Vegetative Endocarditis in Cattle

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Introduction

A case of bovine vegetative endocarditis was described as early as 1841 by Joseph Carlisle V.S. who called for "... a thorough investigation into cardiac diseases... ."[1] In the last 148 years vast progress has been made in cardiac physiology and pathology; however, bovine endocarditis is still commonly misdiagnosed until necropsy if it is diagnosed at all. This misdiagnosis is probably due, in large part, to the similarity of the clinical signs of endocarditis with the clinical signs of other diseases, especially traumatic reticuloperitonitis and pneumonia. Another factor contributing to the misdiagnosis of endocarditis is that primary cardiac disease is rarely among the initial diagnostic rule-outs of bovine diseases. Good figures on morbidity are not available, but one study found the lesions of vegetative endocarditis in cattle carcasses to be approximately 16 times greater than the diagnosis of endocarditis by veterinarians in the same area.[2] In any case, it seems that vegetative endocarditis is as common and as economically important as some of the better known and more often diagnosed diseases of cattle.

Background

The term vegetative endocarditis comes from the typical lesion evident at necropsy. The lesions often have a verrucose surface and range in size from barely visible to several cm in diameter. They are reported to be most common on the right AV valve although all four valves as well as any part of the endocardium may be affected.[3] The lesions are believed to cause clinical disease by interfering directly with heart function[4] as well as by thromboembolism in other body systems.[5,6,7] Bacteria are often present within these lesions and are believed to be the etiologic agents. Early studies found *Streptococcus spp.* to be the most commonly isolated organisms,[2] but more recent studies have isolated *Corynebacterium pyogenes* most commonly.[3,5,7] In either case, *Corynebacterium pyogenes* and *Streptococcus spp.* account for approximately 80% of the positive cultures. It is presently thought that the formation of these vegetative lesions is most commonly preceded by recurring bacteremia due to chronic septic conditions.

The history and clinical signs of vegetative endocarditis vary greatly with the stage of the disease and secondary organ systems involved. The most common reasons for presentation are reported to be recurrent or persistent fever, anorexia, decreased milk production, weight loss and chronic lameness.[2,3,4] Tachycardia, a loud pounding heartbeat, and cardiac murmurs are also common early clinical signs. The murmurs are usually systolic and louder over the right body wall.[2,8] As the disease progresses, signs of congestive heart failure, such as ventral edema, dyspnea, and distension or pulsation of the mammary and jugular veins, become more evident.[3] In general, the clinical signs will increase in intensity if proper therapy is not instituted.

A confirmed diagnosis of vegetative endocarditis is difficult to achieve without necropsy. CBC results usually show a non-regenerative anemia indicative of chronic inflammatory disease and a mild leukocytosis. The serum chemistry abnormalities noted are usually due to the secondary involvement of other organ systems. Electrocardiographic studies have been done but have not found results that are diagnostic of endocarditis.[10,11] Ultrasonic imaging of the vegetative lesions is possible in some cases.[10,12] However, it is not a practical tool in bovine medicine at this time. One of the best diagnostic tools that *is* practical is blood culture. Fortunately, commercial kits containing media and suitable for shipping to bacteriological laboratories are now available. Blood culture, when positive, has the advantage of also allowing antibiotic sensitivities to be performed. It is important to remember that blood culture is not 100% sensitive or 100% specific.

Treatment of vegetative endocarditis usually consists of long term (at least 4-6 weeks) antibiotic therapy. Penicillin has been shown to be effective in some cases.[3] Treatment is seldom successful and the costs of long term treatment should be evaluated with the value of the animal in mind before treatment is initiated.

Case Reports

The following cases are presented in order to illustrate the varied history, clinical signs, test results and progression of bovine vegetative endocarditis.

