

Sleep disorders



조 규 호

연세대세브란스병원

case 1: 반복적인 의식소실을 주소로 내원한 38세 남자

M/38

C.C : 일시적인 의식소실 (“필름이 끊긴다”)

Onset : 2014년 가을

P/Hx

- HTN/DM/Tbc/hepatitis (+/-/-)
- **Pituitary prolactinoma** → Endo : Dostinex(cabergoline), Adipex(phentermine)
- Dyslipidemia

S/Hx

- Alcohol (-) Smoking (-)
- Occupation : 건설 현장 업무

171cm 126kg BMI 43.09

(2006년 110kg)

Brief Hx.

2011년 시야장애 주소로 Pituitary prolactinoma 진단.

2014년 가을 부터 잠깐씩 의식소실 발생함. (2-3회/달)

2015년 7월부터 빈도 증가. (1회/1일)

→ 주로 오전 11시~오후 4시경

→ 거의 항상 일할 때 (서 있을때 주로) 생긴다

→ 앉아 있을 때는 고개 숙인 자세. 서있다가 쓰러질 뻔함.

→ 주변에서 보았을 때 잘 알아채지 못하고 가끔은 왜 서서 졸고 있냐고 할 때도 있음.

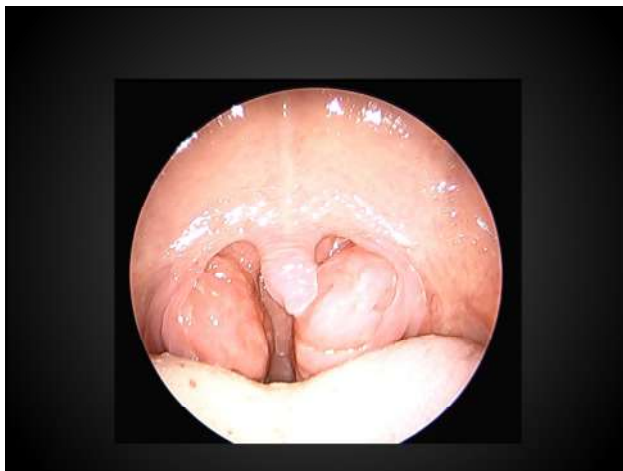
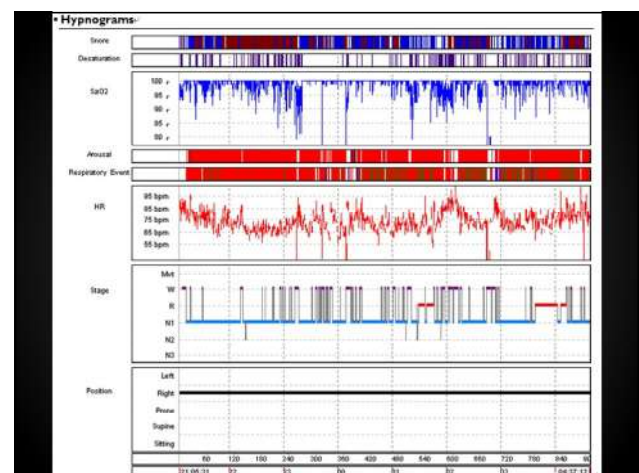
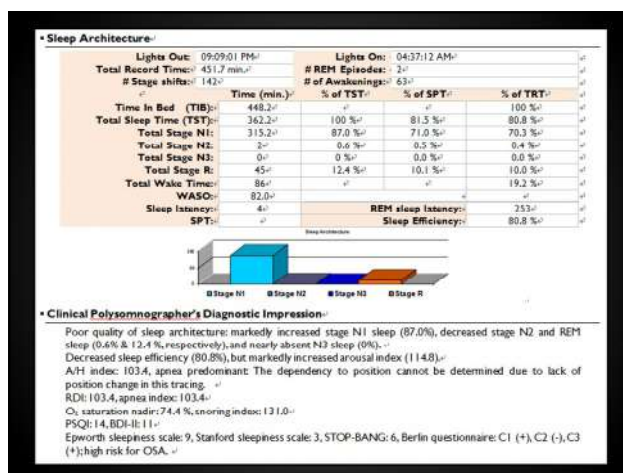
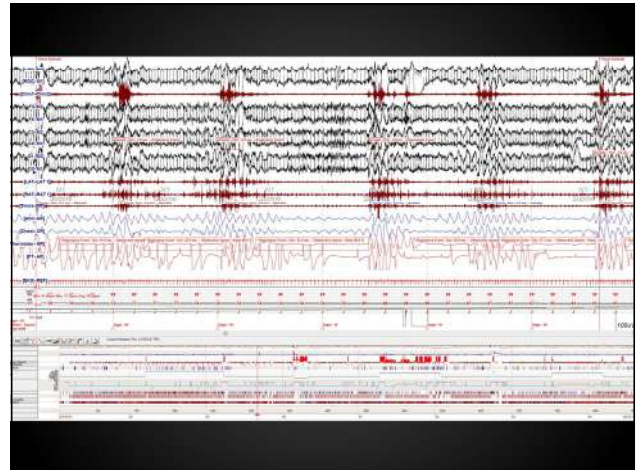
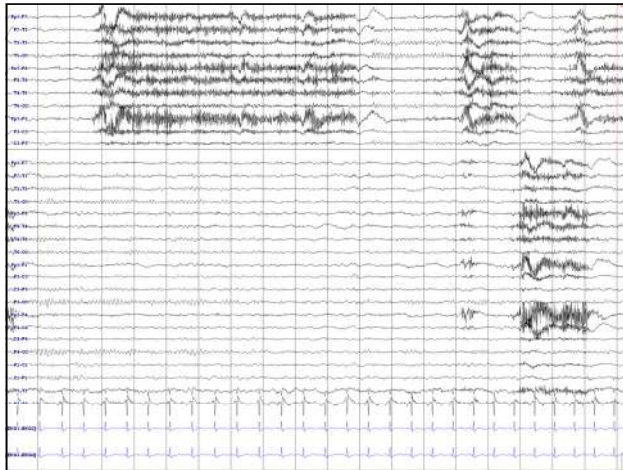
2015.9.10 운전하다가 의식 소실. 5-10초. 전봇대에 부딪히기 직전 의식 차렸음.

