Seizures and Palliative Medicine

Palliative Medicine ECHO Conference

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Mr. X

Mr. X is a 65 year old male

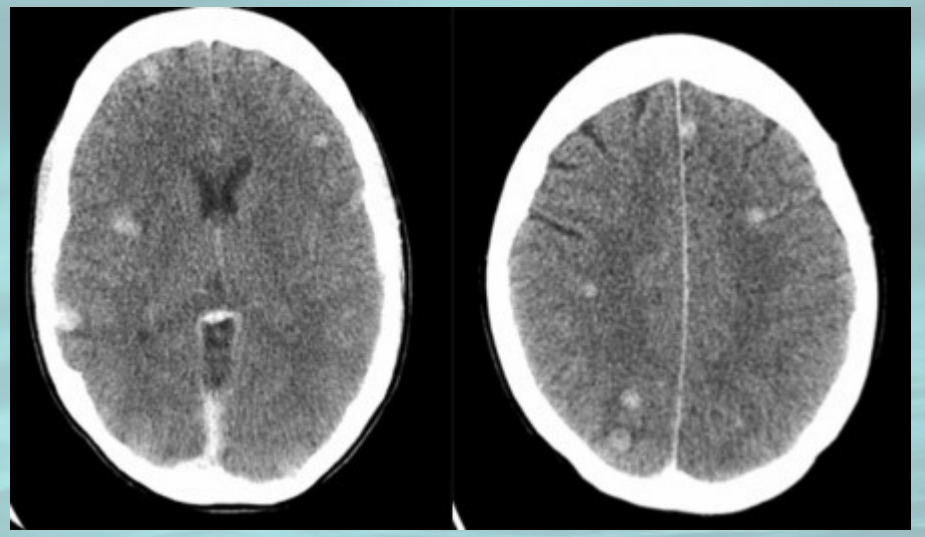
- Stage 4 non small cell lung cancer
  - Recently diagnosed brain metastases
- Whole-brain radiotherapy one month ago
- Low dose dexamethasone daily 4 mg
  - Being weaned after irradiation
- Had tonic-clonic movements in left arm
  - Lasted 3 minutes

Mr. X

- Medications
  - Decrease in dexamethasone past 2 weeks
  - Addition of hypoglycemic agents 3 weeks ago
- Left sided paresis
  - Preceded the diagnosis of cerebral tumors
  - Worsened

What are the differentials?

Mr. X



- Blood work
  - No biochemical anomalies.
- Repeat CT scan of brain
  - Increased edema and stable size of metastases

What is treatment?

Should Mr. X be on seizure prophylaxis?

INTRODUCTION

At risk population:

Ischemic stroke

Intracerebral hemorrhage

Neurodegenerative diseases

Non-neurological conditions such as terminal liver, kidney, or respiratory failure

Challenges

- Events are unwitnessed by professionals
- Differential diagnosis and treatment can be difficult.
- Even witnessed events can be mistaken for delirium or agitation
- Postictal state
- Treatment

Diagnosis

- Description of ictal signs and symptoms, is the most important diagnostic tool in epileptology

- In Prospective study Stefan et al. found less clonic elements and a higher proportion of non-convulsive status epilepticus in elderly patients.

Diagnosis

Ictal symptoms included:

- Impaired attention and concentration (90%)
- Bewilderedness
- Impairment of goal-directed action
- Speech reduced to simple semiautomatic phrases or gestures.
- Low amplitude fragmentary myoclonic jerks, typically in the face, eyelids, or hands, and at times associated with hand automatisms

Technical Examination

- Epileptiform discharges on EEG
- Role of MRI
- CT head which in contrast to MRI is less time consuming and less burden on patient, can show gross edema or tumor

Technical Examination

- Location of diagnosis
- Non Convulsive Status Epilepticus
- EEG + Treatment = Diagnosis of NCSE

- LAB TESTING
- Role of CK elevation
- No use of serum pro calcitonin in palliative settings.
- AED levels is useful if intoxication is concerned but it is rare and should be avoided.

Anti Epileptic Therapy

Treatment Principles:

Respecting Patient Resources and Wishes

Target Levels of QoL

Considering the Current and Future Requirements of Therapy

Ensuring Practicality:

Acute Management of Seizures and Convulsive Status Epilepticus

- Limiting Benzodiazepine to Status Epilepticus or series of seizures.
- Patients should be acutely treated when a generalized seizure lasts longer than 5 min or two or more seizures occur without regaining preictal level of consciousness in between event.

Choice of treatment of SE will depend on the patient′ s location: hospital, hospice, or home care.

- In either setting, the first step of treatment (0–10 min) is administration of benzodiazepines

- No Formal recommendations for starting doses in palliative.

Hospital setting

- Initial management SE in the palliative = The general treatment recommendations for SE.

- In established SE (10–60 min), intravenous drugs [e.g., phenytoin/fosphenytoin, valproate (VPA), LEV, phenobarbital (PB)] are most commonly used, although there is no class I evidence for choosing one over the other. Among those VPA, LEV, and lastly additional lacosamide (LCM) seem to be effective and safe alternative

- Refractory and super-refractory SE are treated with anesthetics with a markedly lower success rate and a high morbidity and mortality.