Case 1

A 2-year-old Brangus bull was presented to the UMC-VTH on 1-29-88. The history was of a recurrent fever (up

to 106.5°F), decreased appetite of approximately one month duration. The owner reported a weight loss of approximately 300 lbs and a lack of activity when compared to the other bulls on the same farm. The bull had been treated with erythromycin, dexamethasone and vitamin B_{12}. Each treatment had given only short term relief. During the admitting examination the rectal temperature was 100.7°F. The heart rate was 64 bpm, and the respiratory rate was 32 resp/min. The bull was slightly depressed, but no other physical abnormalities were evident. A CBC showed a fibrinogen level of 1200 and a plasma protein:fibrinogen ratio of 5.75. Serum chemistry showed a slight decrease in total protein and albumin, and a high serum alkaline phosphatate (592 U/L).

On 1-31-88 the rectal temperature was 106.2°F, the respiration was shallow with a rate of 72 resp/min, and the heart rate was 72 bpm. Blood was collected for culture and treatment with dipirone[a] (15mls SQ) and ampicillin[b] (1mg/lb SQ q24h) was initiated. The temperature had returned to normal by 2-1-88.

Because one of the differential diagnosis was a liver abscess, ultrasound of the liver was performed on 2-1-88 but no abnormalities were noted. CBC's were repeated on 2-1-88 and 2-3-88 with the same results as the original CBC. The original blood culture showed no growth. A culture on blood collected 2-3-89 revealed a *Staphylococcus spp.* that showed no resistance to any of the antibiotics tested. Despite continued therapy with amoxicillin, the temperature continued to range from 101°F to 106°F. The heart rate and respiratory rate remained increased and breathing became more labored. The bull became more and more depressed and was euthanized on 2-5-89.

Necropsy revealed an irregular, friable, yellow-tan mass on the leaflets of the right AV valve (Figure 1) and several consolidated lobules within the right caudal lung lobe.

Case 2

A 4-year-old Holstein cow was presented to the UMC-VTH on 9-29-88. Six months previously the cow had developed gangrenous mastitis in the left rear quarter. Two months prior to admission the cow had become anorexic and progressively weaker. The cow had been treated for reticuloperitonitis and pneumonia. On presentation the cow was emaciated, depressed, standing with a hunched back, and had a rectal temperature of 102°F. The heart rate was 100 with loud pounding heart sounds and a grade V out of VI mid-diastolic murmur loudest on the right side. The lung sounds were increased bilaterally and the respiratory rate was 54 resp/min. Blood was collected for CBC, serum chemistries, and culture. The PCV was 18, the fibrinogen level was 1000 mg/dl, revealed increased liver enzymes and a high globulin value of 8 g/dl. Because of the poor prognosis for recovery, euthanasia was elected.

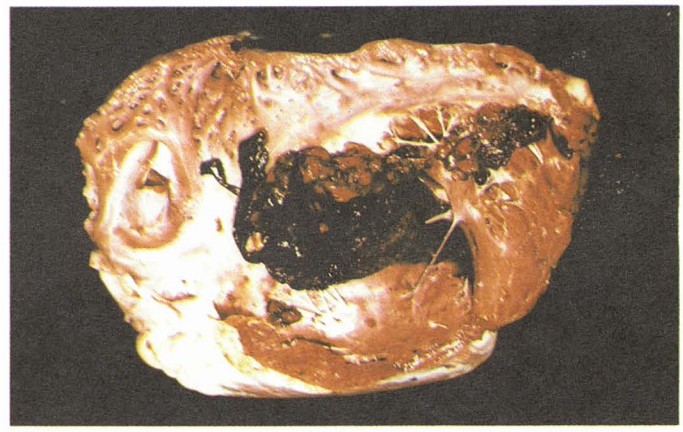

FIGURE 1. Heart of the bull in case 1 at necropsy showing the large vegatative lesion of the right AV valve.

Necropsy revealed multifocal red, roughened areas about 2mm in diameter on the right AV valve, a thrombus adhered to the pulmonic valve, thrombi in the pulmonary arteries, areas of parenchymal necrosis and abscesses in the lungs, and suppurative mastitis with thrombosis of the left mammary vein. Blood culture resulted in growth of *Corynebacterium pyogenes*.

