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The collapsed DKA, cushingoid patient: and other confusing endocrine comorbidities.

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IDEXX

Financial Disclosure

Patty Lathan

I have financial interest, arrangement or affiliation with:

Idexx, Boehringer Ingelheim, Scout Bio:

Consultant, honoraria

Merck Animal Health, Dechra Pharmaceuticals: Honoraria

Bill Saxon Full-time IDEXX Employee







You're on clinics and in walks...

Picture the most flat-out dog you've seen recently...





Everyone's favorite combo:

- Acute (or acute on chronic) pancreatitis
- Diabetic ketoacidosis
- Potbellied Dachshund... Cushing's syndrome, too?

Where would you start?



The plan:



- Forget about Cushing's syndrome for now (unless on tx)
- Basic principles of emergency stabilization
 - LRS good initial fluid choice (has buffer and calcium)
 - QUATs: PCV/TS, BG, electrolytes, lactate, venous blood gases
 - CBC, biochemistries, UA (save samples of additional testing)
 - Resting cortisol if on trilostane
- Confirm pancreatitis within minutes
- Brace yourself/staff for DKA treatment



In clinic diagnosis of pancreatitis

• SNAP cPL

- Screening test: negative result rules OUT pancreatitis
- Positive result *could* be pancreatitis must confirm.

Catalyst[®] pancreatic lipase

- Excellent correlation with Spec cPL and cPLI (and Spec fPL, fPLI)
- Undetectable in dogs with EPI (i.e., specific for *pancreatic* lipase)





Simultaneous treatment for pancreatitis and DKA

- LRS: restore volume, hydration, keep up with ongoing losses, provide maintenance (avoid volume overload)
- Analgesia in *all*: buprenorphine, methadone, fentanyl...
- Maropitant 1 mg/kg SC q24h
- Regular insulin
- Other insulins, e.g., Lispro





Do I have to use regular insulin CRI for DKA

Not necessarily...



Insulin protocols for DKA in dogs

- Regular insulin CRI
 - Add 1-2 U/kg to 240 ml saline
 - BG >400 = 20 ml/h, 0% dextrose
 - BG 250-400 = 10 ml/h, 0% dextrose
 - BG 150-250 = 5 ml/h, 2.5% dextrose
 - BG 80-150 = 0 ml/h, 5.0% dextrose
 - BG <80 = 0 ml/h, 5.0% dextrose, bolus 1 mg/kg 50% dextrose
- Regular insulin intermittent IM injection
 - 0.25 U/kg q 1-2 h
- Lispro insulin? Longer acting insulins (e.g., glargine)?



Additional treatment:

- Enteral nutrition within 48 h of onset of signs of pancreatitis
 - Royal Canin GI Low Fat liquid diet
- Panoquel[®] 0.4 mg/kg IV SID x 3 d, over 15-60 sec
- Monitor <u>potassium</u> and phosphorus, add to fluids prn
 - Monitor PCV/TS
- Bicarb rarely necessary



Crisis over. I still think this dog has Cushing's syndrome. How can I prove it?

This is tricky but we have some tips...

(but first tip is...ABSOLUTELY NOT NOW!!!)



Suspect HAC in a Diabetic







Tip #1: No need to rush. Cushing's testing can and should wait.





Diagnosing Cushing's in known diabetic

- Cushing's most common cause of insulin resistance in dogs
- Suspect when
 - Lack of response to or short or variable duration of insulin
 - PU/PD (USG <1.020) despite decent glucose regulation
 - Hypertriglyceridemia
 - Panting, derm changes, pot belly, hepatomegaly...





Testing for Cushing's in known diabetic

- Wait ≈2-4 wk after start of DM treatment
 - False positives if screen for Cushing's at time of DM dx (stress)
- When weight loss stops (i.e., DM control adequate'ish)
- LDDST if dog stable
- ACTH stim more specific fewer false positives
 - Consider positive with post-ACTH cortisol >?



How much do I lower insulin dose when I start trilostane?



You don't.



Treating newly-diagnosed HAC in a diabetic

- Trilostane, 1-1.5 mg/kg PO BID WITH FOOD
 - No insulin dose decrease needed, usually
- Monitor with ACTH stimulation testing or pre-pill cortisol (if you have experience here)
 - 2 weeks after starting trilostane
 - 1 month later
 - 3 months later
- Focus on control of HAC before fine-tuning insulin
 - CLINICAL SIGNS/CLINICAL CONTROL
 - FreeStyle Libre may allow more rapid insulin dose adjustments



Flipping the script.



You're treating a dog for Cushing's syndrome. Something's not right.

Could it also be a diabetic?









Suspect DM in a known cushingoid when:

PU/PD persists despite cortisol suggesting HAC controlled

- Weight loss
- Blood glucose trending up or mildly increased
- Fructosamine increased
- Check UA in dogs with HAC when signs don't fit



NEXT UP...SUNNY (via email...)

I was hoping you possibly had time to discuss a case. Sunny is a 13 yr old neutered dachshund referred to LSU IM for elevated liver enzymes. After his visit with LSU, we performed LDDST and confirmed Cushings. Initially started Vetoryl at 1 mg/kg BID. Resting cortisol (pre-trilostane) 2 weeks later was 2.7. Clinical signs are not controlled (PU/PD, lethargic at home). I then increased Vetoryl to 2 mg/kg in the morning and 1 mg/kg in the evening. Clinical signs not improving and now owner is reporting urinary incontinence. Resting Cortisol yesterday is 5.0. Other considerations, he has a 4 lb weight loss over the last couple months, currently on Vetmedin and overall just looks terrible.

