Epilepsy & Behavior Reports 17 (2022) 100518

Contents lists available at ScienceDirect

Epilepsy & Behavior Reports

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

Case Report

Cognitive status in a 62-year-old male with lifelong temporal lobe epilepsy and multiple comorbidities

Erin Plumley, Rama Maganti, Bruce Hermann *

Department of Neurology, University of Wisconsin School of Medicine and Public Health, Madison, WI, United States

ARTICLE INFO

Article history:
Received 30 September 2021
Revised 25 November 2021
Accepted 11 December 2021
Available online 17 December 2021

Keywords:
Case report
Temporal lobe epilepsy
Cognition
Behavior

ABSTRACT

This is a case report of a 62-year-old male with lifelong temporal lobe epilepsy presented with an interesting matrix of clinical, cognitive, psychiatric, neuroinaging and psychosocial features. This was one of the cases presented for review and discussion at the ILAE Neuropsychology Training Course as part of a case series discussion and is highlighted to illustrate the potential for neuropsychological resilience in a patient with epilepsy.

Introduction

This patient with temporal lobe epilepsy (TLE) was presented at the ILAE Neuropsychology Summer School as part of the case series discussions. The case involves a 62-year-old, left-handed male with 16 years of education who was admitted to the epilepsy monitoring unit for video-EEG to characterize his drug resistant epilepsy. He is here reported due to his remarkably intact cognitive presentation despite a complicated medical history and inherent risk factors which are typically associated with compromised cognitive function. Unique features of the case included complications of antiseizure medications, complex psychosocial and psychiatric histories, atypical cerebral language dominance, unexpected neuroimaging findings, and largely intact neuropsychological status including memory performance. The neuropsychological evaluation and subsequent presentation and discussion of this patient occurred prior to epilepsy surgery. We now focus on those findings and the questions that were raised, and provide additional information to summarize his subsequent neurological course. Overall, the objective of the report is to spotlight the presence of multiple medical risk factors in an individual and yet demonstrate retention of cognitive reserve to illustrate neuropsychological resilience.

Case report

Medical history

AB is a 62-year-old, left-handed male with a medical history significant for esophageal reflux, tubular adenoma, peripheral neuropathy, and myopia. Sleep was reported to be intact and without problems involving sleep onset or maintenance in the absence of sleep apnea. AB played football in high school and reported a few "hits" from which he was momentarily dazed but without subsequent cognitive, behavioral, or physical sequela. In 2001, he was involved in a motor vehicle accident due to icy conditions, reporting that the airbag deployed. Impact was without loss of consciousness or subsequent neurobehavioral complications.

AB was admitted to the epilepsy monitoring unit for video-EEG to characterize his drug-resistant epilepsy. It was learned that he was the product of a normal pregnancy, labor and delivery, born at term with birthweight unknown. At 6 months of age, he was hospitalized for a severe febrile illness and was diagnosed with meningitis. It is uncertain if seizures were present at that time (the original records were unavailable). His subsequent development was reportedly unremarkable with no history of neurodevelopmental, behavioral, learning, or subsequent medical issues. At age 14 years, he experienced the onset of spontaneous recurrent seizures for which he was started on phenytoin and ultimately remained on for over 4 decades. AB reported that he remained seizure-free during this time. However, there was a very strong suspicion that he experienced recurrent focal onset seizures for which he was amnestic because reliable witnesses reported

* Corresponding author at: Department of Neurology, University of Wisconsin Medical Foundation Centennial Building, 1685 Highland Avenue, Madison, WI 53705, United States.
E-mail address: hermann@neurology.wisc.edu (B. Hermann).