Case 3

A 10-month-old shorthorn heifer was presented to the UMC-VTH on 2-21-89 with a 6 month history of intermittent lameness and unthriftiness that would partially respond to oxytetracycline and sulfas and then relapse. Two and one-half weeks before admission, labored breathing, a nasal discharge, and coughing was noticed. Upon presentation the heifer was alert and responsive but in thin condition. The rectal temperature was 104°F, the heart rate was 80 bpm, and the respiration was shallow with a rate of 50 resp/min. On auscultation there were decreased lung sounds ventrally and increased sounds dorsally. A grade IV out of VI holosystolic heart murmur was present. Blood was collected for a CBC and culture. The CBC showed a fibrinogen level of 900 mg/dl with a plasma protein:fibrinogen ratio of 9.0. Therapy with ceftiofur[c] (50 mg/lb IM q24h) was started.

On 2-22-89 the rectal temperature had decreased to 102°F. Cardiac ultrasound was performed on 2-23-89 and

[a] *Dipyrone[R], TechAmerica, Elwood, Kansas 66024*

[b] *Polyflex[R], Aveco, Fort Dodge, Iowa 50501*

[c] *Naxel[R], Upjohn, Kalamazoo, MI 49001*

revealed left ventricular hypertrophy and an area of increased echogenicity associated with the chordae tendinae of the left ventricle (Figure 2). This area of increased echogenicity was felt to represent a vegetative lesion due to endocarditis. An ECG recorded on 2-28-89 showed sinus tachycardia and a mean electrical axis between 0 and 30°. The culture of the blood drawn on 2-21-89 showed no significant growth. Treatment with ceftiofur was continued during the 8 days of hospitalization. The heifer's rectal temperature remained normal and her heart rate remained elevated between 80 and 120 bpm. Her respiratory rate remained increased (48 - 60 resp/min) but her breathing became progressively less labored after 2-25-89. The heifer was discharged on 2-28-89 with instructions to continue the treatment with ceftiofur for at least 10 more days and to provide a low stress environment.

On 3-28-89 the heifer was readmitted to the UMC-VTH. The owner stated that her condition had deteriorated since the withdrawal of ceftiofur therapy on 3-10-89. Her rectal temperature was 106°F, her heart rate was 120 bpm and her respiratory rate was 60 resp/min. The grade IV of VI heart murmur was still present and a soft cough was noted during the exam. Brisket edema and distension of the jugular veins was evident at this time. The owner elected to discontinue treatment and donated the heifer to the UMC-VTH.

Blood was collected on 3-28-89 for a CBC, serum chemistries, and culture. The CBC showed no abnormalities. There were increases in liver enzymes and a low total protein with a normal albumin level reported on the serum chemistry analysis. The blood culture revealed *Corynebacterium pyogenes*. Culture was also done on blood collected on 3-29-89 and a *Clostridium spp.* was isolated. On 3-29-89 the cow was started on furosemide[a] (2g po q24h) and enrofloxacin[b] (2ml/100lb q24h) by permission of and in conjunction with Mobay Corporation. On 4-1-89 the *Clostridial* growth on the blood culture taken on 3-29-89 was reported and procaine penicillin G[c] (40cc q24h) was added to the therapy. On 4-3-89 treatment with spironolactone[d] (1.0mg/kg po q24h) was added. The rectal temperature of the heifer returned to normal on 3-31-89 but the ventral subcutaneous edema continued to increase and the heifer became progressively more depressed and anorexic. She died early on 4-5-89.

At necropsy there were several liters of amber colored fluid in the pleural cavity and the peritoneal cavity, the lungs were heavy and edematous, and the liver was edematous. The right side of the heart was dilated and the left side of the heart was hypertrophied and dilated. The left AV valve had vegetative lesions and the papillary muscle was necrotic.

