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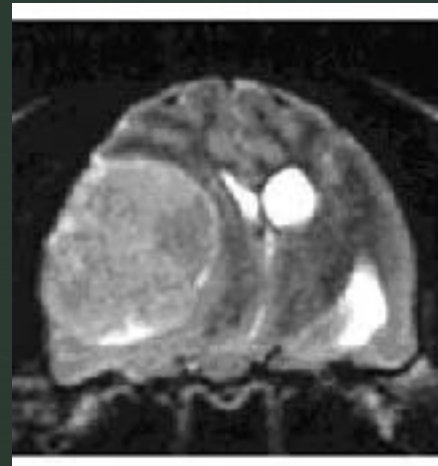


Seizures and tremors: Acute treatment and diagnostic work up



Overview

- Terminology
- Differentiating seizures vs other
- Seizures
 - Acute therapy
 - Differentials
 - Diagnostics
- Tremors
 - Acute therapy
 - Differentials
 - Diagnostics



Terminology

- Seizure: clinical manifestation of a discrete episode of abnormal neuronal activity
 - Generalized – both hemispheres involved, always lose consciousness
 - Focal – only one hemisphere initially affected, variable effect on LOC and responsiveness
- Epilepsy: recurrent seizures of intra-cranial origin
 - Idiopathic – no structural abnormality, other neuro signs, age-dependent onset, known or suspected genetic cause
 - Secondary – identifiable brain lesion
 - Tumor, infectious/inflammatory disease, vascular accident, trauma, hydrocephaly, etc.
 - Cryptogenic – no apparent lesion, but dose not fit idiopathic criteria

Terminology

- Cluster seizures: two or more seizures within 24 hours
- Status epilepticus:
 - Single ictus lasting longer than 5 minutes
 - Two or more separate seizures without complete return to normal in between
- Reactive seizures: seizure brought about by a systemic perturbation
 - The brain itself is normal

Fits, turns, spasms, and spells

- Dogs:

- Seizures
- Tremors
- Syncope
- Vestibular disease
- Behavioral problems
- Sleep



- Cats:

- Seizures
- Tremors
- Syncope - rare
- Vestibular disease - rare
- Obsessive-compulsive disorder
- Pain associated behavior

Which is it?

- Through description of the event
 - Seizures will always have consistent post-ictal period
 - Timing of event with activity or vagally mediated events
 - Elimination
- Through physical exam
 - Evidence of heart/lung disease or arrhythmia
- Through neurologic exam – ideally interictal period
 - Interpret neuro deficits with CAUTION
 - Vestibular disease, persistent neuro deficits
 - Tremors are typically NOT intermittent
- Video of episode



Tremors vs seizures

- Tremors can be very violent and mimic generalized seizures
- Tremors may worsen with stimulation/handling
- Tremors should not alter consciousness
 - Difficult to discern
- Tremors are typically minimally responsive to anticonvulsants

What if you're not sure?

- History of possible exposure to toxins
- Baseline blood work – check for apparent extracranial causes
- ECG (5 minute), BP, chest radiographs, SpO2
- Consider further cardiac work up
- Have owner video event
- Levetiracetam trial

Acute therapy - seizures

- Stop the current seizure
 - Order of drug administration depends on what you have available
- Prevent further seizure activity
 - Particularly important if cluster or status event
 - Consider as immediate therapy if cluster event without current seizure
 - Components:
 - AED therapy
 - Fluid resuscitation
 - Temperature regulation
 - Hyperosmotic therapy



Acute treatment – stop the seizure

Benzodiazepines

- First line therapy for active seizure
- Midazolam & diazepam are equivocal
- 0.5 mg/kg IV up to three times (= 1 ml per 10 kg)
 - Midazolam can be given IM at same dose**
 - Diazepam can be given rectally at twice the dose
- TRANSIENT suppression of seizure activity - minutes
- Consider possibility of tremors if patient does not respond!

Acute treatment – stop the seizure

Levetiracetam

- Incredibly safe drug with minimal side effects
- Generic and cost effective now
- 20-100 mg/kg IV
 - I start w/ 20-40 mg/kg and repeat up to three times
 - Dose a minimum of 60 mg/kg before you consider patient refractory
- Duration of anticonvulsant effect up to 8 hours
 - Can re-dose sooner if needed

Acute treatment – stop the seizure

Phenobarbital

- Profoundly sedating, especially when given parenterally
- 4 mg/kg IV, can give up to 4 times in 24 hours
 - Typically only give 2 doses in a row for an active seizure
 - Monitor ventilation and gag reflex
- If patient on phenobarb already, try to collect a red top before giving so levels can be determined if needed

Acute treatment – stop the seizure

Ketamine

- Use has been reported in humans and one dog
- 5 mg/kg bolus followed by CRI of 5 mg/kg/hr
- Monitor ventilation and gag reflex, especially if combined with other drugs

Acute treatment – stop the seizure Propofol & GA

- Last resort
- Propofol to induce anesthesia then continue as CRI or use inhalant anesthetic
 - 3-5 mg/kg slow IV
 - CRI rate is 100-500 mcg/kg/min
- May cause hypotension and hypoventilation
- Need to intubate and monitor as any anesthesia patient
 - Ventilatory status, HR, SpO₂, BP, EtCO₂, etc.