https://doi.org/10.1016/j.ebr.2021.100518
2589-9864/

observing episodic focal impaired awareness seizures without post-ictal self-awareness. He never experienced a focal to bilateral tonic-clonic seizure. His epilepsy became more problematic in 2005 at age 52 during a phenytoin medication adjustment, and he subsequently experienced an estimated 6 focal impaired awareness seizures per year from that point on. In 2012, his neurological examination revealed impaired position sense and decreased light touch in his feet bilaterally as well as inability to complete heel-to-toe walking--suggestive of a cerebellar effect that was presumably related to the long-term use of phenytoin where, in addition, laboratory tests in late 2012 revealed toxic levels of phenytoin. In 2013 at age 60, he was ultimately switched to levetiracetam 1000 mg BID. He initially reported being seizure-free for about one year, but then reported an increase to 5 seizures per year. As a result, his dose was increased to 1500 mg twice daily in 2015.

AB's seizures are stereotyped and characterized by an aura of a strange, abnormal (unpleasant) metallic taste followed by a vacant stare, unresponsiveness, oral automatisms (lip smacking) and verbalization (saying "what" repeatedly). The duration of the seizures was estimated to be approximately 2 min followed by mild postictal agitation and restlessness. The seizures occurred predominantly at night, 1–2 h after falling asleep. This seizure type occurred twice per month prior to levetiracetam monotherapy. His second seizure type was characterized by a typical aura followed by a sensation of "lightheadedness and an out of the body sensation" lasting 5–10 seconds, and these occurred 1–2 times per month prior to levetiracetam dosage increase. His third seizure type was characterized by a sensation of déjà vu for 5–10 seconds with no associated impairment of awareness.

Psychiatric history

AB reported experiencing episodes of depression throughout his life that tended to occur without warning and that were unrelated to situational factors. These were described as periods marked by sadness, apathy, irritability, "feeling sorry for himself" and a "racing mind" at night. The frequency was unclear, but episodes were more evident when he was working full time, would last for "about a week" and then spontaneously remit and were reportedly exacerbated with the introduction of leviteracetam. He denied that these episodes impacted his occupation or impaired social functioning. When the depressive episode resolved, AB stated that he felt like he was "on a high." There was no clear history of mania or hypomania, suicidal ideation, initiation of psychotropic medication, or psychiatric treatment. Family psychiatric history was notable for post-traumatic stress disorder and alcoholism in his father that was reportedly linked to his military service. Three paternal cousins committed suicide.

Social history

AB and his two siblings were initially raised by his biological parents until age 4 when his mother died. His father remarried and he was then raised with an additional 3 step-siblings and 2 half-siblings. His stepmother was described as verbally, physically and emotionally abusive. At age 14 years, he moved out of the home to live with a brother due to the abuse. AB went on to obtain a Bachelor of Arts degree (biology major) and was employed by a large food corporation for 38 years as a quality supervisor in a laboratory. He reported that he enjoyed his job and retired in December 2012 at age 59. AB has been married for 38 years. He and his wife adopted a son with complex medical issues who passed away at age 33. AB denied changes in cognition or day-to-day functional status and reported driving without difficulty or incident. For leisure, AB runs 4 miles approximately 3 times per week. He denied history of tobacco, alcohol, or other substance use. A past family history of epilepsy was denied.

Evaluation

Neuroimaging. Brain MRI revealed areas of focal encephalomalacia within the left external capsule and basal ganglia and lateral left putamen, believed to represent sequelae of prior intracranial hemorrhage, the timing of which was uncertain, suspected but not confirmed to be possibly linked to his bout of encephalitis. The left hippocampus demonstrated volume loss and loss of internal architecture with increased FLAIR signal. Ventricles and cortical sulci were felt to be mildly prominent, compatible with mild diffuse cerebral and cerebellar volume loss and evidence of old bilateral cerebellar infarcts. There were also small punctate areas of T2-weighted and T2 FLAIR signal abnormality in the deep frontoparietal white matter likely representing small vessel ischemic disease. *FDG-PET* revealed focal moderate hypometabolism within the distal aspect of the left mesial and lateral temporal lobe; hypometabolism in the left caudate, left putamen, and left thalamus, and hypometabolism in the bilateral cerebellar hemispheres.