Case 4

A 2-1/2 year old Polled Hereford bull was presented to the UMC-VTH on 5-2-89. The bull had a high fever (up to 109°F) of 3 weeks duration and had been anorexic for 2 weeks. The bull had been treated with oxytetracycline, ceftiofur, trimethoprimsulfadiazine[e], and flunixen meglumine[f]. The flunixen meglumine had controlled the fever for 3–4 days but the fever continually returned. At the time of presentation the temperature was 102.6°F, the heart rate was 100 bpm, and the respiratory rate was 68 resp/min. Upon auscultation the lung sounds were normal but a grade IV out of VI systolic heart murmur that was loudest on the right side was present. A CBC showed a slightly high fibrinogen level of 700 mg/dl and a plasma protein:fibrinogen ratio of 12.0. Serum chemistry showed a normal globulin level of 5.7 g/dl.

An ECG was recorded and echocardiography was performed on 5-3-89. The ECG showed sinus tachycardia and a mean electrical axis of between (-)120 and (-)150°. On echocardiography large vegetative lesions were seen arising from at least 2 of the leaflets of the right AV valve.

On 5-4-89 the bull again spiked a fever (107°F). Blood was collected for culture and therapy with ceftiofur (18ml IM q24h). The bull's rectal temperature returned to normal on 5-6-89 but the heart rate remained elevated (90–10 bpm) and the respiratory rate remained between 50 and 80 resp/min. Ceftiofur therapy was continued but the bull became increasingly depressed and on 5-7-89 pulmonary congestion and a moist productive cough became evident. The blood culture from 5-4-89 resulted in the isolation of an alpha-hemolytic streptococcus that was susceptible to all antibiotic tested. The rectal temperature began to rise again late in the day on 5-7-89. On 5-8-89 a CBC and serum chemistries were repeated and the results were not significantly different from those obtained on 5-3-89. After 6 days of ceftiofur therapy there was no improvement in the bull's condition and the owner elected to euthanize the bull on 5-10-89.

At necropsy there was a small amount of ventral subcutaneous edema, the cranial surface of the diaphragm was thickened due to edema, and there were multiple abscesses in the left cranial lung lobe. All leaflets of the right AV valve were thickened due to the accumulation of firm, friable, light tan, irregular shaped masses (Figure 3). The three largest masses measured 1-1/2 x 2-1/2 x 3 cm; 2 x 3 x 4 cm; and 2 x 2-1/2 x 6 cm.

[a] *Lasix*[R], *Hoechst-Roussel Agri-Vet Company, Somerville, NJ 08876*
[b] *Baytril*[R], *Mobay Corporation, Shawnee, KS 66201*
[c] *Pfizer, New York, NY 10017*
[d] *Mylan Pharmaceuticals, Morgantown, NY 26505*
[e] *Tribrissen*[R], *Coopers Animal Health, Kansas City, KS 66103*
[f] *Banamine*[R], *Schering Corporation, Kenilworth, NJ 07033*

