AES 2024 ANNUAL MEETING

A Challenging Case

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October 6, 2024

AES AMERICAN EPILEPSY SOCIETY

Child Neurology FOUNDATION Creating a Community of Support

Disclosure

The speakers have no relevant financial disclosures:

- Dr. Fried provides consulting and advisory services for UCB, Virpax Pharmaceuticals and Elsevier
- Dr. Stowe has worked on a medical advisory board with Takeda Pharmaceuticals

Learning Objectives

- Review a case of a patient with epilepsy with complex neurobehavioral and psychosocial phenotype and:

1. Conceptualize pharmacological options for treatment of seizures and behaviors

2. Conceptualize non-pharmacologic options for treatment of behaviors

Case Presentation

- Nathan is a 20-year-old young man with Potocki-Lupski syndrome (PTLS, 17p11.2 duplication disorder) and longstanding neurodevelopmental concerns including nonverbal status, autism spectrum disorder, intellectual disability for which he has been under long-term neurological care. He has had recent onset of seizures.

- He presented as a transfer of care at 17-years-old with the following complaints/concerns:

Hyperactivity/Anxiety Concerns

- Mom has ADHD and generalized anxiety but she identifies that Nathan is "on another level" and constantly fidgeting and moving.
  - She wants to know if something is available to help him calm down and relax
- She is highly interested in "natural" options, like CBD, and knows a friend whose child has severe epilepsy on CBD
  - She has been hesitant to pursue artisanal CBD and medical marijuana on her own
  - She asks about what you know about terpenes
- Mother wonders about influence stimulants may have for Nathan, with her own ADHD managed by extended-release dextroamphetamine/amphetamine
- Clonidine was trialed long-ago without clear benefits

Aggression and "OCD" Behaviors

- His aggression manifests with lots of forceful grabbing behaviors
  - It's known that providers should avoid wearing lanyards and ties
  - Mom cannot walk past him without a grab attempt, and he may chase her
  - This is also observed at school with mostly female personnel
- There has been an up-tick in "OCD" tendencies
  - Wants to have both parents present with him, but mom cannot sit down otherwise he will become agitated/aggressive
  - Has to put things face down (e.g., phones, clipboards, iPads)
- Aripiprazole, risperidone have been tried with lack of clear efficacy

Headache Concerns

- He can become "Dr. Jekyll and Mr. Hyde" with his behaviors. He is "amazing" after he wakes up until about 12pm, but then something happens at noon and he just appears "sensory overloaded" and he becomes "such a grump." He seems to improve around 4pm.
  - Mom has a similar temporal pattern of headaches/migraines, including hemiplegic migraines, for which she takes prophylactic topiramate
- He may forcefully press upon his left eye and gets moodier and different during these times if they try to stop it
- He will also randomly throw up and ruminate and mom wonders if this is because of migraine-related nausea
- Has tried cyproheptadine and gabapentin– ineffective or uncertain benefit

Sleep Challenges

- Family has long utilized melatonin of doses 3-5mg to help him fall asleep, though this was met with variable and inconsistent response.
- He has always had challenges *going* to sleep, as he would stay awake for hours after melatonin administration. However, once asleep he generally stays asleep.
- He twitches "aggressively" at/around sleep onset and has been identified as being a restless sleeper. There are no reports of snoring.
- Family wonders about his sleep quality because he can be grumpy when being woken up for school.

Neuropathy and Other Pain Concerns

- Family has a long clinical note of observations from the OT describing a "mild positive ulnar variance of the left hand" and observations of pulling at his fingers and perhaps some sensory predilection towards shaking and pulling at his third, fourth, and fifth digits.
  - Family wonders if his 'grabbing' behaviors that warrant someone to wrench Nathan's fingers apart may be a sought-out behavior because he cannot effectively communicate this discomfort
  - Historically, he has loved massages of his hands
- Nathan's mother experiences Raynaud's phenomenon and this can be painful and she wonders if this may be something he is experiencing
  - There are no clear skin color changes observed or foot-related symptoms

