Hashimoto's encephalopathy-rare but reversible cause of dementia or psychosis

Encefalopatia Hashimoto - rzadka ale odwracalna przyczyna otępienia i psychozy

Ewa Papuć [1], Ewa Kurys-Denis[2], Witold Krupski[2], Zbigniew Stelmasiak[1]

[1] Department of Neurology, Medical University of Lublin, Poland
[2] 2nd Department of Radiology, Medical University of Lublin, Poland

Abstract

Hashimoto's encephalopathy is a rare condition associated with Hashimoto's thyroiditis. It is also described as steroid-responsive encephalopathy associated with thyroid autoimmunity due to the good clinical response to treatment with steroids. It is an encephalopathy, with acute or subacute onset, which may manifest as dementia, disturbances of consciousness, psychosis, frequently accompanied by seizures, tremor, myoclonus, ataxia, and stroke-like episodes. HE is a rare disease with a recent estimated prevalence of 2.1/100,000. HE was first described in 1966 by Brain et al., and since its first description, more than 100 patients have been reported in the literature as having Hashimoto encephalopathy. Thyroid gland dysfunction in HE may be variable: from patients presenting hypothyroidism, those who are euthyroid to patients with hyperthyroidism. Anti –TPO antibodies are present in 95–100% of cases, and anti-Tg antibodies in 73% of patients with HE. To support the diagnosis CSF protein level should be assessed, which is typically elevated. The treatment of HE is usually with oral prednisone or high dose of intravenous methylprednisolone, which should cause resolution of neurological symptoms. The condition seems to be presently underdiagnosed, so, it is important to have a clinical suspicion for HE in patients with clinical manifestation of dementia or psychosis, as it is a readily treatable condition with good prognosis.

Keywords: encephalopathy Hashimoto, dementia

Streszczenie

Encefalopatia Hashimoto (EH) jest rzadkim schorzeniem związanym z zapaleniem gruczołu tarczowego typu Hashimoto. Jest ona również określana jako encefalopatia reagująca na leczenie sterydami i związana z procesem autoimmunologicznym gruczołu tarczowego, z uwagi na dobrą odpowiedź na sterydy. Encefalopatia ta może mieć początek ostry lub podostry i przebiegać pod postacią kliniczną zespołu otępiennego, zaburzeń przytomności czy psychozy, często z towarzyszącymi napadami drgawkowymi, drżeniem, miokloniami, ataksją lub epizodami udaropodobnymi. EH jest rzadkim schorzeniem o zapadalności wynoszącej 2.1/100,000 osób. Została ona po raz pierwszy opisana w 1966 roku przez Braina, a od czasu tej pierwszej wzmianki, w literaturze ukazały się opisy ponad 100 pacjentów z objawami EH. Dysfunkcja gruczołu tarczowego w przebiegu schorzenia może mieć różną postać, od pacjentów będących w stanie hipotyreozy, poprzez chorych w stanie eutyreozy, aż do pacjentów z nadczynnością tarczycy. Przeciwciała anty –TPO są obecne w 95-100% przypadków, a anty-Tg u 73% chorych z EH. Badaniem dodatkowo wspierającym rozpoznanie jest ocena poziomu białka w płynie mózgowo-rdzeniowym, który w typowych przypadkach jest podwyższony. Leczenie EH polega na podawaniu prednizonu w formie doustnej lub też wysokich dawek metyloprednizolonu, co zwykle prowadzi do wycofania objawów neurologicznych. Schorzenie jest obecnie rozpoznawane zbyt rzadko, zatem ważne jest aby pamiętać o możliwości występowania EH w grupie pacjentów z objawami otępienia czy psychozy, jako że EH może być leczona, a rokowanie jest pomyślne.

Słowa kluczowe: encefalopatia Hashimoto, otępienie

Introduction

Hashimoto's encephalopathy (HE) has been described as an encephalopathy associated with autoimmune thyroiditis (Hashimoto's thyroiditis) or as a steroid-responsive encephalopathy associated with thyroid autoimmunity due to the typical response to treatment with steroids [1,2]. It is an encephalopathy, with acute or subacute onset, which may be accompanied apart from dementia by seizures, tremor, myoclonus, ataxia, psychosis and stroke-like episodes. HE was first described in 1966 by Brain et al. [3] who reported a case of a 48-year-old man with hypothyroidism, multiple episodes of ence-

phalopathy, stroke-like symptoms, and Hashimoto's thyroiditis confirmed by elevated antithyroid antibodies. HE is a rare disease with a recent estimated prevalence of 2.1/100,000 [4]. A reported mean age at onset is 44 years, with about a fifth of cases under 18 years of age, the disease is 4 times more frequent in women than in men (4:1 female/male ratio) [5]. Since its first description by Brain, more than 100 patients have been reported in the literature as having Hashimoto encephalopathy [5].

