Case Report

Serial neuropsychological testing before and after hemispherectomy in a child with electrical status epilepticus in slow wave sleep

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ABSTRACT

Electrical status epilepticus in slow wave sleep (ESES) is typically characterized by neuropsychological deterioration to varying extents. While the syndrome is self-limiting for some, for others it has a swiftly declining course that requires aggressive neurosurgical intervention. Here, we present a patient with ESES secondary to a large left middle cerebral artery stroke in utero who experienced behavioral and neuropsychological deterioration that rapidly progressed. Collectively, her neuropsychological status, EEGs, MRIs, and nature of her ESES warranted a left hemispherectomy to prevent further decline. The patient was seen for four neuropsychological evaluations. Over time, neuropsychological test scores did not adequately capture her degree of impairment and change. Behavioral observations during evaluations and parental reports played a critical role in determining her initial decline and mild post-surgical improvement. For all practitioners, this report illustrates one extreme of ESES. It also illustrates, particularly for neurologists and neurosurgeons, the importance of behavioral observations relative to test performances.

1. Introduction

Encephalopathy with electrical status epilepticus in slow wave sleep (ESES) represents a large spectrum of disorders and is characterized by an EEG pattern consisting of sleep-related activation and diffusion of spike-wave discharges that usually occupy ≥85% of non-rapid eye movement sleep. Onset is typically between ages two and 14 years, and the condition is often self-limiting by adolescence [1–3]. However, a sizable portion of patients with ESES does not experience spontaneous remission, instead suffering rapid irreversible or minimally reversible developmental, behavioral, and neuropsychological deterioration [2]. Mechanisms underlying the presence and severity of neuropsychological impairment remain inadequately understood because the condition is rare, resulting in published research studies with small, heterogeneous samples. Some children require aggressive surgical intervention for seizure control and cessation of cognitive deterioration. A unilateral MRI lesion of structural etiology is among the top factors that produces favorable surgical outcomes [4,5]. The variability in course and presentation of ESES constrains prescription of a precise gold standard for treatment.

This case report describes a girl (BX) who developed ESES secondary to a large in utero stroke. While she initially presented to Neurology with hemiparesis and delay in achieving early developmental motor and language milestones, she subsequently developed clinical seizures and then ESES accompanied by significant neuropsychological and behavioral changes that worsened rapidly. This case illustrates how serial neuropsychological evaluations reflected marked behavioral changes over time that were poorly captured by test scores and that were not fully appreciated initially in surgical decision-making by either the treatment team or patient’s family. Thus, the role of the neuropsychologist in advocating for surgical intervention to prevent further cognitive decline also is highlighted.

2. Materials and methods

2.1. The study subject

For deidentification, patient pseudo-initials were created using a random letter generator. All dates were fabricated, although relationships among dates were maintained because of their importance in understanding when events occurred relative to one
another. All applicable items on the CARE (CAse REports) guideli-
lines checklist1 are reported in this paper.

2.2. Neuropsychological evaluations, measures, and scores

Neuropsychological evaluations were conducted once prior to
neurosurgery and three times post-surgically (i.e., two weeks,
two months, and six months). Table 1 contains all neuropsycholog-
ical measures at each evaluation. Neuropsychological data (per-
formance-based and parent-report scores) are presented in a
simplified format longitudinally, grouped by domain and pre-
sent as percentiles, in Tables 2 and 3. Scores described as “aver-
age” are between the 16th and 84th percentiles. Because the
neuropsychological evaluation two weeks post-surgically was
brief, BX’s parents did not complete questionnaires.

3. Results

3.1. Case presentation

Patient BX was born at 41-weeks gestation after an uncompli-
cated delivery. She initially presented to Neurology at age three
years (i.e., mid-2015) with right hemiplegia and episodic behavior
concerning for focal seizures. Ensuing EEG was abnormal, consis-
tent with a epileptiform discharges over the left central area
reflecting an increased tendency for the expression of focal sei-
zures. Brain MRI several weeks later showed cystic encephaloma-
lacia of the left cerebral hemisphere in the middle cerebral artery
distribution (consistent with remote stroke), smaller left middle
cerebral artery than the right, smaller left basal ganglia than on
the right, and evidence of Wallerian degeneration in the left cere-
bral peduncle. Pre- and post-surgical MRI slices are presented in
Fig. 1. She started oxcarbazepine but continued to have focal
seizures.

