemic steroid treatment.

MATERIALS and METHODS

In this study, we evaluated five pediatric patients diagnosed with Hashimoto's encephalopathy at the pediatric neurology department of two tertiary hospitals in 2013 and 2023. The complaints, clinical signs and symptoms on admission, laboratory findings, preferred treatment methods, response to treatment, and duration of follow-up and short term prognosis were obtained from patient records retrospectively.

The strict diagnostic criteria of our pediatric neurology team were as follows: 1) Encephalopathy with seizures, myoclonus, hallucinations, or stroke-like episodes, 2) At least one positive thyroid antibodies, 3) Imaging findings in favor of thyroiditis, 4) Absence of other neuronal antibodies in serum and cerebrospinal fluid (CSF), 5) Reasonable exclusion of alternative causes (toxic, metabolic, neoplastic), 6) Normal or non-specific changes on brain magnetic resonance imaging (MRI), 7) Complete or near-complete return to the baseline neurologic status with steroid treatment.

Patients who did not meet these criteria were excluded in order not to cause any diagnostic confusion.

RESULTS

Eleven patients diagnosed with Hashimoto's thyroiditis between the specified dates were enrolled. However, there were 8 patients who met all of the seven criteria we created. Three of these patients were diagnosed as classical Hashimoto encephalopathy with seizures, encephalopathy, marked antibody elevations and thyroid ultrasonography findings. Five of the patients were presented due to their different and unusual presentations.

CASE 1

A previously healthy, 8-year-old girl was referred with confusion and repetitive myoclonic jerks. From her history, we learned that she'd been febrile for five days and received antibiotics for a urinary tract infection. On admission, her neurological examination was normal. However, she had three episodes of generalized tonic-clonic seizures within the following two hours. Since the seizures didn't respond to levetiracetam and phenytoin intravenous boluses, midazolam treatment was commenced. She was then intubated and transferred to the intensive care unit. Although direct microscopic examination of the CSF was normal, she was put on empirical cefotaxime and acyclovir treatments because meningoencephalitis couldn't be ruled out. A few days later, she was extubated and retransferred to the pediatric neurology department. Her persistent orofacial myoclonic seizures were treated with clonazepam. On follow-up, she couldn't recognize her family members, saw objects larger or smaller than normal, had hallucinations and purposeless laughing attacks.

Her cranial MRI revealed a signal increase on the bilateral posterior horns in the T2A sequence. Viral serology and culture tests were negative in CSF and plasma samples. Complete blood count (CBC), biochemical and toxicological examination were normal. Laboratory tests for autoimmune vasculitis revealed normal results. Neuroantibody panel for autoimmune encephalitis were negative. While TPOAb was 458 IU/ml (normal:0-45), and thyroglobulin antibody (TgAb) was 56 IU/ml (normal:0-40), she was euthyroid (fT_3:1,94 ug/dl, fT_4:1,10 ug/dl, TSH:2,4 mIU/L). Thyroid ultrasonography (USG) revealed irregularities in the gland contours and parenchymal heterogeneity. Her electroencephalography (EEG) showed slow background rhythm and left frontotemporal epileptiform discharges. She was diagnosed with Hashimoto's encephalopathy and treated with pulse methylprednisolone (1 g/day) for three days, followed by oral methylprednisolone (1 mg/kg/day). On the fourth day of treatment, myoclonic jerks ceased, and psychiatric symptoms disappeared. She had no further complaints for the next 8 months.

CASE 2

A 15-year-old girl with spastic diplegia was admitted with fever, insomnia, purposeless laughing and hallucinations. On admission, she was agitated, with an intermittent lack of orientation and cooperation.

From her history, we learned that she was a 30 weeker 1100 g premature infant and had mild motor-mental retardation. On admission, she had uncontrolled emotional outbursts like purposeless laughing, didn't answer questions, and constantly repeated her name. Except for spastic diplegia due to prematurity, her physical examination was normal. The pediatric psychiatrist didn't observe any psychotic or depressive disorder.

