Spontaneous vegetative endocarditis due to *Enterococcus faecalis* in a Rottweiler puppy

D. Tessier-Vetzel[1], C. Carlos[1], J. Dandrieux[1], H.-J. Boulouis[2], J.-L. Pouchelon[1], V. Chetboul[1]

[1]Unité de Cardiologie d'Alfort et Unité pédagogique d'immunologie-microbiologie, [2]Ecole Nationale Vétérinaire d'Alfort, France

Summary

A 5-month-old female Rottweiler was referred because of a 5-week diarrhea and a sudden onset of a cardiac murmur auscultated by its veterinarian. Definitive diagnosis of bacterial endocarditis was based on ultrasonographic visualization of vegetative cardiac lesions and positive cultures of *Enterococcus faecalis* in blood and urine. Complicating findings were suppurative nephritis and renal infarction. Despite intensive supportive care, the endocarditis and clinical condition deteriorated and the dog had to be euthanized.

Key words: endocarditis – dog – *Enterococcus faecalis* – bacteremia – nephritis

Zusammenfassung

Eine 5-monatige Rottweiler-Hündin wurde wegen Durchfall und eines plötzlich auftretenden Herzgeräusches in die Klinik überwiesen. Die definitive Diagnose einer bakteriellen Endokarditis wurde aufgrund sonografisch diagnostizierter vegetativer Herzläsionen und positivier *Enterococcus faecalis*-Kulturen im Blut und Urin gestellt. Ungünstige Nebenbefunde waren eine eitrige Nephritis und ein Niereninfarkt. Trotz Intensivbehandlung verschlechterten sich die klinischen Anzeichen der Endocarditis und der Hund musste euthanasiert werden.

Schlüsselwörter: Endocarditis – Hund – *Enterococcus faecalis* – Bakterien – Nephritis

History

A 5-month-old 18 kgs female Rottweiler was referred with a 5 week history of diarrhea, progressive lethargy, anorexia, weight loss and a sudden onset of a cardiac murmur. The feces had become watery and bloody two weeks previously. During the last week, the diarrhea was associated with vomiting. The owner reported recent urine discoloration throughout micturition.

Physical examination

Physical examination showed depression, dehydratation and pyrexia (39.8 °C). The mucous membranes were pale and dry. The abdominal palpation was moderately painful and revealed few liquid digestive content. Other physical abnormalities included tachycardia (160 beats/min) with a regular rhythm, and a left apical grade IV/VI systolic heart murmur. Pulmonary auscultation was normal, but respiratory rate was discretely increased (35/min). The association of fever, lethargy and recent onset of a cardiac murmur was highly suggestive of endocarditis (Lombard and Buergelt, 1983).

Complementary exams

The following complementary exams were performed: a complete blood analysis (biochemical panel and blood count), cardiovascular exploration (thoracic radiographs, blood pressure measurements, electrocardiography, echo-Doppler), fecal examinations (fecal flotation and direct smear, canine parvovirus detection via fecal hemagglutination), urinalysis (sediment analysis, protein/creatinine ratio, cultures), abdominal ultrasonography, blood cultures.

Results of diagnostic tests

Biochemical abnormalities included elevated levels of serum alkaline phosphatase (321 U/L; normal: 30 to 120), hypoproteinemia (43 g/L ; normal: 54 to 70 g/L) and hypoalbuminemia (19 g/L ; normal: 25 to 37 g/L). The cell blood count showed a hyporegenerative,

 DOI 10.1024//0036-7281.145.9.432

		Reference values
Haematocrit	*25.6*	• 37–55%
Red blood cells	*4.02*	• 5.5–8.5 10^6/mm^3
Hemoglobin	*8*	• 12–18 g/100 mL
Reticulocytes	*55000*	• 5500–127500/mm^3
Thrombocytes	*450000*	• 200000–500000/mm^3
Total leucocyte count	*52940*	• 6000–17000/mm^3
Immature neutrophils	*6352*	• 0–300/mm^3
Segmented neutrophils	*39176*	• 3000–11500/mm^3
Eosinophils	*1059*	• 100–1250/mm^3
Basophils	*0*	• 0–10–^{9}/mm^3
Lymphocytes	*4235*	• 1000–4800/mm^3
Monocytes	*2118*	• 150–1350/mm^3

Table 1.

normocytic and normochromic anemia, a neutrophilic leukocytosis with a regenerative left shift and a monocytosis (Tab. 1).