2015.09.18 OPD 내원.

2015.9.21-23 신경과 입원함.

Video-EEG monitoring





Diagnosis

1. Severe obstructive sleep apnea
2. Tonsillar hypertrophy

Progress

Tonsilectomy + UPPP
 postop AHI 43.6
 after weight reduction & CPAP
 treatment: minimal symptom

Episodic alterations of consciousness

	EDS	CPS	Syncope
Onset	Usually gradual(min)	Sudden	Variable(sec-min)
Warning	Yes; sleepiness	Yes; aura	Yes; dizziness, diaphoresis, nausea, blurred vision
Duration	5-10min	Usually < 5min	10sec-5min
Postictal	No	Possible	No
Age at onset	<30: Narcolepsy >50: Sleep apnea	Variable	Variable
Long-term course	Chronic	Usually chronic, nonprogressive	Variable
Special identifying features	Sitting, Repetitive activity ↑ "microsleep" with automatism	Focal neurologic abnormality	Usually no motor activity

case 2: 지나친 주간 졸음을 주소로 내원한 52세 남자

세브란스 병원 신경과 조규호

Brief history

▶ 현재 증상 (현재 수면 중에 일어나는 증상과 수면과 관련된 증상 에 대해 자세히 기술해 주십시오)

• 보통은 잠이 많이 오고 자각각각 졸려 6시경에 잠이 들어 22시~3시경까지 잠이 깨고 잠은 잘 못하는 것 같습니다.

• 보통은 심하게 졸려 잠이 들자마자 잠이 떨어지고 일어나는 경우가 많습니다.

