Autoimmunity Reviews 15 (2016) 466–476

Contents lists available at ScienceDirect

Autoimmunity Reviews

journal homepage: www.elsevier.com/locate/autrev

Review

Hashimoto's encephalopathy: A rare proteiform disorder

Giacomo Montagna [a], Mauro Imperiali [b], Pamela Agazzi [c], Federica D'Aurizio [d], Renato Tozzoli [d,*], Ulla Feldt-Rasmussen [e], Luca Giovanella [f]

[a] Department of Pediatrics, Ente Ospedaliero Cantonale, Lugano, Switzerland
[b] Department of Laboratory Medicine, Ente Ospedaliero Cantonale, Lugano, Switzerland
[c] Division of Neurology, Neurocenter of Southern Switzerland, Lugano, Switzerland
[d] Department of Laboratory Medicine, S. Maria degli Angeli Hospital, Pordenone, Italy
[e] Department of Endocrinology, Copenhagen University Hospital, Copenhagen, Denmark
[f] Division of Nuclear Medicine and Thyroid Centre, Oncology Institute of Southern Switzerland, Bellinzona, Switzerland

ARTICLE INFO

Article history:
Received 10 January 2016
Accepted 22 January 2016
Available online 3 February 2016

Keywords:
Hashimoto's encephalopathy
Autoimmune encephalopathies
Autoimmune thyroid diseases
Anti-thyroperoxidase antibodies
Anti-α-enolase antibodies

ABSTRACT

Hashimoto's encephalopathy (HE) is a rare not well understood, progressive and relapsing multiform disease, characterized by seizures, movement disorders, subacute cognitive dysfunction, psychiatric symptoms and responsiveness to steroid therapy. The disorder is generally associated with thyroid diseases and the most common feature is the presence of anti-thyroperoxidase antibodies (TPOAb). Patients are usually euthyroid or mildly hypothyroid at presentation. All age groups can be affected. The pathophysiology is still unclear, especially the link between elevated serum TPOAb and the encephalopathy. Most reported cases occurred in women and girls. Unspecific symptoms, non-pathognomonic laboratory neurophysiology and neuroimaging features make its diagnosis a real challenge for clinicians.
The case of a 16 year old boy, with a clinical picture of HE associated with hypothyroidism, demonstrating an excellent response to high dose steroids is presented together with a systematic review of the literature.

Contents

* Corresponding author at: Department of Laboratory Medicine, Santa Maria degli Angeli Hospital, Pordenone, Italy. Tel.: +39 0434 399213; fax: +39 0434 399906.
E-mail address: renato.tozzoli@aas5.sanita.fvg.it (R. Tozzoli).

http://dx.doi.org/10.1016/j.autrev.2016.01.014
1568-9972/

1. Introduction

Hashimoto's thyroiditis (HT) is the most common form of thyroiditis in both childhood and adulthood [1], with a prevalence of 1.2% [2] and 5% [3,4], respectively. Neurological and psychiatric complications of HT include neuropathy, cerebellar dysfunction, encephalopathy, myxedema, coma, dementia, depression and psychosis [5].

Hashimoto's encephalopathy (HE) is a poorly understood disorder, characterized by unspecific and protean neurological and/or psychiatric symptoms often associated with increased anti-thyroperoxidase antibodies (TPOAb) in serum and sometimes in cerebrospinal fluid (CSF), increased CSF protein concentration, nonspecific diffuse electroencephalogram (EEG) abnormalities, nonspecific magnetic resonance imaging (MRI) features and often but not always responsiveness to corticosteroids. The onset may be acute or subacute and the following course tends to be progressive or relapsing/remitting [6–9].

We present the case of a 16 year old boy with HE together with an extensive review of the literature.

2. Clinical case

A previously healthy, right-handed 16 year old boy was admitted to the hospital after a generalized tonic–clonic seizure, followed by extreme psychomotor agitation, which needed sedation and 48 h of intensive care support. The boy had a normal cognitive development, no history of recent infections or flu-like symptoms, injury, travel, tick bites or academic decline. Vital signs, ECG recording and neurological examination were normal. Laboratory studies including blood count, C-reactive protein, serum electrolytes, lactate and ammonia levels were unremarkable. Urine toxicology was negative. CSF analysis revealed hyperproteinorrachia (855 mg/L; reference range (RR): 200–400), increased albumin (657 mg/L; Upper reference Limit (URL) < 350 mg/L) and a slightly elevated IgG concentration (36 mg/L; RR < 34) without oligoclonal bands. Blood, CSF and urine culture were negative as well as polymerase chain reaction for enteroviruses and herpes simplex viruses in the CSF. Head computed tomography (CT) with and without contrast and MRI showed no abnormal signs. Both electroencephalogram (EEG) and video-monitored-EEG revealed a slowing of the background rhythms localized in the posterior right hemisphere (Fig. 1). During the hospitalization the boy had no further seizure and was discharged home. A follow-up EEG, after three weeks, was normal. The etiology of the encephalopathy remained unexplained for this first episode.