Preventing further seizures AED therapy

- Benzos will only last for minutes – need to have a plan
- Immediately prevent further seizures if status or cluster event
- If having severe cluster event give AED (even if not actively seizing) immediately after neuro exam
- Because of safety profile, levetiracetam is my first choice, after that no particular order

Preventing further seizures AED therapy

- Levetiracetam 20-60 mg/kg IV or PO
 - Oral takes 1-2 hours to peak levels so depends on seizure frequency
- Phenobarbital loading 4 mg/kg IV or PO x 4 doses in 24 hours
 - Oral takes 4-8 hours to peak, so typically given IV
- Benzodiazepine CRI 0.5-2 mg/kg/hr IV
 - Rapid resistance, MUST taper to avoid rebound seizures
 - Only use 1-2 days until something else is loaded
- Ketamine 5 mg/kg bolus then 5 mg/kg/hr IV
 - Only used until something else loaded then tapered off
- Zonisamide takes 3 days to load

Preventing further seizures

Fluid resuscitation

- Hypoperfusion is not uncommon with status/cluster events
 - Deleterious to the injured brain – treat aggressively
 - Prolonged CRT, decreased pulse quality, persistent tachycardia
- Isotonic crystalloids, bolus over 20 minutes
 - 20-30 ml/kg in dogs
 - 10-15 ml/kg in cats
- Hypertonic saline 5 ml/kg over 10 minutes, must follow with IVF
- When in doubt give a fluid bolus!

Preventing further seizures

Thermoregulation

- Hyperthermia is common with frequent or static seizures
- Pursue active cooling if temp >105 ,
 - Especially if patient not conscious
 - Moisten coat w/ cold water and use fan if mild
 - If severe, bathe with cold water until temp <105 then dry
- Severe hyperthermia >108 does not necessarily indicate heatstroke
 - Heatstroke is complex and is not just a result of elevated temperature
 - Warn owners it is possible and monitor for signs



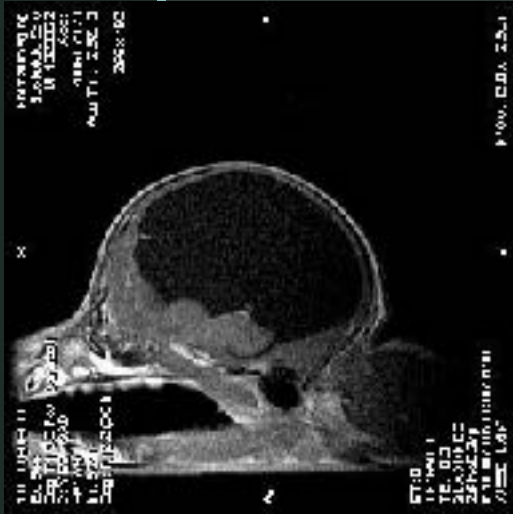
	CPP = MAP - ICP		
Hypertonic saline	↑↑	↑	↓
Mannitol	↓	↓	↓

Preventing further seizures

Hyperosmolar therapy

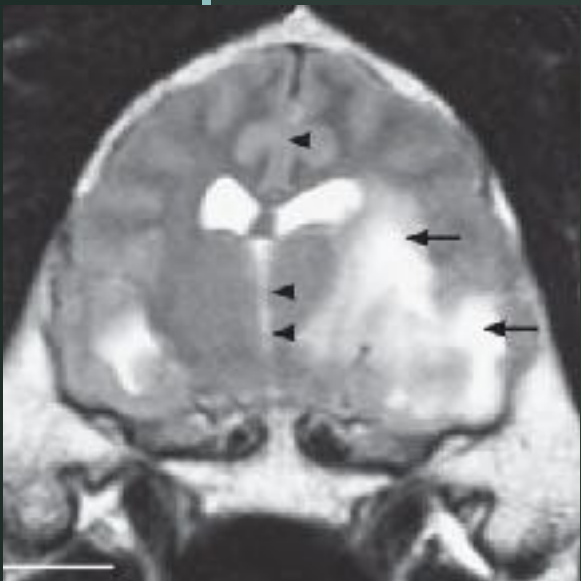
- Seizures can cause cerebral edema, especially status/clusters
 - Recommend for all status events
 - Recommend for clusters unless patient is BAR
- Hypertonic saline 5 ml/kg over 10-15 minutes
 - Also helps restore perfusion
 - Must be followed with IV fluid therapy
- Mannitol 0.5-1 gram/kg over 10-15 minutes
 - Contraindicated if any hypoperfusion present
 - If unable to drink, must provide IVF

Differentials for seizures



- Degenerative: storage disease, thiamin deficiency
- Anomalous: hydrocephaly, lissencephaly, chiari-like malformation, arachnoid cyst/diverticulum
- Metabolic (extracranial): hypoglycemia, hepatic encephalopathy, uremic encephalopathy, hypoxia, hyperlipidemia, hyperthermia, intestinal parasitism, hyperthyroidism, electrolyte changes (sodium & calcium)
- Neoplasia: any primary or secondary neoplasia. Meningioma, lymphoma, glioma, etc.

