Seizures and Epilepsy – Dr Rahul

What are the most sensitive and specific aspects of history taking in diagnosing seizures? 1:04

- Ideally get an eye witness account, can consider requesting for CCTV footage
- Pre-Ictal
  - Suggestive of epileptic seizure
    - § Aura: Premonition or pre-ictal phenomenon; most common would be temporal lobe auras (déjà vu, jamais vu, unusual taste/smells)
    - § Going blank for an extended period of time
  - Suggestive of syncope
    - § Prodrome: Tunneling of vision, cold/sweaty
- Ictal
  - Tonic clonic features
  - Foaming at the mouth
  - Biting of the tongue
  - Loss of consciousness/awareness
- Post Ictal
  - Most seizures which cumulate in a convulsive seizure result in a post ictal amnesic phase (few minutes or longer) – next remembered event might be being in the ambulance/being in the hospital (vs remembering on site events more in keeping with syncope)
- Incontinence not very specific nor sensitive

Physical Examination findings? 6:34

- Tongue bite marks
- Atraumatic shoulder dislocation suspicious for epileptic event

What are the common and important triggers to evaluate for? 7:06

- Sleep deprivation
- Alcohol/benzodiazepine withdrawal
- Intercurrent illness – Febrile illnesses can lower seizure thresholds
- New medications
- Flashing lights – photosensitive epilepsy more common in paediatric epilepsy syndromes than in adults

Role for blood tests? 9:12

- Bottom line is that there isn't a very sensitive/specific blood test
- Prolactin: Has to be taken fairly soon after event (within 30 minutes; may be possible for ward patient), may help to differentiate convulsive vs non-epileptic seizure, but not able to distinguish from syncope; negative prolactin does not exclude seizure
- CK: Non-specific test, many factors can raise CK (exercise, falls, IM injections)
- Lactate: May be raised shortly after a convulsive seizure, but normal lactate does not exclude seizure
- WBC: WBC may be raised also in seizures – raised WBC in seizure does not always equate to infection but it is important to evaluate for infection as a trigger or cause (e.g. meningoencephalitis) of seizure

Role for EEG 12:36

- Indications for an EEG
  - Possible Seizure: Localise where epileptiform abnormality is, pattern may suggest a particular epilepsy syndrome which guides management

    - In known epilepsy: If previous EEGs have been normal or if patient is not back to neurological baseline (to ensure that patient is not having an ongoing non-convulsive seizure)
- Timing for EEG
    - More sensitive the sooner after the seizure
    - If there is a concern of non-convulsive seizures, refer to neurologist – KIV for emergent EEG
- How useful is an EEG in excluding seizures?
    - If there is ongoing event, if EEG is negative, an epileptic seizure is conclusively excluded
    - During inter-ictal state, less definitive in excluding

<u>What work-up should be performed for first onset seizures? 17:38</u>

- Neuroimaging: CT brain usually performed in ED; MRI gives increased resolution
- Glucose – ensure there is no hypoglycemia
- Electrolytes, LFT, toxicology screen
- EEG
- Subsequent investigations like LP (if suggestion of CNS infection) depends on clinical picture

<u>When is an MRI indicated?</u>

- If resource permits, then an MRI has better resolution. MRIs are encouraged in patients who are medically refractory , or there is some suggestion of focality on their EEG or clinically (eg Todd's paresis)
- The epilepsy protocol is a set of MR sequencing and processing parameters to highlight grey white differentiation, thin slices over the mesial temporal structures etc. It has higher detection of subtle abnormalities. It is not a 'must', but would be required eg if contemplating epilepsy surgery

<u>When should AEDs be start for first onset seizures? 19:17</u>

- Definition of epilepsy has evolved over the years – in the past required 2 or more unprovoked seizures
- Nowadays, if there are risk factors in the presence of a first onset seizure, treatment might be warranted
- Indications include:
    - Prior brain insult – e.g. previous MCA stroke
    - Highly abnormal EEG
    - Nocturnal seizure during sleep
    - Major injury as a result of seizure
    - Patient choice/wishes

<u>Figuring out AEDs? 21:57</u>

- How do we choose between the different AED agents?
    - Is a particular epilepsy syndrome identified – e.g. in JME/absence seizures, valproate and levetiracetam is indicated; avoid carbamazepine/phenytoin
    - Side effect profile
    - Cost
- Generally warn patients that they may feel a little drowsy or 'off' for the first few days but this usually settles
- Specific Drugs
    - Levetiracetam (Keppra)
        - § Generally favourable side effect profile, but can still cause mood changes, irritability and insomnia
        - § Costly! – 10x/more per tab compared to sodium valproate/phenytoin

        - Dosing
            - Starting Dose: 250mg BD then increase based on response
            - Ceiling Dose: 1500mg BD
    - Sodium Valproate
        - Significant side effects: Weight gain, tremors, teratogenicity, LFT derangements, thrombocytopenia
        - Dosing: Epilim chrono
            - Starting Dose: To minimize adv effects, consider 300mg OM for 3-7 days and then BD
            - Ceiling Dose: 1500mg BD
    - Phenytoin
        - Significant side effects: Severe cutaneous reaction (SJS/TENS), gingival hyperplasia with prolonged use, hepatitis and haematological abnormalities
        - Dosing:
            - Starting Dose: Oral administration can be once daily if patient of average build 300mg ON. If small or frail, would be lower eg 200. If larger doses eg 400mg or more, consider BD dosing
            - Ceiling dose: Ceiling dosage for this drug would depend on drug levels. I'd say once you're straying past 400mg , you should be guided by levels
    - Carbamezipine
        - Significant side effects: Severe cutaneous reaction (SJS/TENS), drowsiness, ataxia (usually when heading into toxicity)
        - Dosing:
            - Starting Dose: 200mg OM for 1 week, then BD
            - Ceiling Dose: 1600mg daily (usually in split doses)
- Generally start at lowest dose then titrate upwards – based on side effects, efficacy
- Efficacy: 50% reduction in pre-treatment seizure frequency