A subsequent series of speech-language, physical, and occupa-
tional therapy evaluations over the next four months identified
mild speech impairment characterized by articulation errors that
reduced speech intelligibility, age-appropriate receptive and
expressive language skills, balance impairment, fine motor mani-
puation difficulty, and sensory concerns (e.g., hypersensitivity to
lights, need for increased tactile input). Additional parental con-
cerns included inability to toilet independently and excessive
apetite.

3.1.1. Clinical course

About one year after her initial EEG (i.e., mid-2016), video-EEG
(vEEG) was performed and was abnormal due to the presence of
left centro-parieto occipital spikes and low amplitude slowing over
the left hemisphere. She presented to the emergency room for
numerous episodes of status epilepticus (SE) between mid-2016
and mid-2017. Episodes of SE were characterized as focal onset
(left hemisphere) evolving into bilateral convulsive SE of childhood
due to remote brain injury from stroke. Seizures were 3–7 min in
duration, and required rectal diazepam.

BX was educated in a developmental preschool in 2017 with an
Individualized Education Program where she reportedly performed
at or close to grade level. However, seizure frequency and severity
peaked about 1.5 years after her initial presentation (i.e., shortly
after beginning kindergarten). This coincided with abrupt slowing in
academic achievement and significant behavioral changes includ-
ing increased disengagement, repetitive hand motions, drooling, and
behavioral outbursts. Upon returning to school after

1 Checklist available at https://www.equator-network.org/reporting-guideli-
nes/care/.
behavior persisted. Despite these behaviors, scores in language comprehension and auditory working memory improved mildly. While her expressive vocabulary score declined, this was largely a product of perseveration, as she repeated prior responses from another test with varying vocal inflections. Expressive language was markedly qualitatively better (in contrast to her score and relative to the pre-surgical evaluation), characterized by improved intelligibility, adequate expression of her wants, and intact ability to repeat short sentences. Formerly characterized as right hemiplegia, she demonstrated post-surgical hemiparesis. It had been anticipated that motor skills would remain unchanged post-surgically due to motor planning believed to be subserved by her right hemisphere.

### 3.2.3. Post-surgical outpatient assessment 2

BX’s next outpatient neuropsychological reevaluation was two months after surgery, prior to returning to school at seven years of age and during this time she remained seizure-free. BX was highly impulsive, grabbing test materials as soon as they were presented and choosing answers before considering all response options, as well as being inappropriately affectionate at times with faculty/staff, which represented a change in her behavior. Word reading remained significantly suppressed, comparable to a preschooler who had not entered kindergarten. Right-sided hemiparesis remained prominent, although her dominant hand grip strength and grooved pegboard scores improved.

While no other neuropsychological scores improved, BX’s responses on questionnaires greatly contrasted with past and present scores by indicating fewer concerns regarding emotional and behavioral functioning and significant improvement in all areas of adaptive functioning. She also reported several qualitative behavioral improvements including a mild reduction in mouthing objects, increased responsiveness to redirection, consistent independent toileting, and mildly decreased impulsivity (which continued to greatly contrast with what was observed during the evaluation). She denied observing any worsening of behaviors or cognition; however, social immaturity was becoming more apparent due to her lack of progress. An anticipated right homonymous hemianopia post-surgically was confirmed but BX compensated well by turning her head to the right and moving her eyes to the left to scan the right visual field.
3.2.4. Post-surgical outpatient assessment

BX’s final neuropsychological evaluation was six months after surgery (i.e., age seven years, four months). Updated vEEG between neuropsychological evaluations was abnormal (consistent with history of hemispherectomy) but without evidence of epileptiform activity including ESES and she remained seizure-free. Because of continued limited use of her right arm and hand, she was scheduled to begin receiving botulinum toxin A injections three weeks after this evaluation.

BX denied new concerns and continued to report qualitative improvements. However, her responses on the adaptive functioning questionnaire indicated a number of mild declines compared to four months prior. Higher scores two months post-surgically likely were over-estimations of BX’s abilities in the context of seeing several improvements in her daughter’s functioning, while by six months post-surgically, her perception of adaptive functioning had become more realistic. She signified improvement in executive function on questionnaires comparing her pre-surgical evaluation to her 6-month post-surgical evaluation that was not readily apparent during the assessment. However, many of the improvements identified still reflected impairment relative to peers.

