Myxomatous Mitral Valve Degeneration MMVD

Definition: Degenerative valvular disease leading to valve incompetency, left atrial enlargement, volume overload and CHF

Pathology: Expansion of spongiosa valve layer with glycosaminoglycans and proteoglycans. The valve leaflets thicken and roll at the edges. This may affect the chordae tendinea, the valve may prolapse and leak and the chordae may rupture. The tricuspid and aortic valve can also be impacted

Pathophysiology: Mitral valve regurgitation may lead to left atrial enlargement, volume overload, left ventricular enlargement, elevated LA pressure, pulmonary venous distention, left-sided congestive heart failure, and occasionally there is pulmonary venous hypertension

Compensation: MMVD reduces flow to the kidneys which activates RAAS. RAAS increases volume and generates volume overload and eccentric hypertrophy. This leads to an increased stretch, increased contraction and systolic function is enhanced to compensate for regurgitant volume and maintaining cardiac output

Physical Exam Findings: Left apical systolic regurgitant murmur, high velocity blood flow during systole, pressure gradient LV to LA generates plateau character murmur. The severity corresponds to the intensity. You may hear a systolic click due to the prolapsed MV, a high pitch sound during mid-systole, and the patient may have a cough or respiratory distress if in CHF

Electrocardiogram: Typically sinus rhythm, possible APCs, VPCs, A-fi along with patterns of chamber enlargement (P mitrale and LV enlargement causing tall R waves and a wide QRS)

Diagnosis: Signalment, echo, thoracic rads *make sure signs are not referable to another condition, arterial blood pressure management is a crucial part of therapy

Chest Rads: Symptomatic dogs may have rads consistent with CHF

-interstitial to alveolar infiltrates consistent with pulmonary edema, LA enlargement, Pulmonary venous distention

*Most reliable indication of disease severity is LA size assessed with an echo and radiographs (VLAS, VHS)

MMVD Classification Scheme

- Stage A: no evidence of disease but **at risk** (CKCS, breed predilection)
- Stage B – Structural heart disease (**thickening, leakage**) but **no clinical signs** of CHF
    - B1: **no** chamber enlargement or **mild** left atrial enlargement only
    - B2: **Moderate/severe** LA and LV **chamber enlargement**
- Stage C: Past or current episode of **CHF**

- Stage D: End stage disease **refractory** to traditional management of CHF

Treatment

Mainstay is a diuretic (furosemide, torsemide) and Pimobendan (inodilator)

- ACE-Inhibitors (enalapril, benazepril)
- Spironolactone
- Low salt diet
- Amlodipine if hypertensive
- Diltiazem +/- digoxin if there is atrial fibrillation
- Entresto (sacubitril/valsartan)
- Sildenafil if clinically significant pulmonary hypertension

Prognosis

- Prior to CHF – no reliable estimate
- 15 months from stage B2 to CHf with pimobendan
- ~3yrs MST from stage B2 with pimobendane; 2.5 years without
- Pimobendan and ace-inhibition together unknown prognosis
- After CHF onset ~12 months

Dilated Cardiomyopathy

Definition: Heart muscle disease characterized by systolic dysfunction and ventricular dilation (eccentric hypertrophy). This can affect primarily left or both ventricles

Pathology: Severe dilation of the LV, LA and possibly RV. The LV free wall is most severely affected. Myofiber degeneration and necrosis occurs and this all may be in the absence of inflammation.

Etiology: Familial/genetic and nutritional are the most common but other causes such as viral, metabolic, and immune mediated are also possible.

Familial/Genetic PDK-4 and Titin genes (autosomal dominant and incomplete penetrance)

Nutritional: Taurine deficiency, high levels of peas, lentils, other legume seeds or potatoes in pet foods, link is unknown

Pathogenesis: Reduced CO > Neurohormonal activation > Na^+ H_20 retention, vasoconstriction, cardiac remodeling > further reduction in heart function > Increased preload > Progression of disease, CHF

Disease Progression: It may be difficult to ID the asymptomatic phase of this disease, many tests can help but none are perfect. Echo parameters, Holter monitoring, NT-proBNP, C-TNI, PDK4 genetic testing can all help. The prediction of time to CHF is uncertain

Outcomes: Exercise intolerance, Syncope, CHF, Sudden Death

Physical exam findings

- Left apical systolic murmur
- Pulse deficits
- Weak pulses
- Variable pulses
- Tachycardia, Tachypnea, Soft Crackles
- Ascites