EEG monitoring in the Epilepsy Monitoring Unit. AB underwent video-EEG monitoring for 5 days. Interictally, clear epileptiform activity was lacking. Four seizures were captured and semiologically they were preceded by an aura of a metallic taste as well as lightheadedness and then followed by a fearful look followed by automatic behaviors consisting of repetitive lip smacking and fidgeting. He was able to follow commands and recalled objects inconsistently that were presented during the events. Electrographically, the seizure onset was characterized by rhythmic delta activity arising from the left hemisphere that subsequently evolved to rhythmic ictal theta activity that was best seen in the left temporal chain. Seizure duration ranged from 40-60 seconds.

Intracarotid amobarbital procedure. The results revealed intact expressive and receptive language and right-sided hemiplegia and a contralateral visual field deficit following infusion of the left cerebral hemisphere after 100 mg of sodium amytal was injected. Following the Medical College of Georgia protocol (Loring et al., 2005), his memory performance was found to be intact with spontaneous recall of 5 of 8 items with recognition correct on 8/8 items and no false positive errors. The right cerebral hemisphere was not tested.

Cognitive assessment. AB presented with fluent, prosodic, and non-paraphasic speech. His thoughts were goal directed, but tangential during the clinical interview. He appeared mildly disinhibited with sarcastic responses. Affect was euthymic and animated. Performance was intact on measures of performance validity (Dot Counting Test, E-score = 12; Rey −15, score = 13). Supplemental Table 1 summarizes the assessment for which the following trends were evident:

- Estimated general cognitive functioning was average (WAIS-IV 3-short form subtests FSIQ = 94). Single word reading ability was also average (WRAT-4 word reading = 99).
- Verbal and visual learning and memory were intact. AB recalled 7-9-9-13-11 items from a 16-item word list across learning trials, representing high average performance (CVLT-II = SS = 115). Following a delay, he recalled 10 items which improved to 11 with category prompts, representing average performance (SS = 108). Recognition discrimination was high average (SS = 115). On a measure of visual learning and memory, AB recalled 4-6-9 units from a 12-unit geometric display across learning trials, representing average performance (BVMT-R = S S = 91). Following a delay, he recalled 8 of the previously encoded units, representing average performance (SS = 97). Recognition discrimination was within normal limits.

- Language abilities were intact. Visual object naming was high average (BNT = SS = 112) and semantic fluency was average SS= (105).
- Processing speed was average (WAIS-III Digit Symbol-Coding = 90; TMT-A = 97, 0 errors)
- Abnormalities were evident in executive functioning. Visuomotor and mental flexibility were low average (TMT-B = 87, 0 errors). Novel problem solving and concept formation was borderline impaired to low average with 1 category completed and impaired for number of errors and perseverative responses (WCST-64).
- Several self-report measures of mood and personality were completed. Depression screening was unremarkable (NDDI-E raw score = 8). Screening of DSM-IV symptomatology was unrevealing with all scale scores within normal limits (PDSQ). On the MMPI (MMPI-2-RF), AB responded in a valid manner with no elevations across the clinical scales. His responses indicated a higher-than-average level of behavioral constraint, he did not appear indecisive, and a lower than average level of aggressive behavior. Additional elevations were on the following scales: neurological complaints and disaffiliativeness (e.g., prefers being alone).

Overall, the neuropsychological screening demonstrated average general cognitive abilities and intact processing speed, visual object naming, verbal fluency, verbal learning and memory, visual learning and memory, and mental flexibility. In contrast, AB demonstrated abnormality in novel problem solving with a notably increased number of errors and perseverative responses. Findings of executive dysfunction were consistent with his tangential and disinhibited presentation. Interestingly, on a self-report measure his responses were suggestive of an individual who demonstrates an above average level of behavioral constraint indicating that he does not act out impulsively or seek excitement. However, he presented as mildly disinhibited. Further, his responses suggested he was someone who was somewhat asocial and who experienced neurological symptoms. The diagnostic impression included Mild Neurocognitive Disorder (dysexecutive). Although he only had one low executive function score on a measure of novel problem solving, his presentation was also suggestive of executive dysfunction marked by a tangential affect and mild disinhibition.