While BX remained distractible and impulsive, there was progressive improvement. Mouthing objects rarely occurred. Peer relations had improved, and she had developed several friendships at school. At the evaluation, motor skills and appearance were notable for right hemiparesis, wide-based gait during ambulation, right leg bracing, and chronic contracture of her right hand. She initially approached the neuropsychologist as if she was going to hug him immediately, but she self-adjusted her behavior appropriately, a notable behavioral change and demonstration of self-inhibition.

Overall, behavioral observations and test scores were most consistent with one another compared to prior evaluations. BX was able to complete the evaluation without breaks, something she previ-

| Table 2 | Neuropsychological test scores (percentiles). |
|---------|---------------------------------------------|
| Age (Years:Months) | 6:8 | 6:10 | 7:0 | 7:4 |
|                      | Pre-Surgical | 2 weeks | 2 months | 6 months |
| Verbal Intelligence  | 21 | 19 | 7 |
| Nonverbal Reasoning  | <1 | <1 | 4 |
| Word Reading         | 1 | <1 | 7 |
| Language             | 25 | 63 | 9 |
| Comprehension        | 68 | 10 | 16 |
| Expressive Vocabulary| 5 | 9 | 10 |
| Verbal Fluency (Semantic) | 7 | 5 | 9 |
| Visual Perception    | 25 | 16 | 9 |
| Block Construction   | 5 | 16 | 9 |
| Motor                | 3 | 19 | 16 |
| Fine Motor Coordination | 13 | 6 | 8 |
| Tracing              | 95 | 79 |
| Drawing              | 2 | <1 | 7 |
| Grip Strength (Dominant Hand) | 73 | 16 |
| Leg Coordination     | 99 | 79 |
| Attention & Working Memory | 25 | Attempted | Attempted |
| Auditory Attention   | 5 | 16 |
| Auditory Working Memory | 9 |
| Memory               | 37 | 16 | 16 |
| Verbal Memory        | 9 | 9 |
| Delayed Free Recall  | 5 | 16 | <2 |
| Delayed Recognition  | 5 | <1 | <1 |
| Visual Memory        | 9 | 79 |
| Immediate Recognition| 5 | <1 | 16 |
| Delayed Recognition  | Invalid | 16 |
| Visual-Verbal Memory | 16 | 5 |
| Immediate Recall     | 5 | 2 |
| Delayed Recall       | 9 |

| Table 3 | Parent-report scores (percentiles). |
|---------|----------------------------------|
| Age (Years:Months) | 6:8 | 7:0 | 7:4 |
|                      | Pre-Surgical | 2 months | 6 months |
| Adaptive Functioning* | 5 | 50 | 37 |
| Communication        | 5 | 9 |
| Functional Academics | 9 | 25 | 16 |
| Self-Direction       | 9 | 63 | 16 |
| Leisure              | 16 | 50 | 37 |
| Social               | 25 | 25 | 9 |
| Community Use        | 16 | 75 | 9 |
| Home Living          | 5 | 37 | 25 |
| Health and Safety    | 5 | 25 | 9 |
| Self-Care            | 5 | 25 | 9 |
| Executive Functioning** | 99 | 69 |
| Inhibition           | 95 | 86 |
| Initiation           | 97 | 97 |
| Self-Monitoring      | 99 | 76 |
| Task-Monitoring      | 86 | 46 |
| Shifting             | 66 | 16 |
| Emotional Control    | 97 | 79 |
| Working Memory       | 42 | 34 |
| Planning and Organizing | 86 | 76 |
| Organization of Materials | 99 | 95 |
| Inattention          | 99 | 96 | 82 |
| Hyperactivity/Impulsivity | 99 | 99 | 99 |
| Learning Problems    | 99 | 99 | 99 |
| Anxiety/Depression   | 84 | 58 |
| Withdrawal           | 99 | 50 |
| Somatic Complaints   | 99 | 50 |
| Social Problems      | 99 | 66 |
| Rule-Breaking        | 65 | 58 |
| Aggression           | 65 | 58 |

*Higher percentile indicates better adaptive functioning.
**Higher percentile indicates greater cognitive or behavioral concern.

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ously had been unable to do. Other behavioral improvements included generally understanding test directions, appropriately requesting assistance as necessary (e.g., asking the examiner to hold paper in place while she drew), and obtaining averages scores in the areas of verbal intelligence, semantic verbal fluency, visual memory delayed recognition, grooved pegboard, and grip strength. In addition to surgery, therapies, and orthopedic bracing, behavioral and cognitive improvements may have reflected reduced dosages of clobazam and zonisamide, both of which were treatments at the time of pre-surgical and third post-surgical evaluations.

