Neurological Manifestations of Thyroid disease

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Pituitary-Thyroid Axis
Thyroid function

- Thyroid gland is able to store large amounts of hormone, enough for 2-3 months
- Thyroglobulin is stored – cleaved to T4 and T3 and released
- 93% of active hormone secreted is T4 but almost all converted to T3
- T3 is 4X more potent but present in smaller quantities in blood
Thyroid Hormones

- Combine with plasma proteins with high affinity, released slowly to tissues
- Pass freely across cell membrane to cell nucleus, bind to intracellular proteins
- Long latent period before metabolism increases, 2-3 days, max 10-12 days but much faster for T3
Metabolism

- Effect = generalized increase in functional activity
- Increase in basal metabolic rate +60-100%
- All cells of the body affected
  - ↑ carbohydrate/fat metabolism
  - ↑ HR, arterial pressure, respiration, blood flow and CO
  - ↑ muscle and CNS functions
- Effects on other endocrine glands
Hypothyroidism

- Lethargy
- Weight gain
- Dermatologic changes: alopecia, dry hair coat, hyperpigmentation
- Bradycardia
- Cold intolerance
- Anestrus + others
Hypothyroidism

• Myopathy
  • Weakness
  • Stiffness
  • Myalgia
  • +/- elevated CK
  • EMG abnormalities

• Myxedema coma
  • Electrolyte imbalances (↑CO2, ↓Na, hypoglycemia), acid-base disorders and cerebral energy substrate depletion
Hypothyroidism

- Generalized polyneuropathy
  - LMN Tetraparesis
  - ↓ spinal reflexes
  - Megaesophagus
  - Laryngeal paresis/paralysis

- CN Deficits: Peripheral
  - CN VII, VIII, (V)
  - Unilateral ++
  - Central vestibular rare
Blood work abnormalities

CBC
- Mild non-regenerative anemia

Biochemistry
- ↑ Cholesterol
- ↑ Triglycerides
- ↑ CK
- ↓ Sodium (Na)
Diagnosis

- FT4 ED *****
- cTSH
- +/- TT4
- +/- autoantibodies

- TT4
- +/- FT4 ED
Diagnosis

• Low TT4 ALONE is NOT enough to make a diagnosis!
Hyperthyroidism

- Weight loss, Polyphagia
- PU/PD
- Hypertension
- Muscle weakness
- Encephalopathy
- HCM + failure, cachexia
- Blood work abnormalities
Case #1 – Seizures

- “Dexter” - 8 year old MN Beagle x Basset
- 2 weeks ago at groomer, found foaming at mouth
- Presented on emergency for 2-3 generalized seizures
- Blood work rDVM
- Started on levetiracetam and Diazepam CRI
- Transferred to MOVEH for ongoing care
Dexter – Seizures

- PE: 37.3°C, 76 bpm, BCS 4.5/5
- 120-130 mmHg Doppler
- rDVM Blood work
  - RBC: 4.65 x 10^9/L (5.65-8.87)
  - HCT: 27% (37-62)
  - Cholesterol: 8.48 mmol/L (2.84-8.26)
Dexter – Seizures

- Neurological Examination:
  - Mental State: Very sedate and disconnected
  - Cranial Nerves: Absent menace bilaterally, nasal septum markedly decreased bilaterally seems weaker on left side
  - Gait and Posture: Ambulatory with whole body proprioceptive ataxia and paresis, paces constantly once up but requires assistance to stand, paces in large circles to the left
  - Postural Reactions: Inconsistent left side

- Localization: Thalamocortex

- DDx: Vascular accident, neoplasia, encephalitis, cyst, degenerative, toxic, less likely genetic epilepsy
Dexter – Seizures

- Three View Thoracic Radiographs: Suspect neurogenic edema
Dexter – Seizures

• Three View Thoracic Radiographs: Suspect neurogenic edema

• Thyroid profile:
  • T4: 9.3 nmol/L (ref; 13.0 - 53.0)
  • Free T4: <3.86 pmol/L (ref; 7.7 - 47.6)
  • Canine TSH: 5.93 ng/mL (ref; 0 - 0.60)
Dexter – Seizures

- Diagnosis: Hypothyroidism + other CNS?
- Rx Levothyroxine 0.7mg PO BID
- Rx Levetiracetam 750mg PO BID
- Follow up 1 month, MRI if seizures continue
Dexter – Seizures

• Follow up:
  • Seizure free until March 17th – 2 generalized seizures and 4 focal seizures
  • Anemia and biochemical abnormalities resolved
  • Thyroid well controlled, clinically doing well
  • Switched Levetiracetam to Zonisamide June 2016 (IM consult)
  • Lost to neurology follow up…….
Case #2 – Spinal Cord

- “Piper” - 9 year old FS Samoyed
- Slowing down over past year
- Hind end giving out occasionally over 6 months
- Currently taking Metacam
- Acute onset hind limb paresis worse on left
Piper – Spinal Cord

- PE: 37.8°C, 90 bpm, dry brittle hair coat that is thinning, dandruff dorsally, BCS 5/5
- Routine Blood work:
  - RBC: 3.34 x 10^12/L (5.65-8.87)
  - HCT: 21% (37.3-61.7)
  - Cholesterol: >13.42 mmol/L (2.84-8.26)
  - PCV/TP: 25/9.0 Before MRI
Piper – Spinal Cord