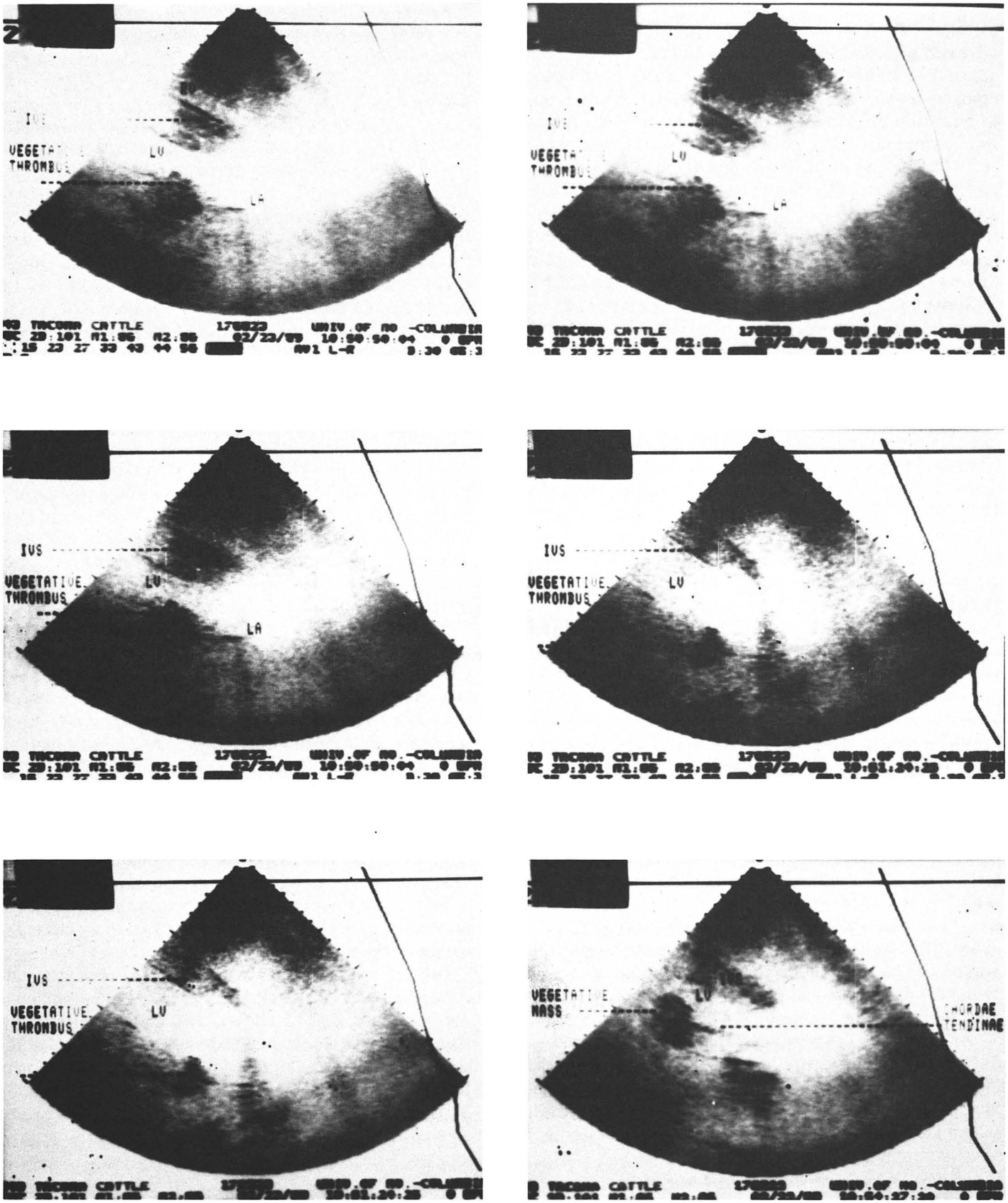

FIGURE 2. Echocardiography image of the heifer in case 3 showing an area of increased echogencity associated with a vegatative lesion on the left AV valve.

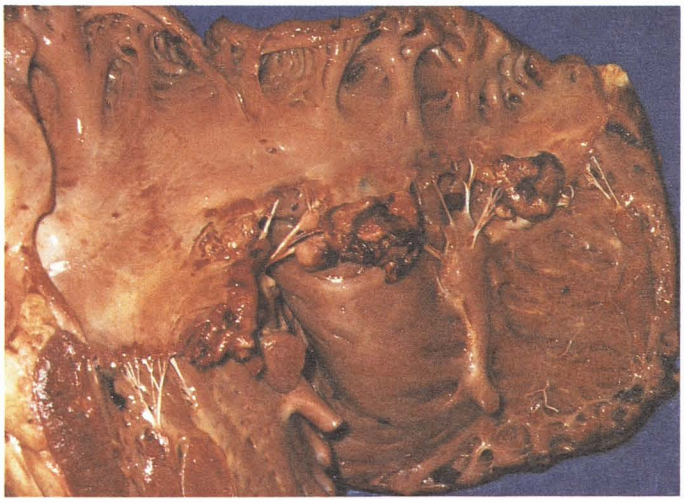

FIGURE 3. Heart of the bull in case 4 at necropsy showing the vegatative lesions attached to the right AV valve.