Survey thoracic radiographs and systemic arterial blood pressure were normal. Electrocardiogram revealed a sinus tachycardia (160 bpm). Echocardiogram was obtained on the standing position, from the right parasternal view, using a 5.0 MHz mechanical sector transducer with M-mode, two-dimensional and Doppler capabilities (Esaote, AU3 Partner, Italy). M-mode and two-dimensional echocardiogram revealed a normal right heart without a tricuspid valve lesion. The mitral valves appeared thickened, irregular and hyperechoic with a large cauli-flower like mass

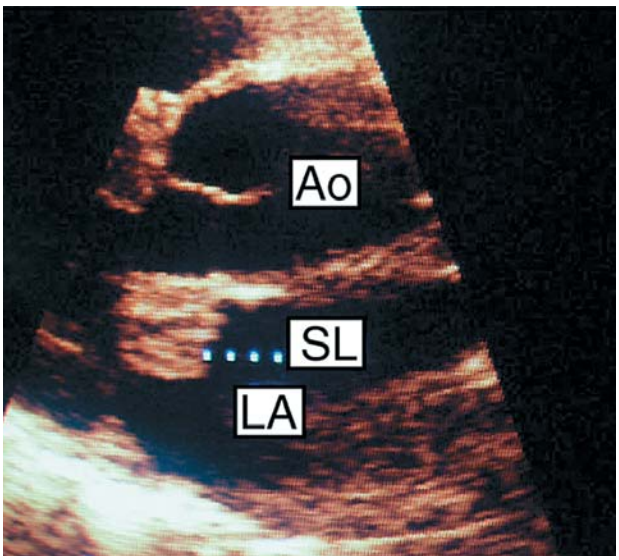

Figure 1: Right parasternal, long-axis, left ventricular outflow-view (Ao: aorta; LA: left atrium). After interrogate several planes, this view shows the maximal thickening of the septal leaflet of the mitral valve (SL). The lesion was a large cauliflower like mass. Maximal measurement of the septal leaflet was 15 mm. A heterogeneous appearance with hypoechoic areas within the lesion is seen.

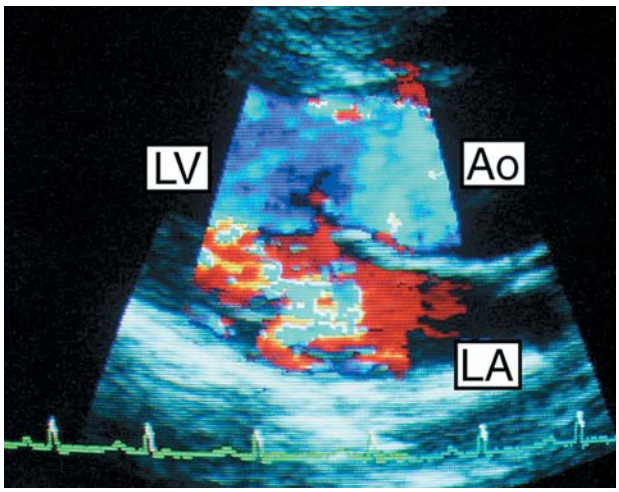

Figure 2: Right parasternal, long-axis, left ventricular outflow-view (Ao: aorta; LV: left ventricle). Color-flow jet of mitral insufficiency. The large vegetative lesion of the septal leaflet prevents proper closure of the cusps. Mitral insufficiency was consequently observed. Greater than 50% of the left atrium (LA) is filled by the aliased regurgitant flow.

(15 mm) on the septal leaflet (Fig. 1). The posterior leaflet presented a 8 mm distal nodule. Color flow Doppler echocardiogram showed severe mitral regurgitation (Fig. 2) without left atrial dilatation. Aortic valve and flow were normal, as well as left ventricular morphology and function.

All fecal examinations were negative. Urinalysis revealed microscopical hematuria and proteinuria with a protein/creatinine ratio of 2,7 (normal < 0,4). Abdominal ultrasonography revealed severe, diffuse, homogenous, echoic and nodular lesions of the left kidney with profound alteration of its architecture. Left renal length was markedly increased (7 cm) with very irregular contours. The perirenal fat was hyperechoic, suggestive of retroperitonitis. The right kidney presented two small, characteristic peripheral images of infarction. Echo-guided percutaneous renal biopsy showed a histological lesion consisting of a severe necrotic and suppurative nephritis. Blood culture confirmed bacteremia *(Enterococcus faecalis)*. The same organism was isolated from urine (10^4/mL).

