CASE REPORT

Neuropsychological assessment as an objective tool to monitor treatment response in anti-N-methyl-D-aspartate receptor encephalitis

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SUMMARY

We report a 1-year follow-up of a young woman with anti-N-methyl-D-aspartate receptor encephalitis. Management of autoimmune encephalitis remains challenging as objective and clinically relevant biomarkers are sought, which allow for the monitoring of treatment response. While further investigation is required, we believe that this case highlights the importance of following a comprehensive neuropsychological profile as a clinically relevant biomarker to guide therapeutic decision-making. By relying on the neuropsychological assessment of the patient, treatment with more toxic medications was avoided and her antiepileptic drug regimen was simplified.

BACKGROUND

Anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis is an increasingly recognised aetiology of previously unexplained encephalitis.[1 2] The syndrome usually develops with a progression of symptoms through psychiatric manifestations, catatonia, amnesia, reduced verbal output, insomnia, seizures, movement disorders, autonomic instability, hypoventilation and eventually coma.[1 3] Primary language dysfunction without frank psychosis is noted in children with anti NMDAR encephalitis, but is more of an atypical presentation in adults.[1 3–5] While initial treatment approaches are prevalent in the literature, long-term treatment and clinically relevant biomarkers used to assess treatment response remain controversial.[3] Modified Rankin Scale (mRS) has been used as a potential marker for outcome. However, more recently it was shown that in patients with autoimmune encephalitis with a 'good' neurological disability outcome (mRS 0–2), 40% still scored below average in adaptive behaviour and 60% reported ongoing neuropsychiatric or neurocognitive symptoms (emotional lability, short-term memory deficits, etc).[4 6] Therefore, the authors suggested comprehensive neuropsychological assessment is superior to a gross six-point '0=no symptoms, 6=dead' scale, to determine optimal treatment and follow-up care of autoimmune patients.

CASE PRESENTATION

We report a 28-year-old functionally normal woman with no neurodevelopmental, psychiatric, medical or substance abuse history who presented with 3-week progressive course of confusion, difficulty recognising family, decreased speech output, right arm and face numbness, and subsequent epilepsia partialis continua of her right hand.

INVESTIGATIONS

Brain MRI showed no significant findings.

EEG showed continuous slowing over the left hemisphere, but no epileptiform discharges. While serum was negative, the cerebrospinal fluid analysis identified NMDAR antibodies. Malignancy screening was negative (body PET and CT, MRI of pelvis and transvaginal ultrasound).

TREATMENT

The patient was started on antiepileptic drugs (AEDs; clobazam, levetiracetam and phenytoin) and immunosuppression with intravenous steroids, plasma exchange and rituximab.

OUTCOME AND FOLLOW-UP

In order to formally assess her cognitive status and to help guide her immunosuppression treatment, a brief targeted neuropsychological assessment was completed 2 weeks following immunosuppression initiation, 1 month post-symptom onset (table 1). Assessment demonstrated incomplete global aphasia and receptive vocabulary less than the 2-year-old age equivalency. The patient was discharged and received outpatient speech and language therapy two times weekly.

At first follow-up (3 months after disease onset), the patient evidenced limited improvement in speech and function on qualitative exam, with fluctuations throughout the day in behaviour and cognition per her family. Fertility preservation and cyclophosphamide were considered, given a seeming lack of clinical or functional improvement.

Neuropsychological assessment was repeated demonstrating clinical improvement in receptive language function, scores improving to the 6-year-old age equivalency (table 1). In addition, continuous EEG monitoring did not demonstrate any epileptiform activity and therefore multiple AEDs were thought to potentially be contributing to fluctuations in performance throughout the day, as opposed to continued disease progression. Cyclophosphamide treatment was not initiated, and an AED taper of clobazam was initiated.

Table 1 Summary of neuropsychological testing results

Neuropsychological assessments	Time 1: 1 month post-symptom onset; 2 weeks post-immunosuppression initiation	Time 2: 3 months post-symptom onset; 10.5 weeks post-immunosuppression initiation	Time 3: 1-year follow-up
Western Aphasia Battery			
Spontaneous speech content	0%	20%	90%
Spontaneous speech fluency	20%	20%	90%
Auditory verbal comp: Y/N Q's	70%	80%	100%
Sequential commands	10%	60%	94%
Repetition	20%	20%	68%
Object naming	0%	30%	85%
Total language score	15/100	30/100	84/100
Peabody Picture Vocabulary Test—Third Edition (PPVT-3)			
Raw score	16/204	80/204	171/204
Age equivalent	<1 year 9 months	6 years 1 month	19 years 1 month

Scores are presented as percentage correct to account for expanded form used at 1-year follow-up.

In subsequent follow-up visits (6 months and 1 year post-disease onset), she appeared markedly improved and the patient and her family reported return to 70% of baseline functioning, and her language improved to a 19-year-old age equivalency. She remains seizure free on a single AED, and immunosuppressed on rituximab. She is presently emotionally and behaviourally stable, and has continued to follow-up with neuropsychological assessment, to inform cognitive progress and guide transition back to independent execution of activities of daily living.

DISCUSSION

Current literature indicates that neuropsychological assessment can aid in the detection and treatment of autoimmune encephalitis.[3 6 7] While further investigation is required, we believe that this case highlights the importance of following a comprehensive neuropsychological profile as a clinically relevant biomarker to guide therapeutic decision-making in autoimmune encephalitis. We reported specifically on neuropsychological language assessment (most relevant to this case), but standardised and reliable neuropsychological assessments are available for assessing the various cognitive domains affected by any autoimmune encephalitis including memory, attention, executive, visual spatial and psychiatric functioning. We believe that by applying these assessments across the various autoimmune encephalitides one can potentially (1) offer insights into disease mechanism of action, (2) inform specific disease course, (3) identify protective and prognostic factors, (4) inform treatment response and medication selection, (5) guide selection of rehabilitative interventions and (6) monitor for indication of disease stability, progression, recovery and/or relapse.

Learning points

- Neuropsychological assessment in cases of autoimmune encephalitis allows for the identification of particular disease-associated cognitive and psychiatric deficits, which may themselves become clinical biomarkers.
- By relying on the objective neuropsychological assessment, treatment with more toxic medications may be avoided and antiepileptic drug regimen may be simplified.
- Neuropsychological assessment may offer insight into disease mechanism, inform disease-specific course and objectively monitor for disease stability, progression, recovery and/or relapse.

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