The diagnostic challenge of slowly progressive autoimmune limbic encephalitis with Alzheimer disease copathology

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Background

CASPR2 autoimmune encephalitis is associated with a broad spectrum of symptoms involving the limbic system such as anterograde amnesia, temporal lobe seizures and behavioral disturbances. Clinical heterogeneity combined with possible slow disease progression makes this diagnosis challenging particularly against neurodegenerative diseases involving the temporal lobe. We report on a patient with progressive cognitive decline, focal epilepsy, positive ATN status and positive for CASPR2 antibodies.

Case presentation

A 67-year-old man experienced recurrent brief episodes of altered consciousness with speech difficulties and head flushing. EEG and MRI were normal; he was diagnosed with focal seizures and treated first with Levetiracetam (500 mg bid), later switched to Lamotrigine 100 due to onset of mood depression associated with short-term memory deficits.

Nine months later, Lacosamide (100 mg bid) was added due to recurrence of focal seizure with tonic-clonic generalization, with EEG showing mild right temporal slowing of rhythm.

At the age of 68, 15 months after the first symptoms, he was seen at the memory clinic for a neuropsychiatric consultation for anxiety, low mood, worse memory and nonfluent speech with recurrence of focal seizure 1 every 2-3 months.

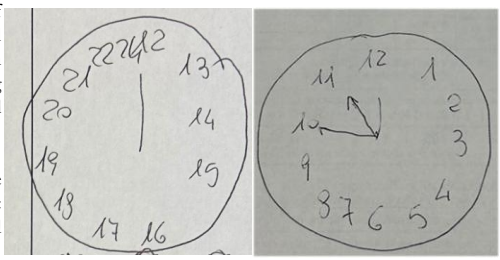

Fig. 1: Clock drawing test before and after treatment. MoCA showed an improvement from 16/30 to 21/30

Neurological examinations showed uncertain wide-based gait and nonfluent aphasia.

Neuropsychological tests revealed a multi-domain cognitive impairment (MoCA score: 16/30) with memory, executive and language deficits (Figure 1).

Blood tests and CSF analysis ruled out metabolic or infectious events (5 white cells); ATN profile was positive (t-TAU 927 ng/L, p-TAU 132 ng/L, aβ42/40: 0,042).

Plasma p-TAU 217 was within normal limits (0,16 pg/L).

Both serum and CSF were also positive for CASPR2 antibodies.

Repeat brain MRI was unremarkable (Figure 2) and EEG confirmed slow activity in the right temporal region. FDG-PET showed higher uptake in the medial temporal lobes (Figure 3). Total body CT and EMG were negative.

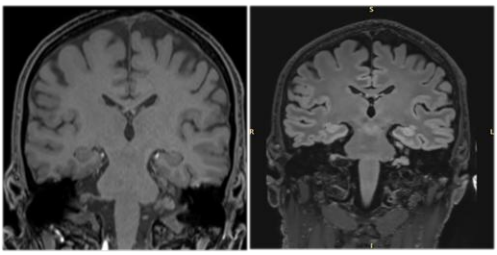

Fig. 2: Repeat MRI (December 2024) in T1 (left) and FLAIR (right) revealed no pathological finding

A diagnosis of probable CASPR2 autoimmune encephalitis was made and high dose steroid therapy combined with e.v. Ig was started with slow steroid tapering.

At follow-up after 4 months after discharge, his cognitive evaluation was improved (MoCA score 21/30) and he had no further seizures. 7 months later, with lowering of steroid to 25 mg/day verbal fluency worsened and gait was more unstable with falls. Neuropsychological evaluation showed no significant change (MoCA score 21/30).

Steroid dose was increased and a second cycle of IgG was prescribed with improvement of gait stability and mood. A second CSF analysis is going to be planned.

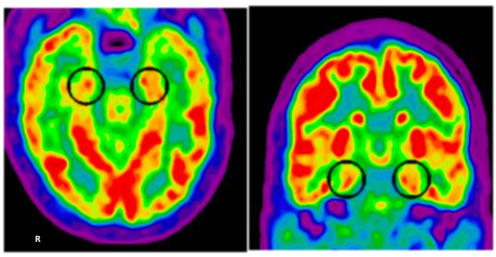

Fig. 3: FDG-PET showing mild hypermetabolism of the amygdala bilaterally

Conclusions

We present a case of an autoimmune limbic encephalitis with slow progression and brain amyloid co-pathology. A repeated CSF analysis will verify whether t-TAU and p-TAU levels had been influenced by the immune-mediated acute inflammatory processes. However, the clinical improvement after immunosuppression points towards autoimmune encephalitis as primary pathology responsible of cognitive impairment.

References:

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