Discussion

Several aspects of this patient's presentation are of interest. AB appeared to suffer an early initial precipitating injury (meningitis and possibly vascular insult) followed by a classic latent period with the onset of spontaneous focal seizures in early adolescence. The precipitating injury was believed to have put him at increased risk for seizures. His seizures were reportedly well controlled for decades, but with variable reporting of frequency per patient and family, but eventually breaking through with clearly subsequent drug resistant epilepsy. Looking forward to retirement, he initiated the surgical evaluation process where structural imaging unexpectedly revealed diffuse abnormalities. In addition to left mesial temporal sclerosis, imaging findings included bilateral cerebellar white matter lesions and focal caudate and putamen lesions with hemosiderin sequelae of prior hemorrhage, though there was no clear history of clinical stroke. Hypometabolism was observed in the left mesial and lateral temporal lobes consistent with his left temporal epilepsy, along with bilateral cerebellar hypometabolism, presumably related to the effects of chronic antiseizure medication, use as well as hypometabolism in the left thalamus and left putamen.

In the context of significant lifelong epilepsy, aging, and diffuse neuroimaging findings, we expected to see considerable cognitive pathology; however, AB arguably demonstrated cognitive reserve with generally spared cognitive abilities, save for mild executive dysfunction. It is certainly possible that more extensive testing might have revealed additional cognitive pathology. It is unclear to what degree the executive dysfunction is reflective of a possible underlying mood disorder, chronic phenytoin use, or related to his cerebral pathology in general, or cerebellar-thalamic-striatal abnormalities in particular given their known link to executive function. Notable of course was his intact verbal learning and memory in the context of left hippocampal sclerosis. AB's right hemisphere dominance for speech and left handedness are of relevance here and could reflect either reorganization of function in the context of his early encephalitis and associated lesions; or, reflective of "natural" reversed speech. Unfortunately, we have no handedness information for his biological family which might have been helpful in differentiation. Interestingly, there appears to be no clear and unequivocal evidence of pathological "crowding out" of nonverbal abilities nor poor right hemisphere mediation of language skills suggestive of reorganization. He demonstrated a personal weakness in visuospatial processing and problem solving when compared to verbal measures, but the significance of this is unclear and may reflect normal variability. Taken together, his cognitive skills were, overall, impressive and arguably not due to exceptional innate ability. He did have a college education and stable work history, however, his work tasks were reportedly rote and routine by design. Further, he led a healthy lifestyle with no history of drug, tobacco or alcohol use, with routine exercise. There is the question as to whether his healthy lifestyle served as a protective factor for his brain health in the context of a complicated neurological history. Given the well-established potential benefits of exercise on brain health and cognition in aging and preclinical neurodegenerative disorders [3,4], as well as the emerging interest and early findings in epilepsy [1,2], it is possible that his lifestyle choices provided some protection against further challenges to his neurobiological integrity and thus contributing to cognitive reserve. It is possible that attention to other potentially modifiable risk factors of interest to the aging community may be of relevance to the cognitive and brain aging processes of persons with epilepsy (c.f., [5]). Future research is needed to determine how often such cognitive resilience is seen clinically and its relative effect size across cognitive domains.

AB demonstrated further resilience regarding his emotional well-being. He experienced lifelong fluctuations of mood in the context of a family history of depression and suicidality, exacerbated by leviteracetam within the context of a difficult childhood home and family upbringing which he eventually fled. In addition, and to his credit, he subsequently obtained a college education, maintained an admirable long-standing employment history with a major corporation, and enjoyed a stable marriage and lifestyle.

Interesting and illustrative points include, but are not limited to, the risk of cognitive change following epilepsy surgery, longer-term cognitive risks associated with aging, and potential cognitive reorganization that may have provided lifelong cognitive protection.