The EEG showed isolated low amplitude synchronous slow wave activities on the frontal areas of the hemispheres. The cerebral MRI, MR angiography, and MR venography was normal except for the congenital hypoplasia of the left transverse sinus and increased signal intensity in the periventricular white matter due to prematurity. These abnormalities weren't associated with the current clinical manifestation.

CBC, biochemical and toxicological examination of the blood and the CSF were normal. Neuronal antibodies were negative in the CSF and plasma samples. Thyroid function tests and thyroid antibodies (TSH: 8.09 µUI/ml, fT_4:1.13 ng/dl, TPOAb: 587 IU/ml, TgAb: 372 IU/ml) were consistent with subclinical hypothyroidism. Pseudo-nodular appearance and increased vascularization in both thyroid lobes favoring thyroiditis were detected on thyroid USG.

The case was diagnosed with Hashimoto's encephalopathy and treated with 1 g methylprednisolone for three days, followed by oral methylprednisolone (1 mg/kg/day) scheduled for 6 months. After one week, purposeless laughing, persecutory thoughts, and echolalia disappeared.

CASE 3

A 10-year-old boy was referred with persistent fever and vomiting for one week, a tendency to sleep, and not being able to talk and walk for the last few days. He had motor mental retardation and left hemiparesis due to acute necrotizing encephalitis at seven months of age. He was able to walk, take wide steps, and build short sentences previously.

On physical examination, he had confusion, disorientation, and discooperation. He was unable to speak, he could not stand, even sitting

was ataxic, deep tendon reflexes were brisk and left hemiparesis was present. He was examined for central nervous system infection, vasculitis, neurometabolic diseases, cerebral venous thrombosis, mitochondrial diseases, and immunodeficiency due to recurrent encephalitis. He was treated with empirical ceftriaxone and acyclovir until the serological and CSF results were negative for viral and bacterial meningoencephalitis.

Neurometabolic examinations were normal. The biochemical analyses of the CSF were found normal except for 0,7 g/L protein and pleocytosis. Direct examination of the CSF for bacterial and viral infections, as well as viral and bacterial serological tests from plasma samples were negative. Bacterial cultures of CSF and blood samples were negative. Plasma immunoglobulin levels and lymphocyte panel were normal for his age. Autoantibodies for collagen vascular diseases and neuronal antibodies from the plasma and CSF samples were negative. Thyroid function tests were normal; however, thyroid antibodies were high (TPOAb:635 IU/ml, TgAb:165 IU/ml). Thyroid Doppler USG revealed an enlarged left thyroid lobe and asymmetrical increased vascularity.

EEG revealed a paroxysmal disorder consisting of synchronous slow waves in the frontal regions of both hemispheres. There was T2 hyperintensity around the anterior horns of the ventricles due to encephalitis sequelae in cranial MRI. MR angiography and MR venography were normal.

The case was diagnosed with Hashimoto's encephalopathy and treated with pulse methylprednisolone (1 g/kg/day) for three days, followed by intravenous immunoglobulin (IVIG) of 1 g/kg for two days. He recovered dramatically after the pulse steroid therapy and started sitting, talking, and walking two days later. The methylprednisolone was administered at 1 mg/kg/day for 3 months and terminated by reducing the dosage for three months. He had no complaint in 1-year follow-up.

CASE 4

A 7-year-old previously healthy boy was admitted to the pediatric emergency department with acute ataxia. He had fever, weakness, vomiting, and headache that started one week before admission. From his family, we learned that he had aggressive behavior for the last 2-3 weeks and had been fighting at school. On physical examination, he had an amimic face and a decreased mental status, he had meaningless speech and he couldn't answer the questions, he could stand upright but couldn't walk due to ataxia. Subsequently, we observed myokymic twitches on his face.