Differentials continued



- Inflammatory: meningoencephalitis of unknown etiology/origin (MUE or MUO)
- Infectious: FIP, FeLV, FIV, rabies, canine distemper, fungal (Cryptococcus), bacterial encephalitis, Toxoplasmosis, Neospora caninum, aberrant Cuterbra larval migration, rickettsial disease
- Idiopathic epilepsy
- Trauma/toxin: head trauma (potentially years after the event), lots of toxins
- Vascular: vasculocclusive or hemorrhagic strokes, hematoma

Idiopathic epilepsy

- Dogs >>>> Cats
- Normal neuro exam after postictal period (interictal)
- Age dependent onset 6 mo – 6yr or 1-7 yr
- Presumed genetic origin – proven in some breeds
 - Many are channelopathies
 - Recommend castration/spay
 - beagle, Belgian tervuren, Bernese mountain dog, border collie, Dachshund, English springer spaniel, Finnish spitz dog, German shepherd dog, golden retriever, Irish wolfhound, Keeshond, Labrador retriever, Logotto Romagnolo dog, standard poodles, and Vizsla
 - High incidence: boxer, Cocker spaniel, Collie, Irish setter, miniature schnauzer, Saint Bernard, Siberian husky, wire fox terrier

Diagnostic plan

- After first seizure:
 - Neuro exam (post ictal for upto 48 hours)
 - Check for extracranial causes: CBC, Chem, UA, FeLV/FIV
- Consider:
 - Toxo/neospira titers
 - Bile acids
 - Other infectious disease – 4Dx, NCSU tick panel, fungal antigen
 - Chest radiographs





Further work-up

- Advanced imaging (MRI) & CSF tap are recommended when:
 - Cat with any seizure frequency
 - Dog with single seizure that has interictal deficits
 - Dog with recurrent seizures, especially if interictal deficits
 - Epileptic patient with sudden change in seizure frequency once therapeutic drug levels have been verified
- If fits criteria for idiopathic epilepsy, presumptive diagnosis and treatment is reasonable but imaging should be offered
- Seizures should be treated regardless of whether owner elects to pursue imaging.

But what if it's a tremor...

- Worse with stimulation (tactile and auditory)
- "With it"
- Poorly responsive to anticonvulsants
- Electrolyte abnormalities, hypoglycemia
- History of possible ingestion

Acute therapy - tremors

- Stop the tremoring
- Further treatment
 - Prevent ongoing tremors
 - Components:
 - Drug therapy
 - Fluid resuscitation
 - Temperature regulation
 - Other therapy

Acute therapy – stop the tremors



- Poorly/minimally responsive to typical AEDs
 - Can give benzos – may give some muscle relaxation
- Treat underlying cause if present
 - Check BG, electrolytes
 - MOST effective
- Methocarbamol 50-100 mg/kg slowly IV to effect

Preventing further tremors

Methocarbamol as needed

- Maximum daily dose 330 mg/kg/day
- I have exceeded this with no apparent adverse effect

Consider IV lipid emulsion (IVLE)

- 1.5 ml/kg IV bolus, then 0.25 ml/kg/min x 60 min
- Low risk – pancreatitis, fat embolism
- Fat soluble toxins – mycotoxins, permethrins, macrocyclic lactones



Acute therapy – tremors

Other therapy

- Hypoglycemia – 1 ml/kg 25% dextrose IV
- Ionized hypocalcemia – 1 ml/kg calcium gluconate over 15 min
- Fluid resuscitation as for seizures
- Thermoregulation as for seizures
- Minimize stimulation: gentle handling, turn down lights, quiet



QUIET PLEASE
PLEASE DO NOT TOUCH

Acute therapy – tremors

Toxicologic considerations



- Dermal decontamination for topical permethrins
 - Want a soap that will strip oils from the coat = dish soap
- Emesis not recommended in symptomatic animals
 - Could consider GA and gastric lavage but probably not very helpful
- Activated charcoal
 - Probably not helpful once symptomatic
 - Do not force feed symptomatic patients
 - Need to follow with IVF therapy if not able to drink

Differential diagnoses - tremors

- Toxins – MANY!
 - Mycotoxins – compost, garbage
 - Bromethalin
 - Permethrins/pyrethrins
 - Macrocyclin lactones
 - Strychnine
 - Metaldehyde
 - Organophosphates
 - Caffeine/theobromine
 - Recreational drugs
- Hypocalcemia most likely
- Hypoglycemia
- Sodium disturbances



Tremors - diagnostics

- Through history – Potential access to...
 - Chocolate, mycotoxins, pyrethrins are most common seen
- CBC and chemistry
 - BG and lytes or blood gas is fastest if available



Questions

