Steroid-Responsive Encephalopathy Associated with Autoimmune Thyroiditis (SREAT): A case report highlighting diagnostic pitfalls and appropriate management.

V. Cavallero [1], M. Pittavino [2], A. Dutto [2], G. Visconti [2], A. Pia [2], A. Papaleo [2] and M. Capobianco [3]
[1] Neuroscience Department ''Rita Levi Montalcini'' (Turin), [2] A.O. Santa Croce e Carle (Cuneo), [3] A.S.L. Martini Hospital (Turin)

Background and Case Presentation

Steroid-responsive encephalopathy associated with autoimmune thyroiditis (SREAT), also known as Hashimoto's encephalopathy (HE), is an uncommon autoimmune neurological disorder characterized by the absence of specific diagnostic criteria [1, 2, 3].

A **67-year-old woman** with a recent diagnosis of **subclinical hypothyroidism and a history of anxiety-depressive syndrome developed transient confusional episodes, accompanied by apraxia and gait disturbances.** Her first presentation to the Emergency Department (ED) was due to the acute onset of objective vertigo.

The clinical picture was initially interpreted as a non-specific episode within the context of a reactive anxiety-depressive syndrome.

One week later, the patient presented again to the ED: her speech was marked by expressive aphasia and a positional tremor in all four limbs was noted, along with an ataxic gait.

Diagnostic Criteria for SREAT – Dalmau et al.

1. Encephalopathy associated with seizures, myoclonus, hallucinations or stroke-like episodes.
2. Mild or subclinical thyroid disease, usually hypothyroidism.
3. Brain MRI is either normal or shows non-specific abnormalities.
4. Elevated serum anti–thyroid peroxidase (anti-TPO) or anti–thyroglobulin antibodies (anti-TG).
5. Absence of well-characterized neuronal antibodies in CSF and serum.
6. Reasonable exclusion of alternative explanations.

Investigations

- Diagnostic lumbar puncture revealed elevated protein levels in the CSF (**127.3 mg/dL**). CSF biomarkers were within **normal limits**. The autoimmune encephalitis panel was **negative** in both serum and CSF.
- Brain MRI with contrast showed **no encephalic abnormalities**.
- EEG was characterized by **bursts of theta slow-wave activity**, occasionally with sharper morphology.
- **^{18}F-FDG PET demonstrated diffuse cortical hypometabolism. Tracer hypofixation was marked in the temporo-parietal areas and moderate in the frontal lobes, with a consistent left-sided predominance** (*Figure 1).*
- Neuropsychological evaluation revealed **multidomain impairments**.

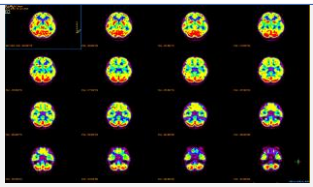

Figure 1

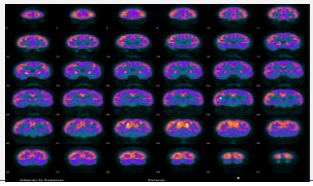

Figure 2

Diagnosis and Treatment

On day 9 of hospitalization, the assessment of thyroid-related antibodies in serum showed elevated anti-thyroid peroxidase (anti-TPO) antibodies **>1300 IU/mL** and anti-thyroglobulin antibodies **23.7 IU/mL**. **These antibodies were subsequently tested in CSF using the same non-standardized method (chemiluminescence immunoassay, CLIA), revealing elevated anti-TPO antibodies of 64 U/mL.**

These new findings supported the diagnosis of SREAT.

High-dose corticosteroid therapy (**methylprednisolone 1 g/die IV**) led to a **rapid and dramatic clinical improvement,** supporting the diagnosis of SREAT.

The patient was discharged **on day 16** with oral prednisone (50 mg/day).

Follow up

- ^{18}F-FDG PET three months after discharge showed residual **mild bilateral temporal hypometabolism** (*Figure 2*).
- A comprehensive neuropsychological assessment conducted two months after hospitalization showed **normal executive, praxic and attentional functions, with short- and long-term memory impairment (RAVLT)**.
- The steroid-based immunosuppressive therapy was **progressively tapered.** Since the 2nd month after discharge, the prednisone dose was reduced to 25 mg/day, after that to 12.5 mg/day by the 6th month.

Discussion

- The case described may be classified as a **type 2 variant of SREAT**, which follows an indolent and progressive course and **can mimic certain forms of neurodegenerative disorders** [4].
- The **^{18}F-FDG PET scan played a relevant diagnostic role.** However, no specific abnormal metabolic patterns have been consistently associated with SREAT in the literature [3, 4].
- The **detection of anti-TPO and anti-TG antibodies** in the CSF supported the diagnosis of SREAT.
- **CLIA is not a standardized method [5]: it may be useful for detecting these autoantibodies in CSF to enhance diagnostic accuracy**.

	June 2024	Follow-up	June 2025 End of FU
Neurological features	Expressive aphasia, positional tremor, ataxic gait, apraxia.	Normal neurological examination.	**Clinical remission.**
NP tests	Multidomain impairments.	Short- and long-term memory impairment (RAVLT).	
Brain ^{18}F-FDG PET	Marked cortical hypometabolism in the temporo-parietal lobes, mild frontal hypometabolism (left>right).	Moderate temporal cortical hypometabolism (predominantly left).	
Thyroid ^{18}F-FDG PET	Hypermetabolism (SUVmax 11.6).	Hypermetabolism with increased thyroid parenchymal volume (SUVmax 17.5).	
TSH (µg/mL)	0.313	6.773	
		Endocrinological FU →	
Prednisone OS (mg)	1 mg/kg	Progressive tapering.	**STOP Prednisone START Cortisone acetate 10 mg/die**
EEG	Nonspecific cerebral dysfunction.	Resolution of the slow-sharp wave abnormalities.	

Take Home Messages

- ✓ **In the differential diagnosis of subacute cognitive decline, consider indolent encephalitic forms such as SREAT.**
- ✓ **Early initiation of a comprehensive workup is essential for achieving a timely diagnosis of SREAT, and the CLIA method can be useful to define the pathophysiology.**

Bibliografia:
1. Graus F, Titulaer MJ, Balu R, et al. A clinical approach to diagnosis of autoimmune encephalitis. *Lancet Neurol*. 2016;15(4):391-404
2. Dalmau J, Graus F. *Autoimmune Encephalitis and Related Disorders of the Nervous System*. Cambridge University; 2022
3. Mattozzi S, Sabater L, Escudero D, et al. Hashimoto encephalopathy in the 21st century. *Neurology*. 2020;94(2):e217-e222
4. Waliszewska-Prosół M, Ejma M. Hashimoto Encephalopathy—Still More Questions than Answers. *Cells*. 2022;11(18):2873.
5. Ferracci F, Moretto G, Candeago RM, et al. Antithyroid antibodies in the CSF: their role in the pathogenesis of Hashimoto's encephalopathy. *Neurology*. 2003;60(4):712-714