Laboratory examinations including CBC, viral markers, toxic compounds, biochemical tests, vasculitic markers, autoimmune and infectious markers, neuronal antibodies from plasma and CSF were normal. Thyroid function tests were normal, but TPOAb was 2435 IU/ml, and TgAb was 145.9 IU/ml. Thyroid USG was compatible with chronic thyroiditis.

Cranial MRI was normal. Isolated sharp wave activities in the centrotemporal part of the left hemisphere were recorded in EEG.

One day after admission, he had right-sided focal seizures and myoclonic jerks in the distal upper extremities. Despite infusions of levetiracetam, phenytoin, and midazolam, seizures could not be satisfactorily controlled. One gram methylprednisolone was commenced and continued for three consecutive days. Then the treatment was maintained at a dose of 2 mg/kg/day. The seizures were controlled on the second day of treatment. He was discharged with levetiracetam and oral low-dose methylprednisolone. Both drugs were discontinued by 6 months and he was followed for a year without any complaints.

CASE 5

A 14-year-old previously healthy girl was referred from the pediatric surgery department due to generalized seizures after an appendectomy operation. From her history, we learned that she had a fever and abdominal pain for the last two days, and she was operated for acute appendicitis. She then had seizures on the postoperative second day and developed hallucinations and purposeless laughing.

Her neurological examination was normal. CSF studies were negative for any viral and bacterial infection. CSF biochemical analysis was normal. Neuronal antibodies were negative in both CSF and plasma. Toxic compounds were negative in plasma and urine. Screening for collagen and metabolic diseases were normal. Thyroid functions tests revealed a hypothyroid state (TSH: 14.7 µIU/ml; fT_4: 0.36 pmol/L) with high-levels of thyroid antibodies (TPOAb: 560.8 IU/ml, TgAb: 122.7 IU/ml). Thyroid USG was compatible with chronic thyroiditis. Levothyroxine was started for hypothyroidism. Cranial MRI was normal, and EEG showed slowing of the background activity. The patient received 1g methylprednisolone for 3 days for Hashimoto's encephalitis. Her psychiatric symptoms improved within one week. Oral steroid therapy was continued for 6 months.

Features of all cases are summarized in Table-1.

Table-1. Features of the Cases with Hashimoto's Encephalitis.