• Neurological Examination:
  • Cranial Nerves: Incomplete PLR bilaterally (iris atrophy)
  • Gait and Posture: Ambulatory with marked hind limb paresis, moderate proprioceptive ataxia, excellent movement in right hind and minimal movement in left hind, left hind is extended and held behind and crossed under the body
  • Postural Reactions: Absent left hind
  • Spinal Reflexes: Weaker withdrawal left hind, increased tone
  • Neck/Back Pain: None elicited even on moderate palpation

• Localization: T3-L3 myelopathy
• DDx: FCEM or other vascular accident, myelitis, neoplasia, IVDD
MRI of the Thoracolumbar Spine:

• The L7-S1 disc bulges dorsally however there is no compression of the cauda equina. There is no other disc protrusion or extrusion along the spinal cord imaged. The spinal cord parenchyma appears normal on all sequences. No bony lesions are noted on STIR sequences.

• Conclusion: Mild L7-S1 intervertebral disc protrusion without associated compression of the cauda equina
Piper – Spinal Cord

• Thyroid Profile
  • FT4 ED: <2.6 pmol/L (9-47.4)
  • T4: 8.4 nmol/L (13-53)
  • T3: <0.62 nmol/mL (0.9-2.1)
  • TSH: 1.43 ng/mL (0-0.6)

• Diagnosis: Hypothyroidism
• FCEM or ischemic infarct due to hypercholesterolemia
Piper – Spinal Cord

- Rx Levothyroxine 0.6mg PO BID
- 1 week recheck; walking but remains paretic needs assistance to get up (obese), anemia improving PCV 27%
- Within 1 month has mild deficits only, doing well, PCV 35%
Case #3 – Vestibular

- “Cookie” – 13 year old FS Pomeranian
- Acute onset trouble walking
- Vomited
- PE: 38.3C, HR 132, 156mmHg
Cookie – Vestibular

- Neurology Examination:
  - Mental State: Bright and alert
  - Cranial Nerves: Mild right head tilt (initial rotatory nystagmus)
  - Gait and Posture: Ambulatory with vestibular ataxia, staggers to the right
  - Postural reactions and spinal reflexes adequate

- Localization: Right peripheral vestibular disease
- DDx: Idiopathic, hypothyroidism, otitis, toxic, neoplasia, encephalitis
Cookie- Vestibular

- CBC and Biochemical profile all within reference limits
- Thyroid profile:
  - Free T4: 4.8 pmol/L (7.7-47.6)
  - Canine TSH: 1.11 ng/mL (0-0.6)
• **Diagnosis:** Hypothyroidism

• **Rx:** Levothyroxine 0.1mg PO BID

• Head tilt and ataxia improved the following day after supplementation and discharged home, lost to follow up
Case #4 - Seizures

• “Chloe” - 13 year old FS DSH
• Several day history of episodes of falling over, loss of balance, lethargy and dazed
• Progressed to several episodes/day
• Normal in between episodes
• Vomited the day before presentation
Chloe – Seizures

• PE: 38.9C, 200 bpm, heart murmur III/VI, BCS 8/9
• Blood pressure ?
• Neurological Examination
  • Mental State: Alert but calm, does seem slightly disconnected but responds to stimuli
  • Cranial Nerves: Menace is present initially but fades after repeated testing on right
  • No abnormalities of gait, posture, postural reactions, spinal reflexes, no pain
Chloe - Seizures

Diagnosis: Suspected seizures

- Extracranial causes…..
- Intracranial…..
Chloe - Seizures

Diagnosis: Suspected seizures
  • Extracranial causes…..
  • Intracranial…..

• Routine blood work:
  • ALP: 62 U/L (ref; 12-59)
  • T4: 145.5 nmol/L (ref; 10-60)
Chloe – Seizures

• Diagnosis: Hyperthyroidism

• Rx Methimazole 2.5mg PO BID

• Follow up: rDVM reports no episodes since T4 back to normal range
Case #5 - Vestibular

- “Socks” - 11.5 year FS DSH
- Indoor/outdoor
- Didn’t come in one night, when found was very wobbly, ‘drunken’
- Decreased appetite
Socks – Vestibular

• PE: 38C, 190, no murmur, BCS 3/5
• 150-155mmHg Doppler BP
• Neurological Examination:
  • Mental state: Bright and alert, responds well, investigates room
  • Cranial Nerves: No head tilt, wide head excursions in both directions, pathological resting nystagmus that changes but is mainly fast phase to the left
  • Gait and Posture: Vestibular ataxia, ambulatory, falls to the left mainly
  • Postural reactions: Appear adequate, leans hard to left when testing
Bilateral Vestibular
Socks – Vestibular

Diagnosis: Bilateral Vestibular

• Extracranial causes…..

• Intracranial…..
Socks – Vestibular

Diagnosis: Bilateral Vestibular

• Extracranial causes…..
• Intracranial…..

• Routine Blood work:
  • Urea: 5.2 mmol/L (5.7-13.2)
  • Creatinine: 66 mmol/L (80-221)
  • ALP: 69 U/L (12-59)
  • TT4: 144.5 nmol/L (10-60)
Socks – Vestibular

• Diagnosis: Hyperthyroidism

• Rx Methimazole 2.5mg PO BID

• Follow up: Initially responded very well, ataxia resolved, back to normal within 1 week
Dogs can’t operate an MRI Machine

But... Catscan