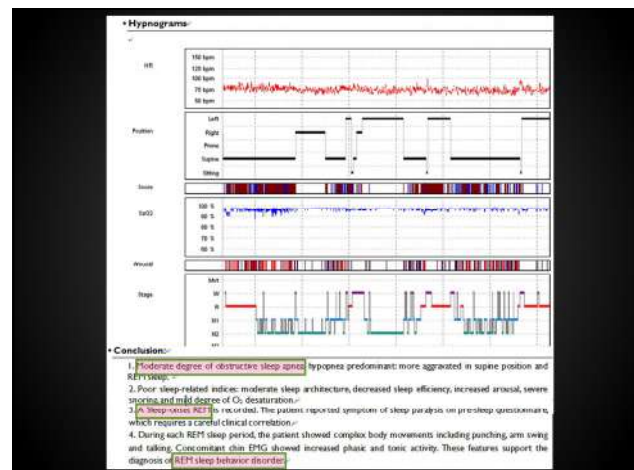
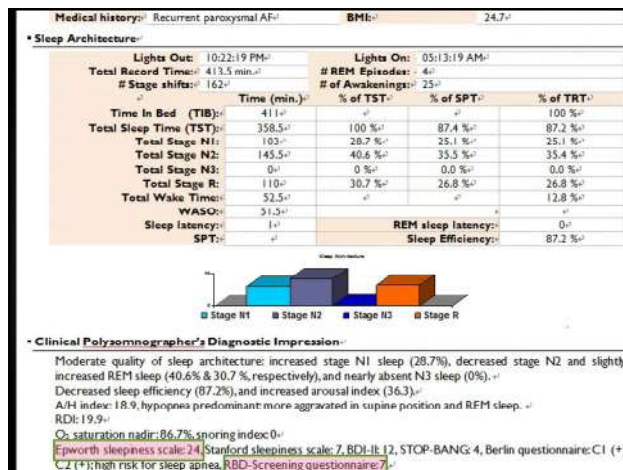
• 때때로 일어나는 졸음에 잠이 들지 않아서 졸려 잠을 못 자는 경우도 있습니다.

• 이 증상이 2014년 10월부터 시작되었습니다.

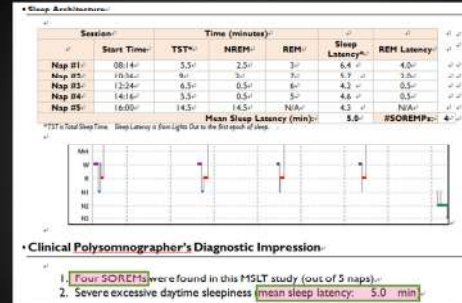
- Past history: paroxysmal atrial fibrillation, S/P RFCA (Nov 2012)
- Smoking: 20 yrs, quit 1 month ago, alcohol: social
- Caffeinated beverage: coffee 1-2 cups
- PSQI 21, BDI-II: 15
- ROS on PSG
 - 아침 기상시 담요 어지러져 있음 (+); suspicion of parasomnia
 - Snoring (+) sleep apnea (-)
 - Daytime Sleep attack (+) - 업무 수행중, 회의중, 컴퓨터 작업중
 - Sleep paralysis (+)
 - Cataplexy triggered by emotions (-)
 - Hypnagogic hallucination (-)

Brief history

- 2014년 10월부터 잤지만 하면 잠이 들었음
- 일하는, 운전 도중 의식을 잃듯이 잠에 빠짐
 - 일상생활을 못할 정도
- 2014년 11월 8일 입원하여 수면다원 검사 및 다수면잠복기 검사



Video

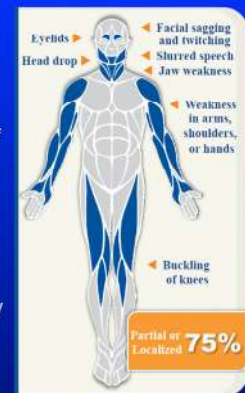


Brief history (2) - Second admission

- 11월 9일 (수면다원 검사 및 퇴원 다음날) 턱을 떨면서 의식을 잃는 event, 반복되어 응급실로 내원
 - 하루 십 수 차례
 - 1분~20분 지속
 - 깨워도 깨워지지 않음
 - 앉거나 누워 있으면 발생
- Brain MRI, SPECT, FDG PET; not remarkable
- Routine chemistry, adrenal function, thyroid function, CSF study; not remarkable

