

MAHIDOL UNIVERSITY
Wisdom of the Land

Difficult to Diagnose Epilepsy Cases

Children and Adolescents

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Annual Meeting Epilepsy Society Thailand 2015

Difficult to diagnose epilepsy cases

- Epilepsy may be misdiagnosed in around 25% of cases.
- Conditions such as syncope, paroxysmal disorders or conversion disorder may be misdiagnosed as epilepsy.
- Alternatively, the symptoms of epileptic seizures may be misdiagnosed as resulting from psychiatric or associated disorders.

Stokes T, Shaw EJ, Juarez-Garcia A, et al. 2004.
Zaidi A, Fitzpatrick AP. 2000.
Smith D, Defalla BA, Chadwick DW. 1999.

Difficult to diagnose epilepsy cases

- The misdiagnosis of epilepsy may lead to human costs such as distress to patients and carers, unnecessary lifestyle changes, social stigma, social and financial deprivation as well as economic costs.
- The annual cost of epilepsy misdiagnosis in England is around £189 million.

All-Party Parliamentary Group on Epilepsy. The human and economic cost of epilepsy of epilepsy in England: wasted money, wasted lives. 2007.



"It is not only the misdiagnosis of whether it is epilepsy or not, it is the misdiagnosis of the type of epilepsy. In paediatrics particularly that is so important, because the multitude of syndromes start in childhood and if you do not make an accurate diagnosis of the type of syndrome you can get the drug treatment wrong and actually make it worse." Dr. Helen Cross

"If somebody is not well trained for taking a good history and dissecting out the points, they are likely to get the diagnosis wrong." Professor John Duncan



The misdiagnosis of epilepsy in people with intellectual disabilities: A systematic review

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Difficult to diagnose epilepsy cases

People with intellectual disabilities are at additional risk of misdiagnosis:

- Stereotypical behaviors
- Drug induced involuntary movement
- Communication difficulties
- Dependence on the observation of carers
- Difficulty gaining an EEG

Seizure
Journal homepage: www.elsevier.com/locate/epilepsie

The misdiagnosis of epilepsy in people with intellectual disabilities:
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Table 4
Events which have the potential to be misinterpreted as epileptic events.

Behavioural^a
Stereotypic repeated blinking or swallowing ¹⁵
Self-stimulatory tics or behaviours
Spontaneous smiling or grimacing, laughing episodes ^{15,20}
Staring spells ^{15,17,18,20}
Inattention, unresponsiveness, going quiet, apparent psychomotor arrest ^{15, 19, 21, 22}
Simulation of convulsions ²³
Physiological^a
Head and/or eye turning ^{1, 2, 20}
Buccolingual movements ¹⁵
Hypnic jerks ¹⁶
Dystonic and tonic posturing, stiffening of limbs ^{15, 20}
Ataxia with falls ¹⁵
Syndromes related^a
Behaviours, motor abnormalities or EEG abnormalities associated with Rett Syndrome (e.g., breath-holding, abnormal hand movements, and unresponsiveness) ²⁴
Symptoms of Sandifer Syndrome ^{10, 21}
Medication related^a
Personality changes due to reduction of antiepileptic medication ¹⁵
Decreased daytime alertness because of side effects of antiepileptic medication or disturbed sleep ¹⁵
Psychological
Conversion disorder ¹⁶

^a Some events could be in more than one category (e.g., head turning and stereotypic blinking could be behavioural or physiological).

Cases:

- **An 8 year-old boy with nocturnal spells and abnormal EEG**
- **A 17 year-old male with congenital heart disease, epilepsy and new onset of nocturnal spells**
- **A 2-year-old boy with tongue biting during sleep**

An 8 year-old boy

Chief complaint: nocturnal spells for one year.

Present illness:

12 months PTA: While being hospitalized for high grade fever, he has developed confusional episode during sleep which occurred every night.

- 30-40 minutes after falling asleep, he would get up, scream inconsolably, try to climb down from his bed and occasionally escape from his bedroom.

Present illness (cont.)

- These episodes last anywhere from 5 – 30 minutes. They occur every night, about 1-2 times each night and may be worsened after tiredness (up to 3 times).
- He could not recall any episode and there is no difficulty in waking him up in the morning.
- Additionally, he snores every night and is very restless in his sleep since he was 3-year-old.

Present illness (cont.)

