Case-based Learning 1
Epilepsy

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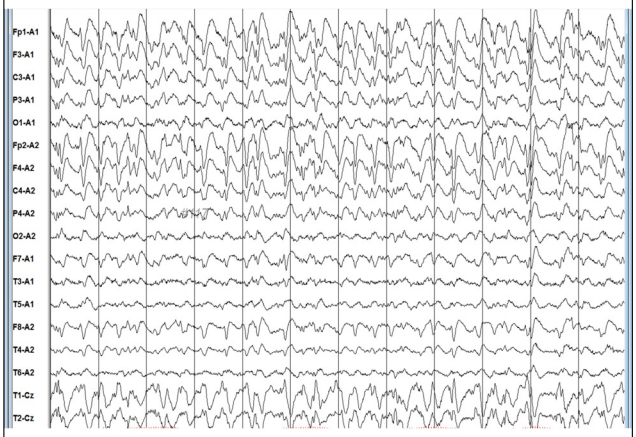
57/M

- C/C : confused & altered mental status for 3 days
- P/I :
  - 3일 전부터 30초 가량 눈에 초점이 없고 불러도 대답하지 않는 증상이 간헐적으로 발생.
    이후에는 의식이 회복되지만 말이 어눌하고 약간 멍한 상태가 지속되고 본인은 기억하지 못함
  - 지속적인 의식혼미가 발생하여 응급실 방문
- PMHx :
  - 최근에 스트레스를 받고 불면증으로 수면제 간헐적 복용
  - 경련, 열성경련 및 외상 없음
- Brain MRI – 특이사항 없음



Absence status epilepticus

- Typical ASE
  - in pts with IGE, >2.5Hz GSW
- Atypical ASE
  - in pts with LGS, <2.5Hz GSW
- Late onset ASE
- Absence status epilepsy by Genton
- Myoclonic absence SE
  - myoclonic jerks of arms
  - 3 Hz SW discharges in the EEG
  - can last hours or even days
  - is usually very resistant to therapy
- Situation related ASE

Typical Absence Status Epilepticus

- Prolonged state of (mildly) altered consciousness
- Bilat. myoclonia may be (eyelid, perioral, arm)
- EEG - continuous or recurrent 3 Hz GSW or GPSW
  - may be slowed in late stage
- In pts with IGE syndromes such as, JAE or JME, PMA
  - 10-25% of absence epilepsy
- In 1/3, ASE is first ever clinical manifestation

Typical Absence Status Epilepticus

- May recur
- In 50%, terminates with GTCSz
- Onset : after puberty or in early adulthood
- Triggering factor : sleep deprivation, alcohol, stress, inappropriate AEDs (CBZ, PHT, GBP, VGB, TGB), AED withdrawal
- Tx : IV BDZs (lorazepam, diazepam), VPA
- Px : usually good seizure control

Absence Status Epilepsy

- Recurrent ASE, infrequent GTCSz, &, rarely, absence Sz
- Similar with typical absence status epilepticus
- Have no clear triggering factor
- No family history of epilepsy
- Interictal EEG – no photoparoxysmal response

Genton, *Epilepsia* 2008

Late onset absence status epilepticus

- occurring in middle-aged or elderly pts
  - late relapse of IGE
  - de novo
- Long term AED Tx is usually not required

Situation-related ASE

I. Drugs such as major neuroleptics but mainly due to benzodiazepine withdrawal

II. Electrolyte and other metabolic disturbances

III. GABA-B agonist-induced absence status epilepticus in patients with epileptic seizures (tiagabine or vigabatrin)

IV. Severe brain anoxia

Comatose or critically ill patients

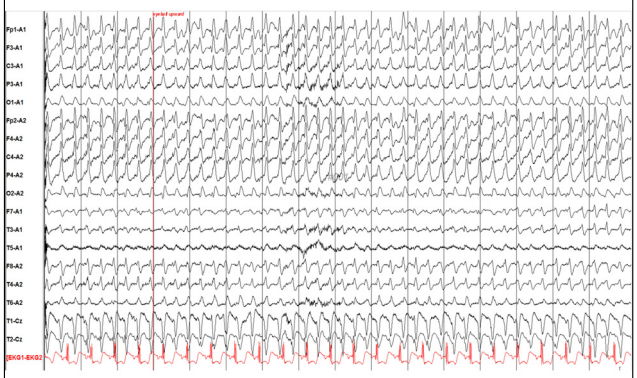
의식저하(52/M)