<u>Focal vs Generalised Seizures? 28:17</u>

- Focality and generality applies to 1. type of epilepsy syndrome vs 2. type of seizure
- Vast majority of seizures that we see are generalized tonic/clonic, but almost all adults who present with a seizure have a **focal onset** which subsequently evolve into GTCs from the focal onset spreading
- Hence appropriate semantics would be: Focal to bilateral tonic clonic seizure
- Clinical Significance
    - GTC – Ongoing GTCs are a medical emergency, the longer the GTC the higher the risk for:
        - Neuronal damage
        - Systemic complications – Autonomic dysfunction due to, rhabdomyolysis, lactic acidosis
    - Focal Seizures – Less life threatening; can generally be managed in the general ward

<u>Dealing with breakthrough Seizures? 32:48</u>

- Do all breakthrough seizures need to be admitted? No, if:
    - Return to neurological baseline
    - No significant injury
    - Reliable caregiver at home
- Repeat brain imaging in known epilepsy is usually not needed, unless:
    - Change in seizure pattern
    - Patient has not returned to neurological baseline

    - Signs of head injury
    - On anticoagulation – TRO ICH
- Drug Levels
    - Check levels if patients present with breakthrough seizure to give an idea about compliance and space for dose adjustment
    - Levels should be checked immediately on presentation – if medications dosed, then levels become difficult to interpret
    - Non-compliance:
        - If detectable in past and now undetectable, suggest non-compliance – subsequently dose and check levels
        - Even if levels are undetectable, need to have detectable doses before on the same dose – then only can conclude non-compliance – could be variable metabolism
        - Note that low drug levels does not equate to non-compliance – may suggest dose inadequacy
    - AEDs for which levels can be checked: Phenytoin, CBZ, sodium valproate, phenobarbitone
- Assessment of patients with breakthrough seizures
    - Compliance
    - Triggers – Sleep deprivation, intercurrent illness
    - Adverse effects of drug
- Medication adjustments for breakthrough seizures
    - Discourage manipulation of AEDs in a reactive fashion as this can cause erratic changes in drug levels
    - If non-compliant/clear trigger, may not need to adjust the dose
    - If decision made for dose adjustment, then aim to keep dose at the newly increased dose – rather than temporarily increasing AEDs then bring the dose back down
    - If acute intercurrent illness, then may consider to use a bridge – e.g. clobazam (standard dose 10mg BD, but in frailer/older patients can consider 5mg BD)
    - Clobazam can be given for prophylaxis against breakthrough seizures – intercurrent infections, menses associated seizures

<u>Status Epilepticus 41:30</u>

- Definition: Unremitting seizure of >5 minutes or 2 successive seizures with no full inter-ictal recovery
- Treatment
    - Benzodiazepine – **Timely intervention is key! Take home message is use whatever is available**
        - Agents
            - Lorazepam: IV 4mg; Most effective from pharmacokinetic (less lipophilic, longer half life)
            - Midazolam: IV 5mg; can give IM 10mg if unable to get IV access
            - Diazepam: IV 5mg
        - Can repeat 2nd benzo dose in 5 minutes if seizure not aborted
    - Anticonvulsants
        - Sodium Valproate – Hemodynamically favourable
            - Loading: 20mg/kg over 1 hour (~1g)
            - Maintenance: 400mg Q8H
        - Levetiracetam
            - Loading: 1500mg over 5-10 minutes
            - Maintenance: 500-1000mg BD (assuming normal renal function)
        - Phenytoin

        - Loading: 20mg/kg over 30 minutes
        - Maintenance: 100mg 8H
    - If first agent doesn't work, can consider loading a second agent
  - Next step will be anesthesia induction – Ideally should be done in the ICU with airway secured: Options include midazolam, propofol, barbituates
- Always evaluate for post-ictal recovery after abortion
- If seizure is happening in front of you, don't wait, attempt to abort

Following up with Patients? 46:50

- Seizure frequency
- Medication compliance
- Adverse effects to medication
- Ascertain if seizures were provoked or unprovoked
- Pregnancy plans – Potential teratogenic effect of anti-seizure medication
  - Folic acid if child bearing potential
  - Most unfavourable – sodium valproate (highest risk of teratogenicity, may affect IQ of children, risk of autism)
- Blood Tests: FBC, LFT – No specific guidelines; Repeat blood tests 6-8 weeks from initiation, once stable – then maybe annually
  - Valproate: Thrombocytopenia
  - CBZ: Hyponatremia
- Do we actively down-titrate AEDs?
  - Based on risk stratification, adverse effects from medication and seizure control
  - If structural abnormality present (e.g. previous CVA/scar epilepsy), more cautious about medication withdrawal because of high risk of recurrence
  - If no structural abnormality – can offer dose reduction with aim to stop if seizure free for > 2 years, but must advise on risk of seizure recurrence

Take Home Points 52:26

- Breakthrough Seizures: Compliance, triggers, drug levels
- Status Epilepticus: Timely intervention is key
- Review patient after seizure has 'aborted' to ascertain return to baseline neurology