- The mother brought him to a hospital where further investigations were performed.
- ❖ EEG: frequent spikes over the right centro-parietal regions
- ❖ MRI brain: normal
- Levetiracetam and subsequently diazepam were given, but neither improved his symptoms.

Sleep history

- Sleep time: 8 PM
- Wake up time: 6-7 AM
- Denies daytime nap or daytime somnolence
- (+) nocturnal enuresis 2 time/week
- (+) snoring, restless sleep
- Bedroom: sharing with parents and one brother

Past history

- Allergic rhinitis
- Otherwise unremarkable

Family history

- (+) sleep walking in mother, disappeared after age of 10 years
- (-) seizure or other neurological condition

Physical Examination

- Alert, well cooperative
- BT 37 °C, BP 95/55 mmHg, HR 80/min, RR 20/min
- BW 26 Kg (P75), Height 125 cm (P50)
- HEENT: **swollen and pale inferior nasal turbinate, tonsils 3+ both sides, Mallampati class III**
- Heart, lungs, abdomen: normal
- No focal neurological deficit



Problem List

Epileptic or non-epileptic event?

Nocturnal spells

Abnormal EEG
(Right centro-parietal spikes)

Problem List

Allergic rhinitis

Snoring
Enlarged tonsils

Restless sleep

R/O obstructive sleep apnea

Problem List

Epileptic seizure or Parasomnia?

R/O obstructive sleep apnea



An 8-year-old boy with “Nocturnal Spells”

- Early phase of sleep (First 1/3 of the night)
- Non-stereotype
- Family History of parasomnia
- **Abnormal EEG**

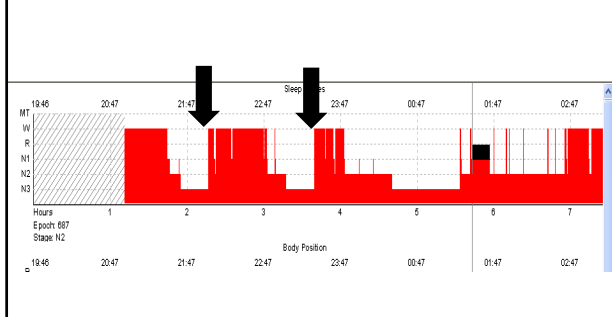
Provisional Diagnosis

❖ Non REM parasomnia with suspected OSA

Differential Dx:

❖ Nocturnal seizures

Hypnogram: events occurred in slow-wave sleep



Polysomnography with Extended EEG

- Sleep efficiency: 50.64%
 - N1 5%, N2 52%, N3 38%, REM 5%
 - Apnea-Hypopnea Index (AHI): 1.2/hr (REM index 8.1)
 - EEG: frequent independent spikes over left and right centro-parietal regions
- Low sleep efficiency
 - Decreased REM sleep
 - Low AHI in total sleep, but high in REM.
 - This study may underestimate severity of OSA due to inadequate REM sleep.
 - Abnormal EEG, but not correlate with the events.

Diagnosis

- Low sleep efficiency (first night effect)
- Mild OSA
 - Allergic rhinitis, tonsillar hypertrophy
- **Non-REM parasomnia**

Treatment

- Reassure, discontinue AEDs
- Rx AR and mild OSA with intranasal steroid
- Rx parasomnia



Management of Parasomnia

- **REASSURE**
- Sleep hygiene
 - regular sleep-wake cycle
 - adequate amount of sleep
- Manage triggering factors
 - Avoid all stimuli that may contribute to partial arousal and trigger an episode e.g. noise, light
 - Avoid extreme exercise, emotional or situational stress
 - Avoid antihistamine, alcohol, antidepressant, sedative
- Environmental safety
- Search for and treat, if present, other sleep disorder, such as OSA, PLMD, RLS
- Scheduled awakening to eliminate sleep walking
- Clonazepam for recurrent and problematic parasomnia

Case Demonstration:

- An 8 year-old boy with nocturnal spells and abnormal EEG
- **A 17 year-old male with congenital heart disease, epilepsy and new onset of nocturnal spells**
- A 2-year-old boy with tongue biting during sleep

A 17-year-old male

Chief complaint: Unusual behavior during sleep for 3 months

Present illness:

Known case hypoplastic left heart with pulmonary atresia s/p Fontan operation

17 years PTA: At age of one month, he was diagnosed with meningitis due to fever with seizure and was put on phenobarbital.