Subsequent course

At the time of the presentation of his case at the ILAE training course AB was still being considered for epilepsy surgery after neuropsychology was no longer involved in his care. His course was as follows: given his drug-resistance, evidence of left hippocampal sclerosis on MRI, ipsilateral hypometabolism on PET, and intact right hemisphere memory, surgical treatment for his epilepsy was recommended as a treatment option. After discussing the pos-

sibilities of a left amygdalohippocampectomy versus laser ablation of the hippocampus, he chose the latter. The initial procedure was performed in 2016 at age 63, 11 months after the initial neuropsychological evaluation and 6 months after Wada evaluation, where the head and body of left hippocampus was targeted. Given that the entire hippocampus could not be ablated in one sitting, a second ablation was performed for the remainder of the body and tail of the hippocampus in 2017 at age 64. He had post-operative complications of a sigmoid sinus thrombosis and deep vein thrombosis that required anticoagulation. He was rendered seizure-free for 2 years but later developed recurrence in the context of an attempted taper of levetiracetam during conversion to lamotrigine monotherapy. Given this failure, he has been maintained on stable dual therapy, lamotrigine 200 mg and levetiracetam 500 mg twice daily.

Conclusions

This case illustrates several unique circumstances, most prominent of which is the degree of general cognitive preservation occurring in the complex setting of right hemisphere dominance for language, intact verbal memory in the presence of left hippocampal sclerosis, diffuse neuroimaging abnormalities with their potential to adversely impact cognitive function, and his complex psychosocial and behavioral history. Limited was information regarding early medical history and long-term collateral information regarding whether the clinical observations of executive dysfunction (e.g., tangentiality and disinhibition) was longstanding or of more recent and worrisome development. Further limited was information regarding the timing of his neuroimaging imaging abnormalities and their link to the presence of behavioral changes. The cognitive battery was somewhat attenuated along with lack of cognitive assessment following his surgery. There were no physician-reported cognitive changes or patient complaints of changes that occurred following surgery which is reassuuring, but the benefits of testing subjective reports with formal assessment are appreciated. Post-operative neuropsychological evaluation would have been helpful to complete the picture of resilience of his cognitive function and serve as an additional datapoint as he continues to age in order to monitor the risk for an atypical cognitive sging course. But nevertheless, the presurgical cognitive assessment will be beneficial should future cognitive concerns arise.

Disclosures

None for any author.

Declarations of interest

None.

Conflicts of interest

The authors of this case report have no conflicts of interest to declare.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ebr.2021.100518.

References

[1] Allendorfer JB, Arida RM. Role of physical activity and exercise in alleviating cognitive impairment in people with epilepsy. Clin Ther 2018;40(1):26–34.
[2] Allendorfer JB, Brokamp GA, Nenert R, Szaflarski JP, Morgan CJ, Tuggle SC, et al. A pilot study of combined endurance and resistance exercise rehabilitation for verbal memory and functional connectivity improvement in epilepsy. Epilepsy Behav 2019;96:44–56.
[3] Dougherty RJ, Jonaitis EM, Gaitán JM, Lose SR, Mergen BM, Johnson SC, Okonkwo OC, Cook. DB. Cardiorespiratory fitness mitigates brain atrophy and cognitive decline in adults at risk for Alzheimer's disease. Alzheimers Dement (Amst). 2021;13(1):e12212.
[4] Edwards GA, Gamez N, Escobedo Jr G, Calderon O, Moreno-Gonzalez I. Modifiable risk factors for Alzheimer's disease. Front Aging Neurosci 2019;24 (11):146.
[5] Gaitán JM, Moon HY, Stremlau M, Dubal DB, Cook DB, Okonkwo OC, et al. Effects of Aerobic exercise training on systemic biomarkers and cognition in late middle-aged adults at risk for Alzheimer's disease. Front Endocrinol (Lausanne) 2021;20(12):660181.