Am I ok to increase to 2mg/kg BID. Should I increase it? Should I culture the urine?







I suspect that you have room to increase with the resting cortisol of 5. But geez, that weight loss is definitely not typical of Cushing's.

Urine culture is reasonable, although checking a chem may be helpful. It's possible he decided to develop DM, as well (would pick that up on UA). Another thought is making sure he doesn't have a macroadenoma causing decreased appetite and lethargy. I assume his appetite hasn't picked up recently? Has it gotten worse?



Update on Sunny...



Good morning. Wanted to let you know Sunny's blood glucose was 612 yesterday with 1+ glucosuria, 1+ ketonuria. No evidence of UTI. ALP has decreased from 9000 to 2600. Also the PrecisionPSL is elevated at 205 (normal is 24-140).



Sent: Friday, January 24, 2025 5:00:01 PM To: Patty Lathan <plathan@lsu.edu>; Robyn N Jolly <rjolly@lsu.edu> Subject: Re: Sunny Welborn

Happy Friday! Hope y'all enjoyed the snow! Wanted to give you an update on Sunny Welborn. I started him on Degludec 0.6u/kg SID (current weight is 11 lbs, so 3 units SID). A few days later when he came in for his Freestyle Libre application, the owner stated that he seems better at home having more energy and eating his full meal. Libre reading was at or above 500 approximately 10 days after starting insulin therefore I increased to 4 units SID. There were a couple readings in the 470 -490 range but the vast majority was 500. It's been 4 days at 4 units SID and readings are still high (majority over 500 but a few readings at 392, 438, 449...).

Should I increase again next week to 5 units SID? What's the max dose of Degludec? Not much info on VIN or Plumbs for me to reference. At what point do you suspect insulin resistance? Do you ever use this BID?



Another dog that was started on degludec over the weekend...







Diabetes mellitus causes weight loss.

Cushing's syndrome does not.



Treatment: DM in Known cushingoid

• Vetsulin[®], NPH BID

- Err towards high end of starting range
- Basal insulin may help decrease glycemic variability
 - Degludec (0.5 U/kg SID to start) or glargine U-300
- Split trilostane to BID dosing if currently SID
 - Same DAILY dose
 - Example: 60 mg SID = 30 mg BID
- Monitor as usual
 - CLINICAL SIGNS, weight, glucose monitoring
 - Cortisol/stims for HAC
- Try not to micromanage DM—focus on clinical signs!



DKA in Known cushingoid

- Acute anorexia, vomiting, dehydration, collapse...
- Check cortisol (+ chem, ideally) first to rule out adrenal crisis
- UA, chem, CBC, pancreatic-specific lipase
- Check for ketones
 - Urine ASAP even few drops for dipstick
 - If no urine use serum from HCT tube on ketone pad of urine dipstick
 - Or check BHB with a ketone meter (Precision Xtra)





Test interpretation practice!



Is an insulinoma causing the hypoglycemia?

- Ruled out other causes?
- Blood glucose <60 mg/dL?
- Submit insulin glucose panel (ratio not helpful)
- If BG on panel >60 mg/dL cannot interpret
- If BG <60 mg/dL...





LOW.

Therefore, if glucose is within reference range or high = insulinoma.



2024 Jan 30 Jan 2024	23		
Result Details 🗸			
Chemistry	1/23/24 6:00 AM		
🛤 🔨 Glucose	a 37	63 - 114 mg/dL	
n 🔨 IDEXX SDMA	b 10	0 - 14 µg/dL	
🛤 🖴 Creatinine	0.7	0.5 - 1.5 mg/dL	
n 🖴 BUN	12	9 - 31 mg/dL	
BUN: Creatinine Ratio	17.1		
🛤 🖴 Total Protein	6.7	5.5 - 7.5 g/dL	
🛤 🖴 Albumin	3.5	2.7 - 3.9 g/dL	
🛤 🖴 Globulin	3.2	2.4 - 4.0 g/dL	
Albumin: Globulin Ratio	1.1	0.7 - 1.5	
ALT	59	18 - 121 U/L	VITIOUSODOUD
n 🖴 ALP	125	5 - 160 U/L	WVC ANNUAL CONFE

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2024 Jan 30 Jan 2	23			
Result Details 🗸			• •	\triangleright
ᄅ Diagnostic result prin	nted 3/18/2024 10:25 PM	Details >		
P Endocrinology	1/30/24 1:35 AM			
Siucose	36.0 63.0 - 114.0 mg/dL			
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Result Details 🗸			
🖶 Diagnostic result pri	nted 3/18/2024 10:25 PM	Details >	
Endocrinology	1/30/24 1:35 AM		
🔨 Glucose	36.0 63.0 - 114.0 mg/dL		
🔨 Insulin	>200.0 5.2 - 41.5 ulU/mL		
 Insulin: Glucose Ratio 	725 14 - 43 RATIO		



Is primary hyperparathyroidism causing the hypercalcemia?

- Ruled out other causes?
- IONIZED calcium increased?
- Submit iCa PTH panel (+/- PTHrp)
 - DIFFERENT TUBES!!!! CALL LAB!!!
- If iCa normal cannot interpret
- If iCa increased...





Ask 'what should PTH be when iCa increased?

LOW.

Therefore, if PTH is normal or high = primary hyperPTH.













Thank you!



Thank you!





Thank you!