Treatment

A first treatment consisted of fluid therapy, metoclopramide hydrochloride (Primperid, Sanofi) in constant-rate infusion, nifuroxazide (Ercéfuryl, Sanofi), aluminium hydroxide (Phosphalugel, Yamanouchi-Pharma) and diosmectite (Smecta, Ipsen). Fever associated with suspected endocarditis justified initiation of intravenous broad-spectrum bactericidal antibiotics (enrofloxacin and ampicillin sodium) (Defrancesco, 2000).

Outcome

During waiting for bacterial culture results, no control of fever could be achieved. The size of the mitral valve doubled despite treatment. When the dog developed septic shock five days later, the owners opted for euthanasia. Autopsy confirmed the cardiac and renal lesions.

Discussion

In our case, hemorrhaged gastroenteritis and presence of *Enterococcus faecalis* in blood and urine cultures are consistent with bacteremia of intestinal origin (Macintire, 2000), responsible for vegetative mitral endocarditis, suppurative nephritis and renal infarction. Incidence of infective endocarditis in dogs remains not precisely known. Its actually published estimation ranges from 0,04 to 0,58% (Sisson and Thomas, 1984; Buchanan, 1992; Lombard and Buergeld, 1993; Sisson, 1994). One study reports the diagnosis of about 5 cases per year of endocarditis in canine patients in a veterinary teaching hospital (Kittleson et al.,1998). Infective endocarditis in cats is more rarely described (Kovacecic et al., 2002). Published breed related risk factors are slight and probably related either to the occurrence of some predisposing congenital heart defects or to overrepresentation of popular breeds (Miller and Sisson, 1999). Dogs affected by infective endocarditis are most often large (more than 15 kg), adult and purebreed dogs. As Rottweiler is predisposed to subvalvular aortic stenosis, this breed could be considered predisposed to infective endocarditis. Aortic stenosis was not detected on echocardiography in this puppy. The breed of this dog remains so incidental. However, according to different studies and conversely to human medicine data (Calvert, 1982; Sisson and Thomas, 1984; Calvert et al., 1985), many cases of infective endocarditis in small animal medicine seem to occur on apparently normal macroscopicaly cardiac valves.

Many predisposing factors of endocarditis are recognized. Damaged vascular endothelial surface and ability of bacterium to adhere to this damaged endothelium remain the two major promoters of infective endocarditis. Lesions of vascular endothelium can be produced with high velocity, turbulent blood flow, as observed with valvular stenosis or insufficiency. High pressures drive high velocity blood flows. This explains the typical location of infective endocarditis on aortic or mitral valve leaflets. Some bacterial species have well-developed mechanisms of attachment to damaged endothelium. Organisms that most frequently cause endocarditis in the dog adhere best to heart valves *in vitro* (Gould et al., 1975). These species are *Staphylococcus aureus* (posses fibronectin receptors), *E. Coli, β-hemolytic streptococci, Corynebacterium, Pseudomonas aeruginosa* and *Erysipelothrix rhusopathiae* (Miller and Sisson, 1999; Kittleson, 1998). Studies have shown that *enterococci* adhere also well to heart valves *in vitro* (Gould et al., 1975), which explains their implication in infective endocarditis and their use to induce experimental endocarditis.