Discussion

These four cases illustrate the many different presentations of bovine vegetative endocarditis. All four of the cases were presented for chronic conditions. This seems to be representative of the majority of cases although apparent sudden deaths have been reported.[1,2] In 2 of the cases (case 1 and case 4) persistent fever and anorexia were the primary complaints. In case 2 the primary complaint was that the cow had been "doing poorly" for several weeks. All of these complaints are in keeping with published reports of common initial complaints in cases of vegetative endocarditis.[2,3] Case 3 was presented with the primary complaint of respiratory problems. This type of presentation is less common but is also discussed in the literature.[3,4] The history of case 3 also included intermittent lameness which was reported in about half of the cases reviewed for one study.[8] The painful, arched stance of case 2, which is similar to the stance seen in traumatic reticuloperitonitis, often occurs with vegetative endocarditis.[4] The pain seen in some cases of vegetative endocarditis is thought to be due to the gross infarction of internal organs.[2] In cases 3 and 4 there were definite signs of congestive heart failure before death while in cases 1 and 2 the most severe signs were due to pathology of the respiratory system.

Non-regenerative anemia of chronic inflammatory disease, hyperfibrinogenemia, and a leucocytosis due to neutrophilia and monocytosis are reported to be typical findings.[2,3,8] However, neither leukocytosis nor anemia was present in any of these four cases. One review reported that hyperglobulinemia was more consistently present in cattle with chronic inflammatory disease than elevated leucocyte counts or increased fibrinogen levels.[8] Of the four cases presented here only one (case 2) showed hyperglobulinemia while fibrinogen levels were increased at least slightly in all four cases. On a bovine leukogram the plasma protein:fibrinogen ratio is often used to indicate inflammation. A ratio of <10 is said to be indicative of chronic inflammation. In three of these cases (cases 1, 2 and 3) the plasma protein:fibrinogen ratio was <10. In the other case (case 4) the ratio was 12.

Sinus tachycardia and right axis deviation (between -178° and -137°) were consistent findings in one study of ECG findings in four cases of bovine endocarditis.[10] Atrial fibrillation has also been a reported finding in bovine endocarditis.[11] ECG recordings were run only for cases 3 and 4. Sinus tachycardia was present in both cases but right axis deviation was present only in case 4. Atrial fibrillation was not present in either case. Positive blood culture results were obtained in all 4 cases presented but not every culture yielded growth. This makes it apparent that blood culture can be negative in the presence of active infection.

Every episode of bacteremia in cattle does not lead to or reflect the presence of endocarditis. This makes it apparent that false positives can occur when using blood cultures as a test for endocarditis. It is best not to consider blood culture as a test for endocarditis, but as a test for bacteremia which, if positive, is consistent with the diagnosis of endocarditis.

Corynebacterium pyogenes was isolated from blood culture in two cases (cases 2 and 3). An alpha-hemolytic *Streptococcus* (case 4) and a *Staphylococcus spp.* (case 1) were also isolated from blood culture. All of these isolates were consistent with previously reported isolates from the blood of cattle with vegetative endocarditis.[2,3] In case 3, the second blood culture grew a *Clostridium spp.*. On necropsy of this cow necrotic myositis of the papillary muscle within the left ventricle was evident. To this date, *Clostridium spp.* has not been associated with vegetative endocarditis but has been linked to acute mural endocarditis of the right ventricle.[5] In this case (case 3) it seems likely that both *Corynebacterium pyogenes* and *Clostridium spp.* contributed to the pathology of the endocardium.

