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BACTERIAL ENDOCARDITIS

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OBJECTIVES

1. Be able to list common sources of infective organisms.
2. Be able to list the predisposing factors for development of endocarditis.
3. Outline the proposed pathogenesis of subacute and acute Bacterial Endocarditis.
4. Be able to list and understand the pathogenesis of the cardiac and extracardiac manifestations of Bacterial Endocarditis.
5. Know which valves are commonly affected and descriptions of their associated murmurs.
6. Be able to list two etiologic agents commonly seen in the different domestic species.
7. Outline a diagnostic protocol and a treatment protocol for an animal suspected to have bacterial endocarditis.

ENDOCARDITIS

Bacterial endocarditis is infection of the endocardium and/or valves of the heart. The reported incidence ranges from 0.06-6.6% in dogs at necropsy, however the actual incidence is likely much less than 2% of all cardiac diseases in dogs. As a proportion of overall cardiac diseases in horses and cattle, endocarditis is higher, maybe 5-15% of all cardiac diseases in these species. Valvular stenosis or insufficiency may result from endocarditis, although insufficiency is more common. Endocarditis is also well described in horses, cattle, swine, cats, primates and a variety of other species.

Etiology and Pathogenesis

1. Microbiologic agents:

a. Dog - *Staphylococcus aureus, E. coli, B-streptococcus, Bartonella sp., Corynebacterium* sp., *Klebsiella* sp, *Pseudomonas aeruginosa*, *Erysipelothrix rhusiopathiae*, *Aerobacter aerogenesis* and other enteric gram negative organisms, and anaerobes.
b. Cat - Staphylococcus, streptococcus, Bartonella sp., and enteric gram negatives.
c. Horse - Streptococcus equi, Strep zooepidemicus, Actinobacillus equi, Meningococcus sp.
d. Cattle - alpha-hemolytic streptococci, Corynebacterium pyogenes, Blackleg, Mycoplasma mycoides.
e. Pigs - Erysipelothrix insidiosa, Streptococcus sp, gram negatives.
f. Lambs - Streptococcus sp and E. coli.
g. Llama/alpaca - Listeria

2. **Source of infection** - The source is often difficult to identify, however organisms may originate from normal body flora, localized extracardiac infection or generalized sepsis.

    a. Extracardiac infections - skin and subcutis, bone, urinary tract, prostate (especially in dogs), mouth, liver, intestine, colon, traumatic reticulitis, metritis and mastitis, strangles infection in foals. IV catheters in all species, especially non-sterile injections in cattle.
    b. Dental extractions - Are frequently implicated (and rarely proved) to be the source of infection; caused by transient bacteremia of normal flora.

3. **Valves affected and predispositions** - Occurrence is higher in large breed male dogs > 4½ years of age.

    a. Dog and cat - the mitral and/or aortic valve is most commonly involved.
    b. Ruminants - the right AV valve is most commonly affected.
    c. Horse - commonly have aortic valve or mitral valve affected, but tricuspid involvement has been reported.
    d. Pig - mitral and aortic

4. **Predisposing factors:**

    a. Immunosuppressive agents - i.e., glucocorticoids and chemotherapeutics
    b. Inappropriate or inadequate antimicrobial therapy, including chronic antibiotic/corticosteroid combinations.
    c. Indwelling IV catheter.
    d. Prior valvular disease - it is difficult to induce BE in dogs with normal valves. Dogs with subaortic stenosis are at increased risk to develop bacterial endocarditis. However, degenerative valvular disease is very common in dogs and has been only weakly associated with BE
    e. Allergic factor - made in reference to equine endocarditis similar to occurrence of human rheumatic heart disease.
    f. Bacteremia resulting from any infectious site.

5. **Pathogenesis**

    a. Subacute Bacterial Endocarditis - mechanism proposed for SBE. It seems likely that these factors are important in the development of BE, although all of these criteria are not necessary to produce BE.
        - Previously damaged cardiac valve or hemodynamic situation in which a jet effect is produced by blood flowing from a zone of high pressure to a zone of low pressure, i.e. abnormal blood flow.
            - Lesions localize on aortic valve, mitral valve chordae tendinae; left atrial endocardium associated with subaortic stenosis, aortic and mitral regurgitation.
            - The lesions tend to form in the area of lower pressure.
        - A sterile platelet-fibrin thrombus - origin is not clear but could be due to abnormal valvular stress or endothelial injury leading to exposure of collagen and resulting in platelet aggregation
        - Bacteremia - as previously mentioned
            - Transient bacteremia or normal flora
            - Extracardiac sites
            - Leads to colonization of the platelet fibrin thrombus
        - A high titer of agglutinating antibody against the infecting organism - this increases the size of the inoculum by clumping bacteria.

b. Acute bacterial endocarditis
    - Might not include previous valvular injury or formation of a platelet-fibrin thrombus due to high virulence of offending organism.
    - Bacteria differ in their ability to adhere to a normal canine valves Enterococci, Streptococci, Pseudomonas aeruginosa have great adhering properties and this may explain the high incidence of infection with these organisms. Staph and Strep have proteases that may produce endothelial injury to aid valve colonization.
    - Acute B.E. is more likely to occur 2o to extra cardiac infection and require a smaller inoculum vs. transient bacteremia of normal flora.