Present illness (cont.)

His seizures were very well controlled and the medication was discontinued at aged of 3 years.

10 years PTA (after 6+ years of no medication): He had recurrent seizures, characterized by clonic movement of left side of face and left arm. Sodium valproate was given.

3 years PTA: After 7 years of seizure free and normal EEG, VPA was slowly discontinued.

Present illness (cont.)

6 months PTA: He had loud snoring and occasional grasping without any witnessed apnea. His weight increased 14 kg in 2 years.

3 months PTA: He has had nocturnal spells which were not similar to his previous seizures. "restlessness, body turning lasting 10-30 seconds" These occurred 1-3 times every night. After the episode, he might wake up or return back to his sleep without any recall.

Sleep History

- Sleep time: 8 PM
- Wake up time: 5.30-6 AM
- Denies daytime nap, daytime somnolence
- Denies morning headache
- Bedroom: sleep in the same room with parents

Past History

- Congenital heart disease s/p surgery at age of 2 and 7 mo, currently on warfarin and captopril
- Intellectual disability, IQ = 76
- Otherwise are unremarkable

Family History

- (-) epilepsy, parasomnia
- Unremarkable

Physical Examination

- Alert, well cooperative, follow simple command appropriately, **obese**
- BT 37 °C, BP 128/64 mmHg, HR 86/min, RR 20/min
- BW 66 Kg, Height 156 cm, **BMI 27.1 kg/m²**
- HEENT: Not pale, anicteric, **short neck**,
acantosis nigricans, tonsils 1+ both sides,
Mallampati class IV
- No focal neurological deficit except for intellectual disability



Problem List

Hypoplastic left heart syndrome with PA s/p surgery

Post-meningitis with recurrent epilepsy, off AED

Obesity and snoring R/O OSA

Nocturnal spells

Diagnosis of Nocturnal Spells

- Brief spells, stereotype
- Variable time across the night
- Snoring and obesity R/O OSA

Differential diagnosis

Secondary parasomnia
(confusional arousal from OSA)
Nocturnal seizure

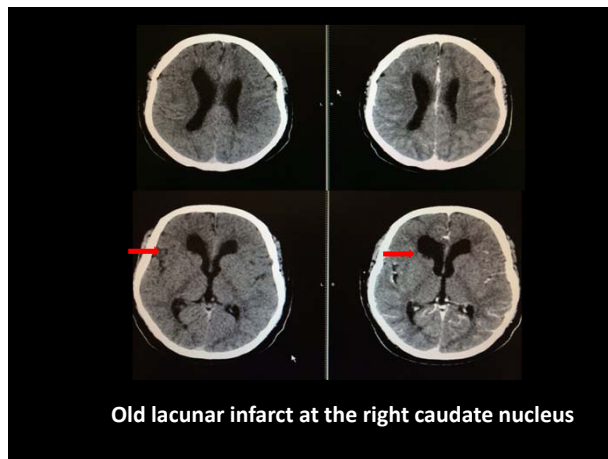
Overnight Video-EEG/PSG

EEG:

- Interictal: few spikes over left and right frontal regions (Fp1, Fp2).
- Ictal: 3 habitual spells captured, consistent with frontal lobe seizure

PSG:

- Cannot perform respiratory monitor due to non-cooperation



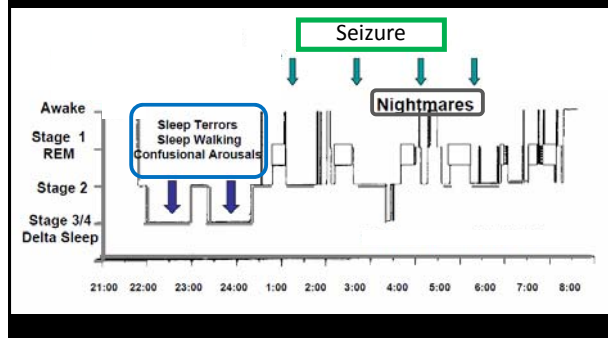
Final Diagnosis: Nocturnal frontal lobe epilepsy

Management

- Control seizure with topiramate
- Diet control and weight reduction



Parasomnias vs Epilepsy



Comparison of Clinical and video-EEG/PSG of Parasomnia and Nocturnal Frontal Lobe Epilepsy

