Rare Sleep Disorders

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Case #1

- 2 week old baby, full term
- Cyanotic and having apnea episodes with feeding
- Normal brain and CXR
Case #1

Marked, rapid desaturation during feed and especially with transition to sleep
Case #1

- CO2 = 110 Torr
- Treated with BiPAP
Case #1

Marked, rapid desaturation during feed and especially with transition to sleep
Case #1

• PSG showed shallow breathing, central apneas with desaturations and elevated CO2

• What is this?
CCHS (Ondine’s Curse)

- ~170 children worldwide
- Areas of brain fail to provide ventilatory drive during sleep
- Diminished ventilatory responses to CO2 and hypoxia during both sleep and wake, lack of perception of asphyxia, do not arouse to respiratory stimuli
Congenital Central Hypoventilation Syndrome (CCHS)

- Rare autosomal dominant (PHOX2B)
- Integration of CO2 by medullary chemoreceptors
- Newborn >> Childhood >> Adulthood
- No primary lung, cardiac, brainstem or neurologic disease
- 2/3 require ventilator only during sleep
- PHOX2B gene regulates Autonomic Nervous System development
CCHS clinical presentations

- Newborn: cyanosis, ALTE(BRUE), Seizure
- "Late" onset (>1 month): respiratory failure with URI
- Autonomic: temperature instability, sweating, pain insensitivity
- Respiratory: hypoventilation, very decreased arousal
- Cardiac: assytole, PAC’s, PVC’s
- GI: constipation, dysmotility, Hirschsprung’s
- Neuro: mood instability, ? Decreased IQ
- Ophthalmologic: decreased pupil response, strabismus
- Neural crest tumors: neuroblastoma, ganglioneuroma
Case #2

• 16 yr old boy previously healthy
• Febrile illness followed by two episodes of excessive sleepiness (up to 15-16 hours per day for several days in a row)
• When awake during episodes, he was irritable, confused and ate large quantities of food
• Each episode lasted 7-8 days and he was completely normal in between
Case #2

• What is it?
  • Narcolepsy
  • Drug use
  • Idiopathic hypersomnia
  • Kleine-Levin Syndrome
Kleine-Levin Syndrome

• First described in 1862
• Very rare (one in a million, literally)
• Most commonly in adolescent or teenage boys (4:1 boys:girls), 81% in second decade
• Majority are primary (no identifying organic cause)

» Huang YS, Arnulf I. Sleep Med Clin. 2006
Kleine-Levin Syndrome

- Recurrent episodes of hypersomnia
- Associated with cognitive and behavioral changes
- Behavioral changes are severe: irritability, hyperphagia, hypersexuality
Kleine-Levin Syndrome

• Precipitating events
  – Majority of first episodes occur in Fall and Winter
  – 89% remember an event prior to first episode like URI with fever
## Kleine-Levin Syndrome

### Table 1

Frequency of symptoms during episodes of Kleine–Levin syndrome

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Percentage (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypersomnia</td>
<td>100</td>
</tr>
<tr>
<td>Cognitive disorders</td>
<td>96–100</td>
</tr>
<tr>
<td>Abnormalspeech</td>
<td>60–94</td>
</tr>
<tr>
<td>Confusion</td>
<td>51–91</td>
</tr>
<tr>
<td>Amnesia</td>
<td>48–66</td>
</tr>
<tr>
<td>Hallucinations</td>
<td>14–27</td>
</tr>
<tr>
<td>Delusions</td>
<td>16–35</td>
</tr>
<tr>
<td>Eating behavior disorders</td>
<td>80–95</td>
</tr>
<tr>
<td>Megaphagia</td>
<td>62–66</td>
</tr>
<tr>
<td>Increased drinking</td>
<td>6.4–16</td>
</tr>
<tr>
<td>Hypersexuality</td>
<td>48–53</td>
</tr>
<tr>
<td>Increased masturbation</td>
<td>29</td>
</tr>
</tbody>
</table>
Kleine-Levin Syndrome

Table 1  ICSD-3 diagnostic criteria for Kleine-Levin syndrome

Criteria A–E must be met:
A. The patient experiences at least two recurrent episodes of excessive sleepiness and sleep duration, each persisting for 2 days to 5 weeks.
B. Episodes recur usually more than once a year and at least once every 18 months.
C. The patient has normal alertness, cognitive function, behavior, and mood between episodes.
D. The patient must demonstrate at least one of the following during episodes:
   1. Cognitive dysfunction
   2. Altered perception
   3. Eating disorder (anorexia or hyperphagia)
   4. Disinhibited behavior (such as hypersexuality)
E. The hypersomnia and related symptoms are not better explained by another sleep disorder, other medical, neurologic, or psychiatric disorder (especially bipolar disorder), or use of drugs or medications.
Kleine-Levin Syndrome

Table 2  Differential diagnosis of Kleine-Levin syndrome

- Primary psychiatric illness (i.e., atypical depression, bipolar disorder, schizophrenia)
- Sleep-disordered breathing
- Narcolepsy
- Menstruation-related hypersomnia
- Complex partial seizures
- Klüver-Bucy syndrome (bilateral temporal lobe lesions)
- Metabolic encephalopathies
- Herpes simplex virus encephalitis
- Lyme disease
- Intermittent porphyria
## Kleine-Levin Syndrome