Pathophysiology of Cardiac Manifestations

1. **Valve destruction and dysfunction**
    a. Valvular insufficiency - aortic and mitral leads to volume overload of left heart (left ventricular eccentric hypertrophy with left atrial enlargement) and associated signs of left heart failure (pulmonary edema) and associated murmurs. Tricuspid and pulmonic causes right heart failure (venous congestion, jugular vein distention/pulsation, ascites, etc).
        - Mitral - holosystolic murmur - common in dog and cat.
        - Aortic - diastolic decrescendo murmur, common in horse, dog, and cat; in the dog and cat this murmur is highly suggestive of BE when present. Aortic insufficiency is also associated with a wide pulse pressure or bounding pulse.
        - Tricuspid - Systolic murmur, typical in cattle.
    b. Valvular stenosis - if lesion is large enough to cause functional obstruction. Stenosis of aortic valve causes systolic crescendo, decrescendo systolic murmur ("to and fro" murmur, common in dog and horse); stenosis of mitral valve causes diastolic rumbling murmur (less commonly ausculted).
    c. Abscess formation around the valve ring is possible – AV block.

2. **Extension of the infection to the myocardium, conduction system, coronary arteries, or pericardium**
    a. Myocarditis - may result from bacterial embolization or from small thrombi from the vegetative lesion that leads to multiple myocardial abscesses or infarcts. Myocarditis is associated with cardiac arrhythmias (APCs or VPCs).
    b. Aortic valve ring abscess with infection of the septum, may lead to heart block or VSD.
    c. Abscess and rupture of papillary muscle or ventricular septum (rare).
    d. Pericarditis from extension of the myocardial infection (infrequent).
    e. Can see elevation of serum CK and AST with myocarditis.
    f. Portions of the vegetation can dislodge from the valve (thrombi), enter the coronary circulation and lead to coronary arterial obstruction with myocardial infarction. Ischemia may manifest as S-T segment abnormalities (typically ST segment depression).

Pathophysiology of Extracardiac Manifestations - these may be the predominant clinical signs, therefore one must keep a high index of suspicion for BE.

1. **Bacteremia and fever**
    a. BE may present simply as "fever of unknown origin."
    b. BE causes recurrent episodes of bacteremia, triggering release of endogenous pyrogen and leading to fever. Recurrent bacteremia also causes secondary infection of other tissues (see below)
2. **Metastatic infection and arterial embolization/infarction**
    a. Can lead to life threatening septicemia.

b. Intermittent shedding of bacteria or septic thrombi from infected valves leads to metastatic infection in many tissues. Tissue dysfunction may also result from infarction by septic or bland (sterile) emboli. Tissues commonly affected (besides the heart) include:
    - Kidney - can lead to pyelonephritis, renal infarcts, or renal failure
    - Spleen - splenic infarcts or abscesses common, but difficult to recognize clinically.
    - Joints - septic embolization of joints
    - Brain and meninges - cerebral infarcts or meningitis.
    - Large thrombi may also occlude larger vessels such as iliac arteries, causing posterior paresis.
    - Disseminated abscessation of virtually any tissue is possible.

c. Left-sided B.E. has greater mortality than right-sided B.E., right sided BE is more likely to result in pneumonia

3. Immunologic phenomena

a. Humans may develop positive titers for:
    - ANA – antinuclear antibody test
    - Rheumatoid factor
    - Coombs test

b. Veterinary literature has documented similar serologic findings, suggesting that autoimmune phenomena or immune complex disease can result from BE. These findings likely result from high levels of circulating antibody against the infectious agent or secondary to damage to normal tissues. Although these findings probably represent abnormal immunologic activity, steroids should never be used in the therapy of this disease. These tests, if anything, add confusion to establishing the diagnosis of BE and again, signal the multisystemic nature of this disease.

Clinical Presentation

Animals exhibiting bacterial endocarditis may present with a variety of clinical signs. Recurrent fever, malaise, lethargy, anorexia or poor appetite, shaking, poor performance or exercise intolerance, unthriftiness, and poor milk production are non-specific signs that may be noted in any species. Cardiac manifestations are also common, especially the presence of a murmur (especially a new murmur). In more advanced cases, arrhythmias, syncope, congestive heart failure or coughing are noted. Extra cardiac manifestations will include shifting leg lameness, swollen joints, kidney disease, and abdominal pain due to splenic or intestinal infarction. Petechia or ecchymosis due to vasculitis or embolism are possible, especially notable in ocular vessels. Major peripheral arterial occlusion can result in weakness, paresis, absent pulse, coolness, ischemic contracture, ischemic neuropathy and pain in the affected limb. Common clinical signs in the dog and the relative frequencies from one study are noted below.