	NREM parasomnia	NFLE
Age at onset	Usually < 10 yrs	Variables
(+) Family Hx	60-90%	Up to 40%
Attacks per night	1 or 2	3 or more
Episode per month	< 1 -4	20 -40
Clinical course	Tends to disappear by adolescence	Often stable with increasing ages
Episode duration	Seconds to 30 min	Seconds to 3 min (often < 2 min)
Semiology of movement	Variable complexity, not stereotyped	<u>Highly stereotyped</u>

Derry CP, et al. Epilepsia 2006

Comparison of Clinical and video-EEG/PSG of Parasomnia and Nocturnal Frontal Lobe Epilepsy

	NREM parasomnia	NFLE
Trigger factors	Sleep deprivation, febrile illness, alcohol, stress	Often none identified
Associated condition	OSA	Often none identified
Ictal EEG	Slow waves	Often normal or obscured by movement, less than 10% frank epileptiform discharge
Times of episode during sleep	First third of night, but usually after 90 min of sleep	Any time, but may occur in first 30 min
Sleep stage when event occur	N3, occasionally N2	Usually N2

Derry CP, et al. Epilepsia 2006

Case Demonstration:

- An 8 year-old boy with nocturnal spells and abnormal EEG
- A 17 year-old male with congenital heart disease, epilepsy and new onset of nocturnal spells
- A 2-year-old boy with tongue biting during sleep

A 2-year-old boy

Chief complaint: Tongue biting during sleep for 6 mo

Present illness:

6 months PTA: The mother has noted that he bit his tongue during sleep both days and nights. It occurs every day, several times per night. Afterward he will occasionally wake up and complain of pain in his mouth. He has ulcers at tips and on both sides of his tongue.

Present illness (cont.)

- This mainly occurs first half of the night and occasionally later half.
- The mother denies any seizure or jerky movement.
- He was seen by a dentist and "close bite" was diagnosed. He was put on mouth guard at night but his symptoms did not get better.
- No other self-injurious behavior.

Sleep history

- Sleep time: 8 PM
- Wake up time: 6-7 AM
- Daytime nap 2-3 hours/day
- Denies daytime somnolence, snoring
- (+) restless sleep, sleep talking
- Bedroom: sleep in the same room with parents

Past History

- Unremarkable
- Fullterm, no perinatal complication
- Normal development for age

Family History

- (-) seizure, parasomnia or other neurological condition

Physical Examination

- Alert, well cooperative
- BT 37 °C, BP 95/55 mmHg, HR 80/min, RR 20/min
- BW 11.6 Kg (P75), Height 86.3 cm (P50)
- HEENT: **tonsils 2+ both sides, Mallampati class III, old ulcers at tip of tongue.**
- Heart, lungs, abdomen: normal
- No focal neurological deficit



Differential Dx of Tongue Biting During Sleep

Diagnosis	Sleep stage	Symptoms	Reference
Nocturnal seizure	Any, N2*	Hypermotor, stereotype	
Rhythmic movement disorder of sleep	Sleep onset	Gradually disappear when older, may have head banging, rocking	Vasiknanonte P, 1997
Sleep bruxism	N1, N2	Rhythmic involuntary contractions of masticatory muscles, teeth grinding	International classification of sleep disorder 2nd
Facio-mandibular myoclonus	N1, N2 (REM)	Sudden forceful myoclonus of masticatory muscle, followed by orbicularis oris and oculi, isolation or in clusters	Aguglia, 1991, Kato, 1999, Senevirante U, 2011

Differential Dx of Tongue biting during sleep

Diagnosis	Sleep stage	Symptoms	Reference
Hypnic myoclonus	REM	Associated with limbs movements	Kimura et al, 2000.
Geniospasm	Awake, sleep (N2) Decreased in REM	Sporadic, AD, infantile onset, increased with stress	Kharraz, B, 2008 Jarman PR, 1997
Psychogenic	Awake		

Take home message

- To evaluate nocturnal event, a careful history is needed.
 - Time of sleep-wake occurrence
 - Precipitating factors: emotions, sleep deprivation, tiredness
 - Duration and frequency of episodes
 - Other accompanying features: pallor, diaphoresis, papillary dilatation, posturing
 - Factors associated with cessation or following the event
- Documentation of the episode with home video recording**
- Video-EEG/PSG recording in selected cases

Thank you for your attention