Seizure History

- Nathan had **no clear history of seizures** prior to establishing care with you
- Periodic EEG evaluations in his youth have demonstrated robust interictal abnormalities.
  - His last EEG from 2011 showed frequent generalized 3Hz spike-wave discharges in runs lasting up to 15-28 seconds. Multiple push button events for jerky body movements and body stiffening were not associated with ictal correlate.
  - Previously prescribed:
    - levetiracetam – became very irritable and discontinued
    - valproate – demonstrated food refusal and was discontinued

Seizure Story Begins

- June 2021, Nathan was in a portable hot-tub and he suddenly froze and began leaning to the left. His eyes rolled back, he was stiff all over without shaking and mom observed this as a "definite seizure." It lasted 1-2 minutes in total with being "off" the rest of the day.
  - Preceding the event, he had a headache and was acting "off."
  - Family wished to hold off on antiseizure medication treatment and pursuing EEG.
  - Neuroimaging was requested and was unrevealing.
- His second seizure occurred in December 2022 and was observed by dad.
  - He developed a "thousand-yard stare" and leaned backwards his eyes rolled up, mouth went open and he went limp for 1-2 minutes.
  - Per dad, "It looked like he had died." He then came to and sat on toilet for 15 minutes and appeared confused and lethargic.
  - Because of the time between events, family again wishes to hold off on ASMs.

Seizures Ramp Up in 2024

- 1/9 at 1045am – while walking with staff at school, he stopped abruptly, leaned over, and his lips and ears became cyanotic for 35 seconds
- 3/21 at 4:45pm – laying on couch and his eyes rolled back into his head, his breathing appeared to stop, his lips were blue and he became stiff and head extended with subtle twitching lasted 2.5 minutes
- 4/5 at 4:42pm – experienced a tonic seizure lasting 2 minutes with eyes rolling up, rigid and stiff body with arched neck, turning grey/white and lips and ears go blue, making gurgling breaths like he was struggling to breathe

Social History and Background

- Nathan has a loving and very supportive family and is typically accompanied by both parents to his visits. Dad is there to help "get the exam done" and then will excuse himself and Nathan so that the concerns may be effectively reviewed between mom and you.

- While family has successfully attained guardianship, they do not have a *Rogers* Guardianship, which is a Massachusetts-specific statute that limits the use of certain treatments such as antipsychotics.

Discuss Amongst the Groups

1. What are some pharmacological options to consider for his complaints?

2. What are some non-pharmacological options to consider for his complaints?

3. What are some community resources to consider in support of this patient and his family?

Clinical Summary

- 20yo with PTLS (17p11.2 duplication disorder), autism, intellectual disability and:
  1. Increasing seizure frequency and not currently on antiseizure medication
  2. Behavioral challenges including hyperactivity and aggression
  3. Possible headaches
  4. Possible nerve pain/behavioral hand-pulling complaints
  5. Sleep challenges, primarily sleep initiation

Within the groups (pharm, non-pharm, resources), consider the following:

- What are some ideas to help manage these seizures?
- What are some ideas to help with the agitation and behaviors?
- What are some ideas to help with the headache/migraine/pain concerns?

What Did I Do?