Though bacteremia is an obligatory event in the genesis of infective endocarditis, the initiating and responsible episode of bacteremia is most often not identified in dogs. Morever, bacteremia is a common process, which remains rarely complicated with infective endocarditis. Origin of bacteremia in infective endocarditis can be various, but involves frequently the gastrointestinal and genitourinary tracts or chronic suppurative processes. Bacterial translocation is the suspected origin of bacteremia in this Rottweiler puppy. This process would be implicated in the development of bacteremia. However, its significance remains still unclear and translocating bacteria (included *enterococci*) have been also found in healthy dogs (Dahlinger et al., 1997). Medical (intravenous or urinary tract catheterizations, immunosuppressive drug therapy) and surgical procedures are distinctly known to promote bacterial endocarditis. Dental procedures present a high risk of complicated endocarditis in human patients with preexisting valvular lesions. This promoter of bacterial endocarditis has not been proved in canine patients. *Enterococcus faecalis* is a gram-positive saprophyte coccus, which belongs to the normal microflora of the gastro-intestinal tract of dogs, cats and also humans. The particular resistance of *enterococci* to adverse environmental conditions has led to the emerging role of these bacteria in nosocomial infections in veterinary medicine (especially in veterinary teaching hospital) as well as in human medicine (Greene and Prescott, 1998; Boerlin et al., 2001). Implication of *enterococci* in systemic infections (bacteremia, endocarditis) and localized infections (abdominal cavity, genitourinary, nervous system and soft tissue) are considered most frequent (Remedios et al., 1996; Greene and Prescott, 1998; Koutinas et al., 1998, Adamo and Cherubini, 2001). However, only few studies have been published on enterococcal infections in companion animals (Boerlin et al., 2001). Although experimental endocarditis has been induced in dogs with *Enterococcus faecalis* (Sapico et al., 1972; Gould et al., 1975), spontaneous endocarditis with this organism has not been well described in small animal medicine.

Even if *enterococci* are not as virulent as *streptococci*, infection with these bacteria remains problematic, as they are very difficult to eradicate from host tissues because of natural and acquired resistance to many

antimicrobials. Reference antibacterial chemotherapy of enterocci infections consists of an association of penicillin or ampicillin with aminoglycosides (Greene and Prescott, 1998). Despite *in vitro* susceptibility of enterococci to trimethoprim-sulfonamide, this antimicrobial choice is not effective *in vivo*, as enterococci can circumvent the block in folate synthesis. Finally, the use of avoparcin, a vancomycin-related glycopeptide, as a growth factor for food-producing animals has led to the development of vancomycin-resistant enterococci. This causes a major human health problem, as vancomycin-resistant enterococci are implicated in environmental and hospital infections. Vancomycin-resistant enterococci have been also isolated from the feces of healthy dogs and cats (Devriese et al., 1992).

As in this case, definitive diagnosis of bacterial endocarditis is based on positive blood cultures associated with well established clinical signs, laboratory abnormalities and ultrasound visualisation of vegetative cardiac lesions. Leukocytosis, monocytosis and anemia are the most frequent hematological abnormalities associated with endocarditis (Calvert, 1982). In this case, an extreme neutrophilic leucocytosis (neutrophilia greater than 50000/mm^3) with a severe left shift was present. The degree of increase in band neutrophils is considered as a direct indication of the severity of the associated disease. Localized purulent processes such as abcessation are recognized to stimulate greater neutrophilic responses than generalized infections or septicemias (Smith, 2000; Gaunt, 2000). When endocarditis is so suspected, observation of an extreme neutrophilic leucocytosis invites always to consider even a primary suppurative process or to suspect infective emboli dissemination due to endocarditis complications. In this case, extreme neutrophilic leucocytosis was attributed to severe necrotic and suppurative nephritis due to infective emboli. Monocytosis is an inconsistent finding, which may reflects a response to mediators of inflammation. Finally, hematological results are not only important for diagnosis. They are although useful in the evaluation of the seriousness of the infective endocarditis. Classical biochemical changes associated with endocarditis include hypoalbuminemia, elevation of serum alkaline phosphatase, blood urea nitrogen and creatinine (Woodfield and Sisson, 1989). In this dog, a mild hyporegenerative anemia, a small ALP elevation and a total proteins decrease were observed. These laboratory abnormalities are most likely the result of a combination of the age of the dog, the severe gastrointestinal disease and the renal lesions (loss of proteins and blood).

Prognosis of active infective endocarditis is poor. Estimated survival rate is 20% (Calvert, 1985). Complications of active infective endocarditis have set in systemic embolization and metastatic infection, immune-mediated disorders, septic shock and the resultant multiple organ dysfunction syndrome (MODS). Animals can thus die from heart disease (sudden lethal arrhythmias or heart failure) as well as from systemic infective complications. Even if eradication of infection is possible, heart failure can result from large aortic lesions or from severe mitral insufficiency. Other patients die from embolic complications, which frequently involve the kidneys. Human echocardiographic studies have shown that patients with large vegetations (diameter more than 10 mm, as found in the mitral valve of our dog) have a higher risk of infective emboli dissemination (Baxley, 1994). It has also been demonstrated in man that the persistence or increase of vegetation size during the treatment (as seen here) worsens the prognosis (Rohmann et al., 1991;Vilacosta et al., 2002). The prognosis is also worsened when there is association of a large valvular vegetation with embolic complications and persistent fever despite adequate antibacterial therapy (Kittleson, 1998; Karth et al., 2002).