One month later he complained of nausea, photophobia and an intense cold sensation. The parents also reported new-onset irritability, loss of short-term memory and inability to concentrate. Physical examination revealed an axillary temperature of 34.1 °C and a sporadic unintentional bilateral fine hand tremor. Thyroid dysfunction was suspected and confirmed by an increased TSH concentration (19.4 mIU/L; RR: 0.4-4.0), and a decreased fT4 concentration (7.1 pmol/L; RR: 7.5-21.1). Ultrasound examination showed an enlarged thyroid gland with a hypoechogenic pattern and hypervascularity by color-Doppler (Fig. 2). Serum TPOAb and anti-thyroglobulin antibodies (TgAb) were increased (10,640 IU/mL; RR < 60.0 and 55.5 U/mL; RR < 33, respectively). Thyrotropin receptor antibodies (TRAb) and other markers of autoimmunity

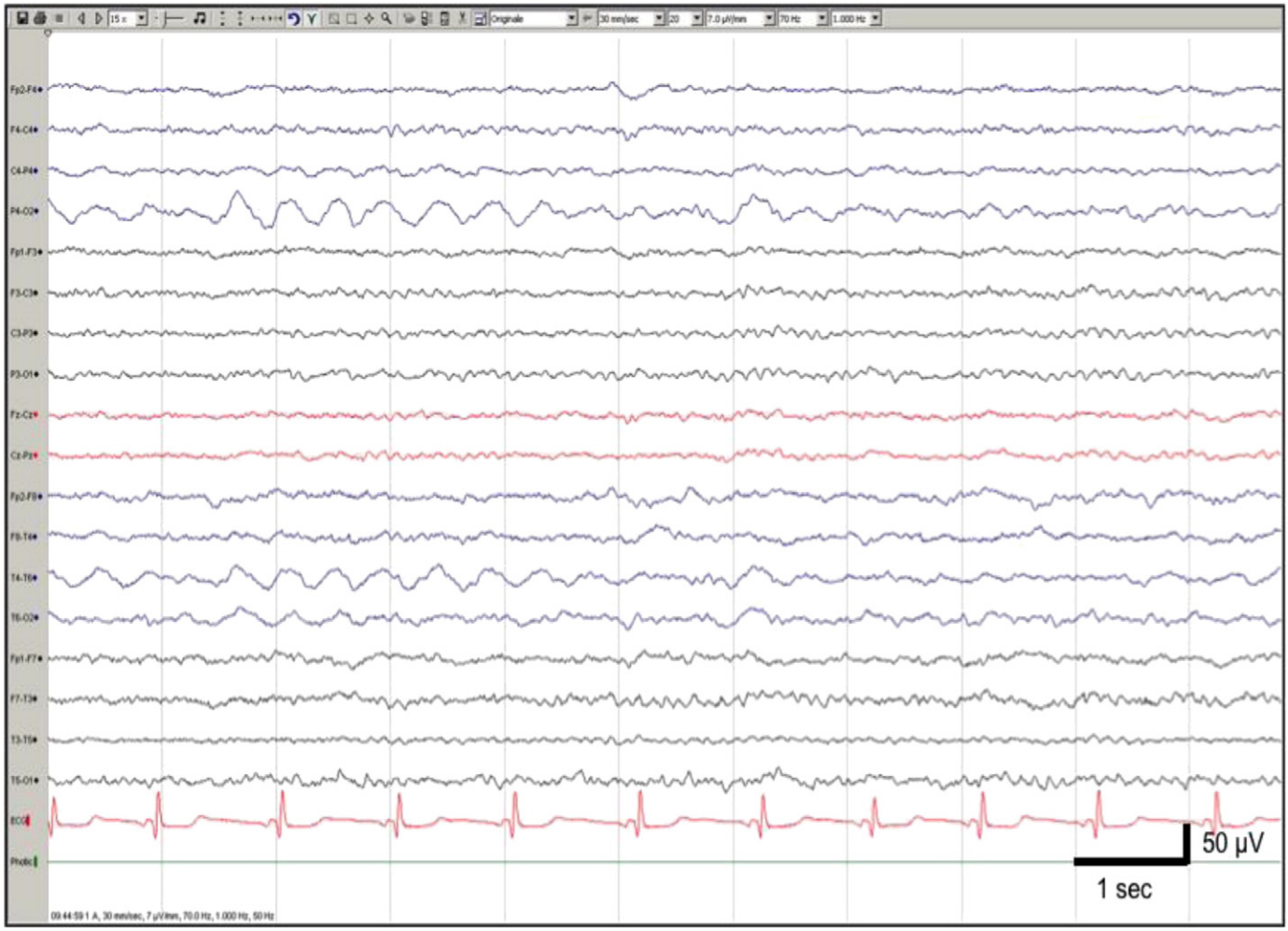

Fig. 1. Scalp EEG at presentation (longitudinal bipolar montage, patient awake) shows slowing of the background rhythms localized in the posterior right hemisphere.