Two types of clinical course of HE have been suggested: relapsing/remitting, also referred to as vasculitic type, which manifests with encephalopathy and stroke-like episodes, and diffuse progressive type, which has an insidious onset and progressive course with occasional fluctuations and manifests with psychiatric symptoms and dementia. Each type may also manifest with tremor, myoclonus, seizures, stupor or coma [6]. Encephalopathy usually develops within days, and the majority of cases present with a relapsing/remitting course, tremor, transient aphasia, seizures or even in status epilepticus, hypersomnolence and gait ataxia. Also commonly seen are myoclonus, psychosis, and stroke-like episodes. In the children population the clinical findings may be variable but in adults a progressive cognitive decline is typical, usually with confusion, seizures, and hallucinations [7].

Diagnosis

Thyroid gland dysfunction in HE is variable despite similar neurological findings. In a recent review of the literature, 35% of patients with had subclinical hypothyroidism; 22% were euthyroid and not on levothyroxine; 20% had overt hypothyroidism; and 8% were euthyroid on levothyroxine, 7% had hyperthyroidism and for 6% thyroid status was unknown; what is interesting 1% did not have thyroid gland disease [5]. Some of the patients improved on treatment with levothyroxine alone, while 40% improved following combined treatment with levothyroxine and steroids [2].

Antithyroid antibodies which should be regularly checked in the serum of Hashimoto's thyroiditis patients include antithyroid peroxidase antibodies (anti-TPO) and antithyroglobulin antibodies (anti-Tg). The prevalence of those antibodies in the general population has been reported at 11% (5–20% in normal older adults, especially in females, and 2–10% in young adults) [5,6]. In the above review multiple antibodies were checked in 71% of cases with HE and 24% reported a normal value for one of the antibodies [2]. Anti-M and anti-TPO were present in 95–100% of cases, and anti-Tg in 73% [2].

Additionally, in the majority of cases of HE an elevated CSF protein level and almost no nucleated cells/mm^3 can be found, but oligoclonal bands are seen frequently. The elevated CSF protein elevation can be mainly observed during exacerbations [8].

The EEG recording shows usually diffuse or generalized slowing or intermittent rhythmic delta activity in the frontal region (FIRDA), nevertheless triphasic waves, focal slowing, epileptiform abnormalities or photoparoxysmal responses may be also seen.

On neuroimaging examinations (CT or MRI) we can observe focal subcortical white matter abnormalities, cerebral atrophy, and diffuse subcortical or focal cortical abnormalities. Approximately 50% of patients with HE have nonenhancing brain MR imaging abnormalities with increased signal intensity on T2 and fast fluid-attenuated inversion recovery (FLAIR) in the white matter as well as dural enhancement [2] which may resolve with treatment. DWI is able to detect small, active, ischemic lesions which are not not detected by conventional MR imaging. These DWI changes are also seen in CNS vasculitis [8,9]. All these changes ma resolve after treatment with steroids. Single photon emission computed tomography (SPECT) studies show focal hypoperfusion in the majority of cases, global hypoperfusion in some and sometimes normal findings. Both EEG and neuroimaging studies in HE may be abnormal but are nonspecific.

On neuropathological examination lymphocytic vasculitis of venules and veins in the brainstem [13,15] or diffuse perivascular lymphocytic infiltration, as well as diffuse gliosis involving mainly gray matter may be observed [14].

The etiology of HE is thought to be autoimmune due to its association with other autoimmune disorders (like myasthenia gravis, glomerulonephritis, primary biliary cirrhosis, splenic atrophy or rheumatoid arthritis), the presence of inflammatory findings in CSF, and good response to treatment with steroids [6,14,15]. A possible mechanism of pathogenesis suggested that HE is an autoimmune cerebral vasculitis, perhaps related to deposition of immune complex. Another possible mechanism can be acute disseminated encephalomyelitis (ADEM) with a presumed T-cell mediated lymphocytic vasculopathy accompanied by blood-brain barrier damage [8].

Treatement

In the treatment of HE immunomodulatory agents (mostly steroids) and/or thyroid-acting agents (mostly levothyroxine), as well as antiepileptic drugs for seizures and status epilepticus should be used [14]. Treatment of HE usually consists of high dose oral prednisone (50–150mg/day) or high dose of intravenous methylprednisolone (1 g/day) for 3–7 days, which typically results in resolution of neurological symptoms (including reduction of refractory seizures). To avoid recurrences a slow taper of prednisone over weeks to months can be given to a patient [15].

Refractory cases with recurrences or those who fail to respond to the above therapy should be placed on long term treatment with prednisone, azathioprine, cyclophosphamide, methotrexate, periodic intravenous immune globulin (IVIG), plasma exchange or combination of these treatments [1,6].

Normalization of CSF, EEG and neuropsychological testing serve as a good indicators of treatment efficacy.

Conclusions

The condition seems to be presently under diagnosed. Therefore, it is important to have a clinical suspicion for HE as it is a readily treatable condition that carries a good prognosis.

References

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Correspondence address

Dr n med. Ewa Papuć
Katedra i Klinika Neurologii UM w Lublinie
ul. Jaczewskiego 8 , 20-954 Lublin
Tel. 81-7244-720, Fax. 81-7244-540
e-mail: ewapap@yahoo.pl