Residual Cognitive Weaknesses in a Case of Treated Seronegative Autoimmune Encephalitis

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Background

- Autoimmune encephalitis (AE) refers to a group of syndromes involving brain inflammation due to autoimmune activity and is associated with acute cognitive impairment.
- While several identified AE-associated antibodies (e.g., NMDAR) can be detected in cerebrospinal fluid and blood serum, many patients who respond well to treatment do not have the AE-associated antibodies.
- This causes challenges in diagnosis and treatment and has led to limited literature prognosticating cognitive outcomes following treatment in cases of suspected seronegative AE.
- We describe a case of seronegative AE in a patient with lingering cognitive symptoms after resolution of acute symptoms post-immunotherapy.

Methods

- Patient is a 25-year-old female with a history of ulcerative proctitis who presented with suspected AE in the context of seizure, fever, balance difficulties, and personality changes.
- While antibodies were not detected, she was diagnosed with AE based on presentation, inflammatory markers, and neuroimaging and was treated with steroids, intravenous immunoglobulin, and plasma exchange.
- Patient presented for neuropsychological assessment 10 months later with lingering cognitive complaints.

- ***Neuropsychological Test Battery:***
  - Wechsler Abbreviated Scale of Intelligence-II (WASI-II)
  - Wechsler Test of Premorbid Functioning (TOPF)
  - Wechsler Adult Intelligence Scale IV (WAIS-IV) Digit Span subtest
  - Repeatable Battery for the Assessment of Neuropsychological Status (RBANS), Update, Form A
  - Trail Making Test
  - Wisconsin Card Sorting Test-64 item (WCST-64)
  - Verbal Fluency Tasks
  - TOMM
  - Beck Depression Inventory II (BDI-II)
  - Beck Anxiety Inventory (BAI)
  - Minnesota Multiphasic Personality Inventory-2- Restructured Form (MMPI-2-RF)

Results

Performance Validity

Test	Score
TOMM Trial 1	50
WAIS-IV Digit Span RDS	8
RBANS EI	3

General Functioning

Test	Score
TOPF	SS = 115
WASI-II VCI	SS = 109
WASI-II PRI	SS = 97
WASI-II FSIQ-4	SS = 104
WASI-II Split	BR = 15-20 %
RBANS Immediate Memory	SS = 83
RBANS Visuospatial	SS = 102
RBANS Language	SS = 87
RBANS Attention	SS = 56
RBANS Delayed Memory	SS = 80
RBANS Total	SS = 77

Visuospatial Functions

Test	Score
WASI-II Block Design	T = 43
RBANS Line Orientation	51-75 %ile
RBANS Figure Copy	ss = 9

Learning and Memory

Test	Score
RBANS List Immediate Memory	ss = 7
RBANS List Delayed Recall	≤ 2 %ile
RBANS List Recognition	10 Hits, 0 FPs
RBANS Story Immediate Memory	ss = 7
RBANS Story Delayed Recall	ss = 5
RBANS Story Recognition	12/12
RBANS Figure Recall	ss = 5

Attention, Processing Speed, & Executive Functions

Test	Score
WAIS-IV Digit Span Forward	C% = 97 (LDSF = 5)
WAIS-IV Digit Span Backwards	C% = 56 (LDSB = 5)
WAIS-IV Digit Span Sequenced	C% = 86.5 (LDSS = 5)
RBANS Digit Span	ss = 2 (4 forward)
RBANS Coding	ss = 5
Trail Making Test A	z = -1.9
Trail Making Test B	z = -5.0
WCST-64 Categories Completed	> 16% (4 categories)
WCST-64 Perseverative Errors	T = 47
WASI-II Similarities	T = 59
WASI-II Matrix Reasoning	T = 54

Language Functions

Test	Score
WASI-II Vocabulary	T = 52
Controlled Oral Word Association (FAS)	z = -0.7
Animal Fluency	z = -0.2
RBANS Naming	17-25 %ile
RBANS Semantic Fluency	ss = 5

Mood and Personality

Test	Score
BDI-II	8
BAI	6
MMPI-2-RF Validity Scales	VRIN-r = 63; TRIN-r = 50; F-r = 61; Fp-r = 51; F-s = 50; FBS-r = 42; RBS = 59; L-r = 47; K-r = 38
MMPI-2-RF Higher Order Scales	EID = 57; THD = 63; BXD = 55
MMPI-2-RF Clinical Scales	RCd = 58; RC1 = 59; RC2 = 54; RC3 = 47; RC4 = 65; RC6 = 70; RC7 = 57; RC8 = 52; RC9 = 53
MMPI-2-RF Supplemental Scales	MLS = 52; GIC = 46; HPC = 42; NUC = 70; COG = 54; SUI = 45; HLP = 69; SFD = 65; NFC = 48; STW = 57; AXY = 44; ANP = 54; BRF = 56; MSF = 59; JCP = 57; SUB = 50; AGG = 51; ACT = 53; FML = 74; IPP = 34; SAV = 52; SHY = 50; DSF = 44; AES = 62; MEC = 43; AGG-r = 65; PSYC-r = 63; DISC-r = 51; NEGE-r = 53; INTR-r = 47

Conclusions

- Neuropsychological testing posttreatment revealed weaknesses/variability in attention, working memory, processing speed, and aspects of executive functioning including executive aspects of memory. Language, visuospatial functions, and retentive memory were preserved.
- This case suggested continued frontal-subcortical dysfunction likely related to residual effects of AE.
- Side effects of medications may have also contributed to her cognitive weaknesses.
- This case highlights the need for more research examining cognitive prognosis and expected timelines post seronegative AE treatment, given limited existing research.
- This is an important consideration for interpretations and recommendations from our neuropsychological evaluations.

Additional Notable Case History Information:

- She experienced fever, change in personality and behavior (“emotional outbursts”), and a seizure. She was initially hospitalized at a local hospital for one week and was later transferred to another hospital. She was diagnosed with AE and treated with high dose solumedrol, IVIG, prednisone, and plasma exchange. She was discharged at the end of the month.
- *Cognitive Complaints:* occasional word finding difficulties (once or twice a week), problems with retrieval; some problems with short term memory
- *Other Relevant Issues and Complaints:* some emotional outbursts, which she attributes to clobazam; fatigue 5 months ago, treated with modafinil
- *Other Medical Conditions:* autoimmune proctitis, seizures in the context of AE, history of headaches (dates back to high school), though rarely occur now; auditory hallucinations in the context of AE while she was hospitalized
- *Medications:* Clobazam, levetiracetam, mesalamine, prednisone, pantoprazole, Phenytoin, Vimpat, modafinil
- *Recent Neuroimaging History:*
  - PET brain improved, no focus of significant cortical hypermetabolism
  - MRI brain showed “interval development of a right cerebral convexity extra-axial fluid collection and extension of the left cerebral convexity extra-axial fluid collection. No significant mass effect or midline shift. Persistent diffuse dural enhancement which is nonspecific and may be secondary to puncture, intracranial hypotension, inflammatory or neoplastic etiologies. No new abnormal intraparenchymal enhancement. Stable left frontal developmental venous anomaly. No evidence of hippocampal atrophy or signal abnormality.”
  - aEEGs and vEEGs showed mild generalized background slowing
- *Family History:* unspecified psychiatric problems (second degree relative), ulcerative colitis (first degree relative)
- *Education and Occupation:* Obtained her bachelor’s in finance and works at an advertising firm; took time off in the context of AE but recently returned
- Low score on one of the embedded performance validity measures represents genuine weakness rather than suboptimal engagement

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