Cataplexy in Narcolepsy

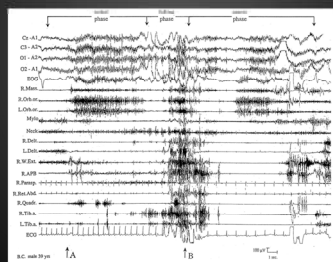
- Second most common symptom of narcolepsy^{1,2}
- Pathognomonic for narcolepsy¹
- Sudden and transient loss or reduction of muscle tone¹
- Triggered by strong emotions¹
 - Laughter, elation, surprise, anger
- Typically partial or localized (~75%)^{2,3}
- Usually short duration¹
- Frequency varies widely¹
- Narcolepsy with cataplexy can be socially disabling and isolating¹



1. American Academy of Sleep Medicine: The International Classification of Sleep Disorders. 2nd ed.; 2005.
 2. Owens S et al. Sleep Med. 2011;12(1):12-18.
 3. Ahmed I, Thorpy MJ. Clin Chest Med. 2010;31(2):371-381.

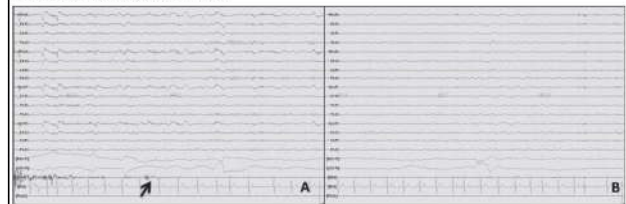
cf) EEG finding during cataplexy:

- falling phase, characterized by a rhythmic pattern of suppressions and enhancements of muscular activity, leading to the fall; atonic phase, characterized by complete muscle atonia
- EEG: persistence of background alpha activity



Clinical Neurophysiology 111, Suppl. 2 (2000) S120-S128

Figure 1—EEG during a cataplectic attack showing (A) transition from wakefulness to sudden atonia in submental EMG; (B) onset of cataplectic attack with REM intrusion



Journal of Clinical sleep medicine 2014;10(2):207

HLA DQ & DR Genotyping

HLA-DQ	serologic	DQ7,DQ6
	allelic(low)	DQB1*03,DQB1*06
	allelic(high)	
HLA-DRB1	most-DRB1*	DRB1*12:02,DRB1*15:01
	less-DRB1*	DRB1*12:01,DRB1*15:04
	less-DRB1*	
	less-DRB1*	
	less-DRB1*	
	less-DRB1*	
	less-DRB1*	

cf. HLA-DQB1*06:02 allele
sensitivity ~95%
Normal population 10-35%
↑ risk for narcolepsy 200 fold

Progress

- IVIg (11/12~11/16) 치료 하였고 Efexor 37.5mg, penid 1T 투약 후 증상 호전되어 퇴원함.
- 2014년 12월 3일 외래
 - Depression 동반되어 Efexor 증량 (75mg)
- 2014년 12월 29일 외래
 - 졸린 것 많이 호전
 - Cataplexy 없음
 - RBD-like symptom은 간간히 있음

Summary

- Old-age onset narcolepsy sx.
 - severe daytime somnolence, cataplexy
 - sleep paralysis (report on questionnaire)
- "Status cataplecticus"
 - (a dozen of cataplexy attack per day)
- Symptom and Test results are consistent with Narcolepsy **except for**
 - (1) the duration of symptom
 - (2) other neurologic disorder (??)