- C/C : comatose mentality after cardiac arrest
- P/I :
  visited ER for dyspnea, oligouria, generalized edema
  → cardiac arrest & coma
  → ventilator & hemodialysis
- PMHx : moderate degree of CKD, DM, HTN, CSAP
- N/Exam
  - isocoric pupil (3mm) without L/R
  - oculo-cephalic reflex (-)
  - no self-respiration

의식저하(52/M)

- Intermittent myoclonus → rivotril & VPA
- On next day
  - L/R (+), oculo-cephalic reflex (+)
  - weak self-repiratory effort (+)
  - semicomatose state
- EEG
- Continuous, generalized 3Hz spike and slow waves

On the next day after arrest



NCSE in Comatose Pts

- Continuous epileptiform or periodic discharges
  - frequent in advanced coma stages
- True NCSE
  - if both EEG & clinical state resolve with vigorous AED Tx
- If no clinical improvement with AED Tx & acute brain insult itself is sufficient to cause coma
  - may not be NCSE, but epiphenomen
  - might represent an end stage of irreversible coma
  - lasts until EEG becomes electro-cerebral inactivity

NCSE proper vs comatose NCSE

- NCSE proper
  - clinical symptoms suggestive of status epilepticus
  - EEG & clinical improvement with AED therapy
- Comatose NCSE
  - continuous epileptiform or periodic discharges in EEG
  - various etiology
  - no clinical motor signs of status epilepticus
  - no clinical improvement with AED therapy
  - Coma-LED - lateralized
  - Coma-GED – generalized

Gerhard Bauer, *Epilepsia* 2010

55/M

- 갑자기 발생한 양팔과 목의 불수의적 움직임
  - 양쪽 팔에서 간헐적인 음성근간대경련
  - 양팔을 들고 있으면 빈번해짐
  - 목의 근간대경련
- 내원 5일 전 감기증세
  - 트라마돌, 클로르페니라민 및 슈도에페드린 복용
- 간혹 증상이 심할 때는 2 회분 용량을 복용하기도 하였지만 일일 100 mg 이하 복용

  (최대허용량: 400 mg/일)

Tramadol

- Centrally acting, synthetic analogue of codeine
  - mu-opioid receptor agonist
  - active metabolite, o-desmethyltramadol, has a far greater affinity (up to 20-fold than codeine)
  - (up to 200-fold than tramadol)
- At peripheral level, inhibits serotonin & NE reuptake

  → mechanism of neurotoxicity in abuse or overdose
- Less abuse potential and less respiratory depression

Tramadol

- Sz can be provoked with tramadol monotherapy
  - in animal and human
  - both at recommended (<400mg) and high doses
  - GTCSz is most common
  - within 24 hrs after intake
- After acute poisoning
  - Sz can be developed in 15-35%
  - debate on the correlation btwn dose & Sz
- Reduced the PTZ threshold but increased the MEST, but not significantly (Bankstahl, 2013 *Neurotoxicology)*

Tramadol

- More common in subjects concomitantly consuming alcohol, anti-psychotics, SSRI or TCA
- Mechanism of provoking Sz ???
  - GABA receptor inhibition
  - H1 receptor activation linked pathway
- Multiple Sz
  - in 7-15%
  - all patients recovered without sequelae
  - unnecessary to administer prophylactic AEDs

47/M

- Known epilepsy pt
  - had taken CBZ 800mg for 3 years
  - Self-stop of CBZ at 3 months ago
  - he developed a GTCSz yesterday
  - → ingested 800mg of CBZ today
  - → What happens ?

Autoinduction of CBZ metabolism

- CBZ is metabolized by CYP3A4, CPY2C8
- CBZ induces CYP3A4
- Hepatic metabolism is significantly increased (2 times) gradually after daily ingestion through 2-6 wks
  - decreases in s-CBZ concentration
  - increases in urinary excretion of CBZ metabolites
  - decrease in elimination half-life (24-36 hr →12-15 hr)
  - with PHT or PB, half-life is reduced to 6 hr