- “Palliative sedation” using benzodiazepines (or alternatively propofol) might alleviate symptoms even if epileptic activity persists

Hospice/Home Care Setting

- Application forms of Lorazepam and Midazolam
- Rectal (If the rectal preparation of diazepam is not available, the IV preparation may be infused rectally via a syringe)
- Intranasal or buccal midazolam or lorazepam or IM-midazolam (Equally effective as IV or rectal form but the data is more robust in Children)

- Lorazepam and Diazepam can be kept at the patient's bedside to allow fast administration if necessary, in cases seizure frequency increases in the last weeks of life.

TABLE 1 | Administration routes and characteristics of antiepileptic drugs relevant for palliative care.

AED	Daily Dose	Special consideration for palliative care	IV	Liquid solution	Suspension	Tablet
Brivaracetam (BRV)	50–200 mg	Mild CYP3A4 metabolism. Probably no clinical relevant interactions	+	+	–	+
Carbamazepine (CBZ)	600–2000 mg	Dizziness, nausea, ataxia Effective for neuralgic pain (200-400 mg/d), decreases: VPA, TPM, LTG, neuroleptics, antimycotic agents, antidepressant drugs, steroid level Increases: diazepam level and effective CBZ- Metabolite Is decreased by: PHT Is increased by: Theophyllin, Cisplatin	–	+	+	+
Eslicarbazepine (ESL)	800–1600 mg (max. 1200 mg when combined with other AED)	Dizziness, gait disturbance, ataxia, hyponatremia Is decreased by: PHT, CBZ Increases: PHT	–	–	–	+
Gabapentin (GBP)	900–3000 mg	Sedation (especially in combination with opioids), therapy of neuropathic pain (900 mg/d) Is increased by: morphine	–	+	+	+
Lacosamide (LCM)	100–600 mg (max. 400 mg when combined with other AEDs)	Dizziness No relevant interactions	+	+	+	+
Lamotrigine (LTG)	100–300 mg	Tremor, sedation (rare), sleep disturbance, mood stabilizing effect. Very slow titration necessary Is decreased by: CBZ, PHT Is increased by: VPA	–	–	+	+
Levetiracetam (LEV)	1000–3000 mg (–4000 mg off-label) mg	Sedation (rare), psychiatric side effects No relevant interactions	+	+	+	+
Oxcarbazepine (OXC)	900–2400 mg	Dizziness, nausea, ataxia (less often when the slow release form is used), hyponatraemia	–	+	+	+
Perampanel (PER)	4–12 mg	Dizziness, somnolence Is decreased by: CBZ, OXC, TPM Decreases: CBZ, OXC, VPA	–	–	–	+
Phenytoin (PHT)	200–350 mg	Dizziness, allergy. Potentially complicated titration Decreases: steroid level	+	–	+	+
Pregabalin (PGB)	150–600 mg	Sedation. No relevant interactions Anxiolytic effect.	–	+	+	+
Topiramate (TPM)	50–200 mg	Sedation, fatigue, lack of appetite, weight loss, paraesthesia, speech disturbances No relevant interactions	–	–	+	+
Valproate (VPA)	1200–2400 mg	Tremor, encephalopathy, mood stabilizing effect. Enzyme inhibition (leading e.g., to increased toxicity of chemotherapy).	+	+	+	+

Application Forms of AEDs

Subcutaneous AED Application

Rectal AED

		Hospital	Hospice/home care	Outcome
Stage 1 5–10 minutes	Early phase Premonitory SE, Impending SE	Lorazepam IV 0.05 mg/kg max. 2 mg/minute, if necessary repeat after 5 minutes	Midazolam buccal or intranasal 0.2 mg/kg (5–10 mg) or Lorazepam buccal or intranasal 0.05 mg/kg or 10 mg IM-midazolam Repeat if necessary	better
Stage 2 10–30 minutes	Established SE	Levetiracetam 30-60 mg/kg IV max. 500 mg/minute, if necessary repeat after 10 minutes and/or additional lacosamide 5 mg/kg IV in 15 minutes *Alternative stage 2:* Valproate 20-30 mg/kg IV max. 10 mg/kg/minute, if necessary repeat after 10 minutes	*In absence of IV route:* 1000–2000 mg levetiracetam in 100 ml 0.9% sodium chloride over 30 minutes SQ if necessary additional: 200 mg lacosamide over 20 minutes SQ Repeat if necessary, or repeat benzodiazepine administration	
Stage 3 30–60 minutes	Refractory SE: SE, that continues despite stage I/II treatment, subtle SE, stuporous SE	midazolam bolus 0.2 mg/kg IV, continuously 0.1–0.5 mg/kg/h or propofol bolus 2 mg/kg IV, continuously 4–10 mg/kg/h	consider palliative sedation	
Stage 4 >24 h	Super refractory SE: SE, that continues despite treatment with anesthetics >24 h	consider palliative sedation	consider palliative sedation	worse

Questions?

Thank you.