4. Discussion

We described the clinical and neuropsychological trajectory of a girl with a severe case of ESES that required left hemispherectomy to alter the course of behavioral and cognitive decline. Our case is in contrast to a recent case report in Epilepsy & Behavior Reports of a child with ESES who demonstrated a different course. In that case, neuropsychological scores showed clear decline and then demonstrated improvement and a favorable outcome with ESES that resolved with treatment before requiring surgery [6]. In our case, although neuropsychological scores remained quite suppressed through serial assessments, qualitative behavioral observations during assessments and parental reports of BX's behaviors captured critical information that otherwise would not have been obtained. While this issue is clear to neuropsychologists, it is not necessarily apparent to practitioners in other fields. As is always the case with neuropsychological evaluations, test score interpretation must occur in the context of patient-specific medical factors and behavioral observations. The present case findings are consistent with those reported in a study with children who underwent hemispherectomy due to ESES in which postoperative neuropsychological testing demonstrated only slight improvement or mixed results. No patients showed significant improvement on testing, but parents generally reported improvements and no further regression [7]. Meanwhile, Kalscheur, Farias-Moeller, and Koop's (2021) case report illustrated a vastly different trajectory of decline followed by significant improvement without surgery.

The precise mechanisms underlying cognitive deterioration in ESES are unknown, but there are several published hypotheses. Among the more compelling hypothesis is that seizures and interictal increases in cerebral blood flow create a self-perpetuating cycle of damage to neuro-vascular coupling [8,9]. Peng et al. demonstrated that the spike wave index from interictal epileptiform discharges during non-rapid eye movement sleep and cerebral blood flow velocity oscillations were at least partially responsible for neuropsychological damage in ESES [2]. BX's abnormal left hemispheric anatomy and neurovasculature may have served as contributors to ESES and lead to her underlying neuropsychological decline.

Fig. 1. T2-weighted MRIs (axial on top, coronal on bottom) demonstrating pre-operative lesion (left column) and post-operative left hemispherectomy (right column).
One of the most apparent limitations of this case report was the lack of consistency in the exact neuropsychological measures utilized at each evaluation. The rationale for test selection at each evaluation was guided by the principle that, because of the relatively short intervals between evaluations, we hoped to mitigate practice effects as not to give a false sense of neuropsychological improvement. However, BX’s behavioral manifestations of cognitive impairment, particularly her inattention and impulsivity, likely would have resulted in minimal, if any, practice effects that would have skewed interpretation, a point highlighted by van Iterson et al. [10].

5. Conclusions

This case report exemplifies the unique but vital contribution neuropsychology can make to understanding the impact of ESES on the developing brain. Anecdotally, our experiences support prior suggestions that all children with ESES should undergo at least two neuropsychological evaluations to assess impairment [11], although the precise neuropsychological tests and time intervals at which assessments occur (e.g., every six months) remain to be determined. Nevertheless, serial neuropsychological assessment, particularly in close proximity to EEG changes or after initiating other treatments such as steroids, may be among the most informative prognostic data utilized in surgical decision-making. Because of the rarity and heterogeneity in presentation of ESES, multi-center reports with common data elements are needed to identify factors predictive of successful outcomes to establish more consistent treatment standards.

Ethical statement

This case was submitted to Akron Children’s Hospital IRB who determined that this did not constitute research because it con-
tained presentation of a single subject’s retrospective data who no longer receives care through the same institutional service. A data use agreement (DUA) was obtained and executed between the two authors’ current institutions. Per the DUA, the manuscript was reviewed and approved by Akron Children’s Hospital.

Author contributions

DP was the primary neuropsychologist responsible for the patient’s care. DP consulted with LS throughout BX’s care regarding data interpretation and treatment recommendations. DP and LS participated in all multi-disciplinary team discussion regarding the patient, and LS also observed the patient’s behavior at one neuropsychological evaluation. DP wrote most of the original draft of the manuscript, created preliminary versions of the tables and figure, and formatted the manuscript to journal requirements. LS wrote portions of the original draft, performed editing on all subsequent drafts of the text, edited tables, and acquired images for the figure.

Declaration of competing interest

Authors have nothing to disclose.

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