	Case-1	Case-2	Case-3	Case-4	Case-5
Age (years)	8	15	10	7	14
Gender	Female	Female	Male	Male	Female
Symptoms/ complaints on admission	Myoclonic seizures Fever Confusion	Fever Insomnia Hallucination	Fever Vomiting Oversleeping Unable to talk Unable to walk	Acute ataxia	Seizure Hallucination Purposeless laughing
History	Receiving antibiotics for 5 days with the diagnosis of urinary tract infection	30 w premature birth 45 days hospitalization Motor-mental retardation Under special education program	Motor-mental retardation and left hemiparesis due to acute necrotizing encephalitis at 7 months of age	Fever, sore throat, headache, vomiting 1 week prior to admission aggressive behavior for the last 2-3 weeks	Fever and abdominal pain for the last 2 days Appendectomy
Neurologic Examination	Loss of memory Blurred vision Hallucination	Spastic diplegia Uncontrolled emotional outbursts	Confusion Lack of orientation and cooperation Aphasia Left hemiparesis Brisk deep tendon reflexes	Decreased mental status Hypomimic face Myokymic twitches on face Ataxia	Normal
CSF Findings	Normal	Normal	Protein: 0,7 g/L Pleocytosis	Normal	Normal
Thyroid Function Tests	TPOAb: 458 IU/ml TgAb: 56 IU/ml TSH: 2.4 mIU/L fT_4: 1.10 ug/dl fT_3: 1.94 ug/dl	TPOAb: 587 IU/ml TgAb: 372 IU/ml TSH: 8.09 mIU/L fT_4: 1.13 ng/dl	TPOAb: 635 IU/ml TgAb: 165 IU/ml	TPOAb: 2435 IU/ml TgAb: 145.9 IU/ml	TPOAb: 560.8 IU/ml TgAb: 12.7 IU/ml TSH: 14.7 mIU/L fT_4: 0.36 pmol/L
Cranial MRI	Increase of signal on the T2A sequence located on the bilateral posterior horn	Congenital hypoplasia of the left transverse sinus Increased signal intensity in the periventricular white matter	T2 hyperintensity around the anterior horns of the ventricles due to encephalitis sequelae	Normal	Normal
Thyroid USG	Irregularities on the thyroid gland contours and heterogeneity on parenchymal echogenicity	Pseudo-nodular appearance and increased vascularization in both thyroid lobes favoring thyroiditis	Enlarged left thyroid lobe and asymmetrical increased vascularity	Findings compatible with chronic thyroiditis	Findings compatible with chronic thyroiditis
EEG	Slow background rhythm and left frontotemporal epileptiform discharges	Isolated low amplitude synchronous slow wave activities on the frontal areas of the hemispheres.	Paroxysmal disorder consisting of synchronous slow waves in the frontal regions of both hemispheres.	Isolated sharp wave activities in the centrotemporal part of the left hemisphere	Slowing of the background activity
Treatment	IV Pulse methylprednisolone (1 g/d-3 days) Oral methylprednisolone (1 mg/kg/d; 3 months)	IV Pulse methylprednisolone (1 g/d-3 days) Oral methylprednisolone (1 mg/kg/d; 3-6 months)	IV Pulse methylprednisolone (1 g/d-3 days) IVIG (1 g/kg- 2 days) Oral methylprednisolone (1 mg/kg/d; 3-6 months)	IV Pulse methylprednisolone (1 g/d-3 days) Oral methylprednisolone (2 mg/kg/d; 6 months)	IV Pulse methylprednisolone (1 g/d-3 days) Oral methylprednisolone (1 mg/kg/d; 6 months)
Respond to Treatment	Yes	Yes	Yes	Yes	Yes

CSF: Cerebrospinal Fluid, MRI: Magnetic Resonance Imaging, EEG: Electroencephalography, TPOAb: Thyroperoxidase antibodies, TgAb: Thyroglobulin antibody, TSH: Thyroid-stimulating hormone, fT_4: thyroxine, fT_3: triiodothyronine, IVIG: Intravenous immunoglobulin

DISCUSSION

Hashimoto's encephalopathy was first described in 1966 by Brain et al., who reported a case of a 49-year-old man with hypothyroidism, who had high thyroid antibodies levels and responded to steroid treatment following the state of confusion and coma caused by the slow progress of symptoms such as dementia (5). Hashimoto's encephalitis is currently defined as acute-subacute encephalopathy, an elevated level of at least one of the thyroid antibodies, and no other reason to explain the existing encephalopathic state (2–5). However, clinicians face a contradiction in such cases. When diagnosed with such few criteria, cases can sometimes be over diagnosed, and some researchers think that thyroid antibodies positivity, which is common in the general population, is detected incidentally in encephalopathic patients (6). Therefore, we developed more strict criteria which are: I. Encephalopathy with seizures, myoclonus, hallucinations, or stroke-like episodes, II. At least one positive thyroid antibodies, III. Imaging findings in favor of thyroiditis, IV. Absence of other neuronal antibodies in serum and CSF, V. Reasonable exclusion of alternative causes (toxic, metabolic, neoplastic), VI. Normal or non-specific changes on brain MRI, VII. Complete or near-complete return to baseline neurologic status with steroid treatment. We saw that patients who met the first six criteria responded promptly to steroid treatment and therefore, we think that the seventh parameter should also be present to support the diagnosis.

In the pediatric population, Hashimoto's encephalitis is frequently observed between the ages of 13 and 18 and mostly in girls by 88% (4). Our patients were between the ages of 8 and 15 and three were girl.