### Table 2

Treatments used in patients with Kleine–Levin syndrome and reported effects\(^{[7,36]}\)

<table>
<thead>
<tr>
<th>Treatments of symptoms during an episode</th>
<th>Response rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stimulants (reduction of hypersomnia)</td>
<td></td>
</tr>
<tr>
<td>Amphetamines</td>
<td>40–71</td>
</tr>
<tr>
<td>Methylphenidate</td>
<td>20</td>
</tr>
<tr>
<td>Pemoline–piracetam–meclofenoxate</td>
<td>25</td>
</tr>
<tr>
<td>Treatments aimed at preventing relapses</td>
<td></td>
</tr>
<tr>
<td>No drug treatment</td>
<td>16</td>
</tr>
<tr>
<td>Phototherapy</td>
<td>0</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>9</td>
</tr>
<tr>
<td>Mood stabilizers</td>
<td></td>
</tr>
<tr>
<td>Lithium</td>
<td>41</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>21</td>
</tr>
<tr>
<td>Valproate, phenobarbital, and phenytoin</td>
<td>20</td>
</tr>
</tbody>
</table>
Kleine-Levin Syndrome

- Associated with CT and single-photon emission CT (SPECT) revealing reduced cerebral blood flow to the thalamus and hypothalamus during episodes
- Spontaneously resolves in 4-8 years.
Case #3

- 55 year old woman goes to ED for “something felt funny in my head”
- Woke her from sleep, had palpitations and sense of fear with it
- Saw a flash of light and heard a loud “crackle, like an electrical explosion”
- PMH: HTN, MEDS: HCTZ
- No symptoms related to sleep previously
Case #3

• What else would you like to know about her?
Case #3

- Had one episode previously
- No alcohol, drugs, tobacco use
- No incontinence with episode
- No h/o snoring, apnea, etc
- Recently has been a bit sleep deprived due to work schedule (shift worker)
Case #3

- Head CT in ED done: normal
- EEG done: completely normal
- PSG done: completely normal
- Tox screen done: completely normal
Exploding Head Syndrome

- **ICSD-3: sensory parasomnia**
  - Diagnostic criteria:
    - Complaint of a sudden loud noise or sense of explosion in the head at wake-sleep transition or upon awakening
    - Abrupt arousal from the event, often frightened
    - Not associated with any complaints of pain
Exploding Head Syndrome

• Variety of sound descriptions:
  – Explosions
  – Roar
  – Crash
  – Yelling
  – Cars driving by
  – Electric short circuit
  – Fireworks
Exploding Head Syndrome

- Visual disturbances (10%)
- Intense heat
- Aura of electrical sensation
- Generic light flashes
Exploding Head Syndrome

- Can be only once or up to several times per week
- Prevalence unknown:
  - 13.8% psych patients
  - 10% sleep disorder patients
  - 10.7 % healthy controls
Exploding Head Syndrome

• Risk Factors:
  – Stress
  – Emotional tension
  – Malaise
  – Age over 50
Exploding Head Syndrome

- PSG and EEG show no epileptiform activity
- Alpha and short bursts of theta seen
- Typically occurs when transitioning from wake to sleep
- Patients however report this happening during sleep
Exploding Head Syndrome

• Etiology: many theories:
  – Eustachian tube pertubation
  – Bried partial complex seizures
  – w/d from BZP or SSRI
  – Transient calcium channel dysfunction
Exploding Head Syndrome

• Important to remember: EHS is more distressing than painful, if pain occurs another condition may be the cause.
• No known treatment is available but several tried (TCA, Ca Channel blockers, anticonvulsants)
• Reassurance important for these patients.
Case #4

• 45 yr old woman c/o increase weight despite trying to diet. No snoring and has very good sleep habits.
• Fatigue increasing during the day, recently had episode of insomnia after a cross country trip
• Medications: Zolpidem prn insomnia
• No other medical history
Case #4

• Weight has increased 25 # in the last 6 months
• She exercises at the gym (cardio) one hour three times a week
• No change in eating habits
• Lives with two teenage kids and often finds dirty dishes in the sink in the morning and “runs out of food more often than previously”
Case #4

- PMH: sleep walking as a child
- PE normal except BMI is now 28 and was lower last year.
Sleep-Related Eating Disorder

- Most patients unaware of eating during the night
- Zolpidem is the hypnotic most often associated with SRED
- If not due to medication, SRED may not be associated with amnesia. Patients report not being hungry but have “urge” to eat and feel that eating helps them fall back asleep
Sleep-Related Eating Disorder

• Risk factors:
  – h/o sleep walking
  – RLS/WED (45%)
  – Depression (40%)
  – More often in women
  – Can be treated with pramipexole or topiramate
Sleep-Related Eating Disorder

- Can be dangerous due to cooking
- Stopping zolpidem in this patient cured the condition.
Sleep-Related Eating Disorder

• Other medications associated with SRED:
  – Zolpidem (Ambien)
  – Zopiclone (Zimovane, Imovane)
  – Zaleplon (sonata)
  – Triazolam (Halcion)
  – Midazolam (Versed)
  – Risperidone (Risperdal)
  – Olanzapine (Zyprexa)
Summary

• Rare sleep disorders are important to recognize and hear about
• Many patients with rare sleep disorders go through years of tests/treatment for other things before getting appropriate diagnosis