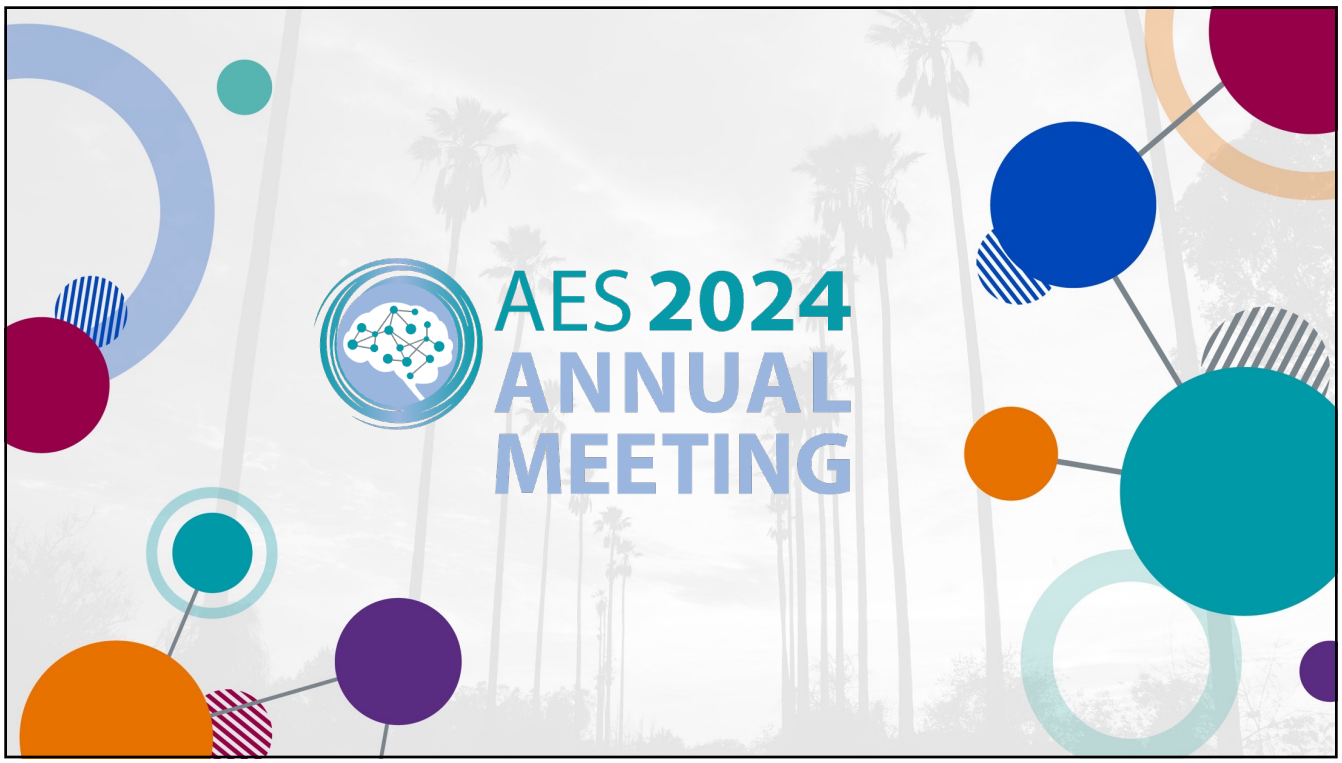
- In the course of treatment of possible headaches/migraines as well as concerns about anxiety and neuropathy → duloxetine
  - Cyproheptadine was added by his GI physician to help with persistent rumination with some positive results
  - Clonidine was trialed for sleep initiation with good benefit but did not help with daytime behaviors
  - Sertraline tried for anxiety/OCD → his mood quickly worsened
- Family pursued medical marijuana and felt like this was exceptionally helpful for mood and school data corroborated reduction in grabbing behaviors. Through trial and error they settled on different tinctures based on time of day.

What Did I Do?

- Once seizures came in full force, family discontinued medical marijuana. Lamotrigine was chosen as first line ASM
- Early/low dosing was "magical" with regards to behaviors but not effective for seizures
- Once achieving lamotrigine level of ~7, he was felt to be moodier, sullen, and he still had a breakthrough seizure
- Decision was made to add valproate and reduce lamotrigine
  - Behaviors are presently "great" and our last visit he was his most calm and cooperative

Impact on Clinical Care

- When prescribing antiseizure medications, be mindful of prospective side effect profiles and the prospective tolerability/intolerability of such side effects
- Families of the nonverbal child do their best to try and interpret their children's symptoms and behaviors, and this can often be through the lens of personal experiences and biases
  - Liaise with these experiences and biases, educate, inform, and collaborate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