ECG findings

- Typically, sinus rhythm or sinus tachycardia
- Frequently L-sided VPCs
- May see atrial fibrillation
- Patterns of LVH (wide QRS complexes, left axis deviation)
- Wide P waves are possible with left atrial enlargement

Radiographic Findings

- Global cardiomegaly
- LV enlargement
- LA enlargement
- +/- CHF
    - Pulmonary edema
    - Pleural effusion
    - Ascites

Echocardiogram

- Gold Standard!
- Reduced fractional shortening (systolic function)
- Increased heart size (LA and LV dilation with LV wall thinning)
- Mitral regurgitation due to annular stretch

- Mitral valve thickness should still appear normal

Nutrition and DCM

Most likely linked to a taurine deficiency (measure whole blood and plasma taurine levels)

Other nutritionally mediated causes may include boutique, exotic ingredients, and grain free diets. Any diet with legumes/potatoes as a major ingredient. Cause and effect relationship has not yet determined

Treatment of suspect nutritionally mediated DCM include testing taurine levels and supplementation +/- l-carnitine in addition to swapping to a food that avoids suspect ingredients and has rigorous quality control and diet trial testing

Treatment of Occult DCM

- Pimobendan! *especially for Dobermans
- Cardioprotective therapy may have some benefit
  - ACE-inhibition if volume overload is observed
  - Salt restriction, fish oils, exercise restriction
  - Beta blockers (benefit in humans, but less evidence in dogs)

Treatment of DCM and CHF

- Diuretics (furosemide) – address increased preload
- Pimobendan – improve systolic function
- ACE-inhibitors – reduce preload and afterload as well as provide cardioprotective benefits and slow remodeling
- Spironolactone – to provide cardioprotective benefits and slow remodeling
- Diltiazem +/- digoxin if atrial fibrillation is observed
- Anti-arrhythmic drugs (sotalol, mexiletine) if ventricular ectopy is observed

Prognosis

Occult DCM – Difficult to assess, likely months to years

DCM in CHF – 9-12 months with currently recommended therapy (including pimobendane)

Canine ARVC (Arrhythmogenic Right Ventricular Cardiomyopathy)

Description: Heart muscle disease with characteristic right ventricular tachyarrhythmias and fibro-fatty infiltration of the RV. It may spread to involve the left heart as it progresses and lead to syncope and sudden death. This disease rarely leads to heart failure.

Pathology: Fibro-fatty infiltration of the RV +/- LV. The adipocytes are replaced by fibrosis and the RV free wall thins. There is also myocytolysis.

Diagnosis: Holter monitoring is the only antemortem gold standard for the diagnosis of ARVC

<100 VPCs are normal for boxers

100-300 VPCs are Equivocal

>300 VPCs of RV origin in 24 hrs or complex RV ectopy

Diagnostic confidence can be gained by genetic mutation testing and breed, breed predisposition and response to therapy

Types of ARVC

Type I: Asymptomatic, hut Holter results meet the requirements

Type II: Collapse/Syncope due to more severe arrhythmias but normal echo phenotype

Type III: LV systolic dysfunction on echo (rare, DCM-like)

Prevalence of ARVC

- Familial disease in Boxers (GENETIC!)
- Rarely described in other breeds (English Bulldogs, Pitties, Labs)
- Cats can also get this!

Etiology: Genetic disease of the desmosomes (cardiac cell adhesion). Autosomal dominant pattern of inheritance with incomplete penetrance in the boxer. No other breeds are found to have this same mutation so their etiologies remain unclear

Mutation test available for boxers: Buccal swab, EDTA blood but it is key to remember that this disease has incomplete penetrance and mutation free does not equate to disease free and vice versa

Physical Exam Findings

- Normally these dogs have a normal physical exam
- Typically, they have normal thoracic rads without any structural changes
- Usually accompanied by a normal echocardiogram
- Disease severity is best characterized by Holter monitoring
- Occult disease is identified by Holter monitor and genetic testing

Treatment

- If symptomatic (syncopal)
- If CHF – treat as DCM
- If asymptomatic but ventricular arrhythmias meet the criteria of malignancy discussed
- Sotalol 2-3 mg/kg PO q12h +/- Mexiletine 5-8 mg/kg PO q8hrs
- Fish oils?

Prognosis

- Generally good
- Bad if + for homozygous for striatin mutation
- Bad if structural disease is observed (type III)
- Sudden death is frequent, unclear if therapy helps prevent this
- Therapy is aimed to reduce the risk of sudden death (unproven) and control clinical signs (syncope)