- Cardiac murmur (74%) - Systolic (74%), Diastolic (13%)
- Fever (70% to 83%)
- Sinus tachycardia (41%)
- Vomiting (35%)
- Lameness (34%) - Shifting (18%)
- Ventricular arrhythmias (27%)
- Heart failure (16%)
- Renal Failure (11%)
- Sudden death (8%)
- Myopathy (4%)

Clinical Pathology

1. Leukocytosis is common in dogs (82%). Neutrophilia with or without a left shift may be present, a monocytosis is common.

2. Anemia of chronic infection - normocytic, normochromic; usually non-regenerative.

3. Elevation of serum alkaline phosphatase activity has been reported in 48% or affected dogs and was more common in dogs with gram negative infections. Endotoxin is reported to affect hepatic excretory mechanisms.

4. Hypoalbuminemia or hypoproteinemia has been reported in up to 51% of dogs with BE. This may result from sepsis, reduced hepatic function with reduced synthesis, immune mediated vasculitis, embolic vasculitis, or endotoxin induced increases in vascular permeability causing transcapillary leak.

5. Hypoglycemia is also fairly commonly reported (24%) in dogs, however is uncommon in the absence of either hypoalbuminemia or elevated SAP.

6. Azotemia due to prerenal or renal causes (10%)

7. Pyuria, hematuria and proteinuria due to renal infarction, metastatic pyelonephritis, glomerulonephritis, or underlying UTI or prostatitis.

8. Elevation of serum CK and AST may be seen with myositis or myocarditis

Diagnosis

1. *EKG*
   a. Conduction disturbance - AV block, ventricular arrhythmias
   b. Voltage changes = cardiac enlargement
   c. Deviation of ST segment

2. *Radiography*
   a. Cardiac - variable and may be normal. Changes compatible with valvular insufficiency such as left atrial or ventricular enlargement.
   b. Pulmonary - May be normal or CHF or hematogenous pneumonia (most common with tricuspid or pulmonic valve endocarditis).

3. *Clin Path* - See above; consider joint fluid changes, CSF changes.

4. *Echocardiography* - thickening, "shaggy", hyperechoic valve echoes, abnormal valve motion and flutter. May not always be able to visualize small vegetations. A presumptive diagnosis can often be established on the basis of echocardiographic findings, pending the results of blood cultures.

5. *Positive cultures* - Blood cultures are the preferred method of diagnosis. These must be multiple cultures (aerobic and anaerobic) taken aseptically. Best results reported during fever spike or just before the fever spike, although 88% positive cultures were obtained when multiple samples were taken. Many people obtain urine cultures at the same time, joint cultures should be obtained if joints are affected.

Treatment

Long term high doses of appropriate antibiotic, preferably based on positive blood culture with known sensitivity. If available, then parenteral (preferably intravenous) high dose broad spectrum antibiotic therapy is indicated. Therapy initiated while pending cultures usually includes either a penicillin or cephalosporin in combination with an aminoglycoside. Treatment for 4-6 weeks is appropriate.

Corticosteroids are contraindicated and reduce survival. Twelve percent survival if given steroids vs. 40% if rapid diagnosis and initiation of appropriate therapy.

Prophylactic antibiotic therapy

Patient's undergoing dental extraction or other procedures associated with bacteremia such as gastrointestinal or urogenital manipulations that also have underlying heart disease have indication for prophylactic antibiotic therapy.

Prognosis for BE is always guarded, the prognosis is worse if CHF or large vegetative lesions are present. The prognosis is also worse for animals with aortic valve endocarditis and aortic insufficiency. The prognosis for animals with gram negative sepsis is worse. If the disease is caught early and there is little damage to the valve then some animals will have a prolonged survival time.

REFERENCES

1. Current Veterinary Therapy XIV, Bonagura JD Twedt DC (eds), Saunders Elsevier 2009 MacDonald KA. Infective endocarditis

2. Textbook of Veterinary Internal Medicine. Ettinger SJ, Feldman EC (eds). Elsevier 2010 Olsen LH, Haggstrom J, Petersen HD. Acquired Valvular Heart Disease.

3. Small Animal Cardiovascular Medicine. Kittleson MD, Keinle RD. Mosby 1998 Kittleson MD. Infective Endocarditis

4. Calvert CA, Greene CE, Hardie, EM. Cardiovascular infections in dogs: Epizootiology, clinical manifestations and prognosis. *JAVMA* 187:612-616, 1985.

5. Sykes JE, Kittleson MD, Chomel BB et al. Clinicopathologic findings and outcome in dogs with infective endocarditis :71 cases. J Am Vet Med Assoc 228:1735, 2006

6. Sykes JE, Kittleson MD, et al. Evaluation of the relationship between causative organisms and clinical characteristics of infective endocarditis in dogs: 71 cases (1992-2005) J Am Vet Med Assoc 228:1723, 2006

7. Maxson AD, Reef VB**.** Bacterial endocarditis in horses: ten cases (1984-1995). Equine Vet J. 1997 29:394-9