Echocardiography has been used to successfully diagnose endocarditis both in cases 3 and 4 presented here as well as in other studies.[2,10,12,13] In humans echocardiography has proven to be a highly specific test (few false positives) but not as sensitive a test (more false negatives) as blood culture for the diagnosis of endocarditis.[14]

It is currently thought that chronic septic conditions play an important role in the pathogenesis of vegetative endocarditis.[7] In these four cases the cattle had been chronically ill for at least 3 weeks (case 4) and up to 6 months (cases 2 and 3) before presentation to the UMC-VTH. In case 2 there was a history of gangrenous mastitis,

and in case 3 there was a history of respiratory disease. In both of these cases, the original illness may have provided the chronic infection that was necessary for the development of vegetative endocarditis. In cases 1 and 4 the original clinical signs were not specific to any particular disease or organ system. Vegetative endocarditis can be both the result and the cause of disease in other organ systems. In many cases it is difficult, if not impossible, to definitively say which was the original disease.

Treatment was attempted in three (cases 1, 3 and 4) of the four cases presented. In case 2 treatment was not attempted due to the duration and the severity of the clinical signs. In the three cases that were treated antibiotics were used. In case 3 a diuretic was also used during the second round of therapy. In one recent study, 9 of 31 cases of vegetative endocarditis were successfully treated with antibiotic therapy.[3] Of the four cases presented here, only one (case 3) showed any response to therapy. In case 3 the cow seemed to improve in response to the original therapy but relapsed and died after the original therapy was discontinued.

Endocarditis was evident at necropsy in all four cases. The severity of the lesions varied greatly but correlated with the clinical signs seen in the animal before death.

Summary

Vegetative endocarditis due to bacterial colonization of the endocardium has been known to occur in cattle for many years. Currently it is thought that abscesses or chronic infection plays an important role in the pathogenesis of the disease. The earliest clinical signs are usually non-specific and closely resemble those of other disease entities such as traumatic reticuloperitonitis and pneumonia. Affected cattle typically present with a history of recurrent fever, anorexia, weight loss, and depression of a few weeks to several months duration. Intermittent or shifting leg lameness without external trauma is sometimes associated with endocarditis. Tachycardia, systolic murmurs and loud pounding heart sounds are common findings upon physical exam. If untreated the clinical signs usually increase in intensity and signs of congestive heart failure often become evident. The CBC changes usually seen with endocarditis are those due to chronic inflammation. In the cases discussed here, hyperfibrinogenemia and a decreased plasma protein:fibrinogen ratio were the most common findings. Serum chemistry abnormalities are dependent upon the organ systems secondarily affected. Blood culture is a practical and useful tool to aid in the diagnosis of endocarditis. However, it is important to interpret the results of blood culture in keeping with the other clinical findings. The most commonly recovered organisms are *Corynebacterium pyogenes* and *Streptococcus spp.*.

Treatment of vegetative endocarditis in cattle is seldom rewarding because the diagnosis is often made late in the course of the disease. If treatment is going to be attempted it should consist of high levels of antibiotics for periods of 4 weeks or longer. Diuretics should be included for animals showing signs of congestive heart failure. The success of treatment depends heavily upon three factors; the right choice of antibiotics, sufficient duration of therapy, and the severity of clinical signs. It is important to realize that while the bacterial infection may be cleared, the vegetative lesions persist and cardiac function may not be improved.

Because of the long periods of therapy required and the poor prognosis for recovery, treatment may not be economically feasible in most cattle. However, some cattle today, because of outstanding genetics, are valuable enough to merit treatment at almost any expense. In these animals antibiotic therapy along with treatment of the congestive heart failure could allow time for the collection of sperm or embryos to be used in artificial insemination or embryo transfer. At the present time very little information about the management of congestive heart failure in cattle is available. Further studies and trials are needed to provide veterinarians with the ability to manage congestive heart failure in these highly valuable animals.

Early diagnosis is the key to successful treatment of vegetative endocarditis. It is only by including vegetative endocarditis among the initial rule outs for cattle showing non-specific signs that earlier diagnosis leading to more successful treatment will be achieved.

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