Summary

Narcolepsy- Diagnostic Criteria ICSD3

- 347.00 (G47.4) Narcolepsy Type 1 (Narcolepsy with Cataplexy):
Excessive sleepiness for 3 months
At least 1 of the following:
 1. Cataplexy, and
on MSLT, MSL <8 mins >2 SOREMPs
(one SOREMP may be on the preceding night's PSG)
 - OR
 - 2. CSF CSF hypocretin-1 levels <110 pg/ml or 1/3 rd the baseline normal levels, and
on MSLT, MSL <8 mins >2 SOREMPs
(one SOREMP may be on the preceding night's PSG)
- In children actigraphy is required before the MSLT.
- 347.00 (G47.419) Narcolepsy Type 2. (Narcolepsy without cataplexy)
Positive polysomnography/ multiple sleep latency test are met, but
No cataplexy is present

Hypersomnia (previously reported) causes of secondary narcolepsy: Head trauma, infection, head trauma, tumor, multiple sclerosis

Status Cataplecticus as Initial Presentation of Late Onset Narcolepsy

Samhita Panda, DM, Neurology

Department of Sleep Medicine and Neurophysiology, Sir Ganga Ram Hospital, New Delhi, India

Narcolepsy, one of the important causes of hypersomnia, is an under diagnosed sleep disorder. It has a bimodal age of onset around 15 and 35 years. It is characterized by the tetrad of excessive daytime sleepiness, cataplexy, hypnagogic/hypnopompic hallucinations, and sleep paralysis. Cataplexy is by far the most predictive feature of narcolepsy. Status cataplecticus is the occurrence of cataplexy repeatedly for hours or days, a rare presentation of narcolepsy. This report

describes an elderly gentleman with late onset narcolepsy in the sixth decade of life presenting with initial and chief symptom of status cataplecticus.

Keywords: Narcolepsy, cataplexy, status cataplecticus, head drop, late-onset

Citation: Panda S. Status cataplecticus as initial presentation of late onset narcolepsy. J Clin Sleep Med 2014;10(2):207-209.

case 3: 지나친 주간 졸음을
주소로 내원한 17세 남자

- 고등학생

- C.C

- Hypersomnolence and unconscious wandering for 10 months

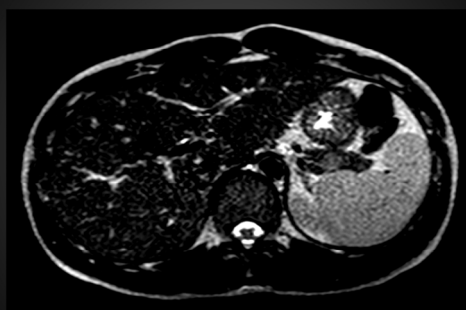
- Present illness

- 10개월 전
운동증 많이 하거나, 잠을 잘 못자면 이후 20시간 가량의 과수면을 하게 됨. 한두 달마다 한번씩 반복됨.
- 4개월 전
수련회 참석 때문에 수면 부족 (< 4hr sleep/night for 2days) 상태에서
버스에서 내린 후 버스 정류장에서 100미터 이상 떨어진 곳에서 배회하고 있는 것을 행인이 발견함. 어떻게 그곳까지 오게 됐는지 기억 못하고, 목격자에게 보호자의 연락처를 알려주었다고 하는데, 이 또한 기억을 못함. 비슷한 일이 한번 더 발생.
- 1주일 전
학교에서 기합을 받은 후 36시간 가량 자다가 GTCS를 하여 인근 병원 ER 방문
- 5일 전
아침식사 거부, 심한 두통, 하던 중 길가 난간을 붙잡은 채 '졸려, 졸려'를 반복하고 있는
채로 발견됨. 인근 병원 ER 방문
- 본원 내과 진료 → 신경과 consultation

Evaluations

- Brain MRI & Routine scalp EEG
 - Normal
- Fasting blood sugar: 29mg/dl
- insulin 7.37 μ U/ml ($\geq 6 \mu$ U/ml)
- C-peptide 2.39 nmol/L ($\geq 0.2 \text{ nmol/L}$)
- Proinsulin 224 pmol/L ($\geq 5 \text{ pmol/L}$)

Abdominal MRI



Abdominal CT & MRI
mass in the pancreas, R/O insulinoma

Treatment & Prognosis

- Surgery
 - Pathology: insulinoma
- 이후 과수면, 주간 졸림증, wandering 사라짐.