There are two types of clinical outset described for adults. While the vasculitic-type causes symptoms such as recurrent hemiparesis, aphasia, ataxia and moderate cognitive impairment, the diffuse progressive type presents with amnesia, hallucinations, and psychotic episodes. The symptoms like seizures, stupor, coma, tremor, and myoclonus may be observed in both types. Pediatric patients are generally referred with a slowly progressing encephalopathy showing symptoms specific to diffuse progressive types such as impaired consciousness, cognitive impairment, underachievement in school, ill-temper, attention deficit, and myoclonic and generalized tonic-clonic seizures (4,7). Four of our patients presented with seizures, and two of them were accompanied by myoclonic jerks. Ferracci et al. reported that the most common complaints of 121 patients were seizures and myoclonus (8). As introduced with many cases in the literature (9-11), two of our patients also presented with status epilepticus. However, even if status epilepticus is controlled, Hashimoto's encephalitis is very likely to be underdiagnosed in children since the post-consciousness period is slow or it’s thought to be associated with previous neurological sequela.

The clinical symptoms of our patients varied widely. Confusion, psychiatric symptoms, seizures, and myoclonus were prominent. Presence of psychiatric symptoms in four patients, especially purposeless laughing attacks in three, was remarkable. In the literature, there are pediatric cases in whom purposeless laughing is defined among the psychiatric symptoms of Hashimoto's encephalitis (10,12).

Four of the patients had a febrile illness before encephalopathic symptoms. Two patients had neurological deficits due to prematurity and acute necrotizing encephalitis. Case 5 had Hashimoto's encephalitis immediately after the appendectomy. Except for one patient, an autoimmune process emerged with triggers such as infection and surgery.

Hashimoto's encephalitis is a steroid-responsive condition. Despite high autoantibody levels, the vast majority of patients are euthyroid (3,13). In our study, except for subclinical hypothyroidism in one patient and hypothyroidism in another, all patients were euthyroid. All patients had ultrasound findings compatible with thyroiditis. Although the pathophysiology hasn’t been completely elucidated, it’s generally recognized that it includes autoimmune cerebral vasculitis, neuronal antibody-mediated reaction, and an autoimmune reaction against the thyroid and central nervous system antigens (11,14). Compared to the literature, we observed fast and effective response to steroid treatment in all patients. Although the antibody titer couldn’t be correlated with the severity of the disease so far, strikingly high thyroid antibodies levels in all of our patients, especially high levels of TPOAb, suggest a relationship between steroid response and antibody titers.

Neuroimaging results are generally normal, and those that reveal abnormalities show mesiotemporal, frontal, or diffuse hyper intense areas, and these findings disappear with clinical recovery (15). While the brain MRIs of three patients were normal, two had sequelae findings related to their underlying neurologic conditions.

The EEG findings include abnormalities such as non-specific generalized slowing and epileptic discharges by 90% (16). While significant slowing of the background rhythm and paroxysmal focal findings were observed in four patients, localized findings were dominant in one patient.

Approximately 50% of cases in the literature have moderate levels of leukocyte and protein in the CSF (4). The CSF examination of all our patients, except for Case 3, were normal.

The rate of clinical recovery with corticosteroids is about 90-95% (17). There's no mutual agreement on the dose and duration; however, the common approach suggests methylprednisolone 1 g/day for 3-7 days, followed by 1-2 mg/kg/day for 2 weeks to 3 months depending on the clinical response (17). Levothyroxine is recommended for cases with hypothyroidism. If no improvement is observed with steroids, other options are IVIG, cyclophosphamide, azathioprine, and plasmapheresis. However, high levels of antibodies may persist despite recovery. Clinical and electroencephalographic improvement, and decrease in pleocytosis in CSF are accepted as a "good response" to treatment (1). All of our patients responded rapidly to high-dose steroids with almost complete recovery. Only one patient required levothyroxine.

CONCLUSION

Hashimoto's encephalopathy may occur with a variety of clinical manifestations. Even if the thyroid function tests of encephalopathic patients reveal normal results, Hashimoto's encephalopathy should be considered and the thyroid antibodies should be examined.

Conflicts of interest: The authors declare no conflict of interest.

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