Hypoglycemia

- Sweating, dizziness
- Confusion, coma, abnormal behavior, seizure
- Hemiparesis, aphasia, etc.
- Various neurologic symptoms

Hypoglycemia d/t insulinoma

Table 1. Other Diagnoses Given to 58 Patients before the Diagnosis of an Insulinoma*

Diagnoses	Number	(%)
Psychiatric diagnosis	3	(5)
Neurologic diagnosis	39	(64)
Cardiovascular accident/transient ischemic attack	8	(14)
Epilepsy	23	(39)
Tumor	3	(5)
Others	4	(7)
Other diagnoses		
Fructosuria mellitur/diabetes mellitus	3	(5)
Myocardial infarction	1	(2)
Alcohol intoxication	3	(5)
"Functional" hypoglycemia	3	(5)

* Data were not available for 1 patient.

Table 2. Timing of Symptoms in Meals, Activity, and Sleep in 39 Patients with Insulinomas

Time of Symptoms	Number	(%)
Before meals	16	(27)
After exercise/exertion	16	(27)
Other meals	12	(20)
No pattern	10	(17)
Sleeping meals	9	(15)
Morning	8	(14)
Nocturnal	8	(14)
Afternoon	3	(5)
Not stated	2	(3)
Stimulomimetic	2	(3)

* Some patients had symptoms at more than a single time or set of circumstances.

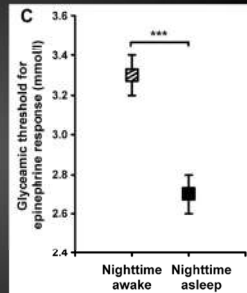
Table 2. Symptoms in 59 Patients with an Insulinoma

Symptom	Number	(%)
Neuroglycopenic symptoms		
Confusion	40	(83)
Personality changes	30	(64)
Dizziness/ataxia	34	(58)
Weakness	33	(56)
Loss of consciousness	32	(54)
Blurring of vision	27	(46)
Anorexia	24	(41)
Dysarthria	19	(32)
Somnolence	18	(31)
Convulsions	16	(27)
Headache	12	(20)
Diplopia	11	(19)
Paresthesias	10	(17)
Coma	7	(12)
Paresis	6	(10)
Autonomic		
Dysphagia	41	(69)
Tremulousness	14	(24)
Polydipsia	7	(12)
Distortion of taste	5	(8)
Other		
Self reported relief of symptoms with food	42	(71)
Weight gain	23	(39)
Hunger	8	(14)
Weight loss	7	(12)
Abdominal pain	3	(5)
Abdominal mass	1	(2)

Am J Med 1999;106:307-310.

Sleep & Hypoglycemia

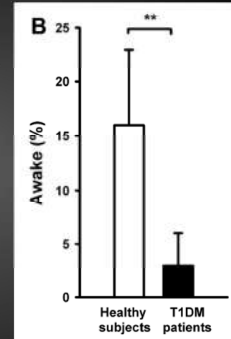
- 55% of severe hypoglycemic episodes occur during nighttime sleep. While asymptomatic in most cases.
 - Nocturnal hypoglycemia: 27-78% in type 1 DM
- Sleep weakens the neuroendocrine defense → nocturnal hypoglycemia



Best Practice & Research Clinical Endocrinology & Metabolism 24 (2010) 801–815

Sleep & Hypoglycemia

- Hypoglycemia triggers awakening in nocturnal hypoglycemia in healthy subjects, type 1 DM frequently fail to awake in the presence of low plasma glucose levels
- Little is known about the frequency of and responses to nocturnal hypoglycemia in type 2 DM



Best Practice & Research Clinical Endocrinology & Metabolism 24 (2010) 801–815