References

Adamo P.F., Cherubini G.B.: Discospondylitis associated with three unreported bacteria in the dog. J. Small Anim. Pract. 2001, 42: 352–355.

Baxley W.A.: Aortic valve disease. Curr. Opin. Cardiol. 1994, 9: 152–157.

Boerlin P., Eugster S., Gaschen F., Straub R., Schawalder P.: Transmission of opportunistic pathogens in a veterinary teaching hospital. Vet. Microbiol. 2001, 82: 347–359.

Buchanan J.W.: Causes and prevalence of cardiovascular disease. In Current Veterinary Therapy XI: Small Animal Practice, Eds. R. W. Kirk., J. D. Bonagura, 1993, 24: 325.

Calvert C.A.: Valvular bacterial endocarditis in the dog. J. Am. Vet. Med. Assoc. 1982, 180: 1080–1184.

Calvert C.A., Greene C.E., Hardie E.M.: Cardiovascular infections in dogs: epizootiology, clinical manifestations and prognosis. J. Am. Vet. Med. Assoc. 1985, 187: 612.

Dahlinger J., Marks S.L., Hirsh D.C.: Prevalence and identity of translocating bacteria in healthy dogs. J. Vet. Intern. Med. 1997, 11: 319–322.

Defrancesco T.: CVT Update: Infectious Endocarditis. In: Current Veterinary Therapy XIII: Small Animal Practice. Eds. R. W. Kirk, W. B. Saunders, Philadelphia, 2000, 768–772.

Devriese L. A., Ieven M., Goosens H.: Presence of vancomycin-resistant enterococci in farm and pets animals. Antimicrob. Agents Chemother. 1996, 40: 2285–2287.

Gaunt S. D.: Extreme neutrophilic leukocytosis. In: Schalm's Veterinary hematology. Eds. B. F. Feldman, J. G. Zinkl and N. C. Jain, Lea and Febiger, Philadelphia, 2000, 347–349.

Gould K., Ramirez-Ronda C. H., Holmes R. K., Sanford J. P.: Adherence of bacteria to heart valves in vitro. J. Clin. Invest. 1975, 56: 1364–1370.

Greene C.E., Prescott J.F.: Streptococcal and other Gram-positive bacterial infections. In: Infectious disease of the dog and Cat. Ed. C. G. Greene Saunders, Philadelphia, 1998, 205–214.

Karth G., Koreny M., Binder T., Knapp S., Zauner C., Valentin A., Honninger R., Heinz G., Siostrzonek P: Complicated infective endocarditis necessitating ICU admission: clinical course and prognosis. Critical Care 2002, 6: 149–154.

Kittleson M. D.: Infective endocarditis. In: Small animal cardiovascular medicine. Ed. Mosby, St Louis, 1998, 402–412.

Koutinas A. F., Heliadis N., Saridomichelakis M. N., Leontides L., Terpsidis K., Christodoulou C. Asymptomatic bacteriuria in puppies with canine parvovirus infection: a cohort study. Vet. Microbiol. 1998, 63: 109–116.

Kovasecic A., Allenspach K., Kühn N., Lombard C. W.: Endocarditis in a cat. J. Vet. Cardiol. 2002, 4: 31–34.

Lombard C. W., Buergelt C. D.: Vegetative bacterial endocarditis in dogs: echocardiographic diagnosis and clinical signs. J. Small Anim. Pract. 1983, 24: 325–339.

Macintire D. K.: Bacterial translocation: clinical implications and prevention. In: Current Veterinary Therapy XIII: Small Animal Practice. Eds. R. W. Kirk., W. B. Saunders, Philadelphia, 2000: 201–203.

Miller M. W., Sisson D.: Infectious endocarditis. In: Textbook of canine and feline cardiology. Eds. P. R. Fox, D. Sisson, N. S. Moise. Philadelphia: W. B. Saunders, 1999: 567–580.

Remedios A. M., Wagner R., Caulkett N. A., Duke T.: Epidural abscess and discospondylitis in a dog after administration of a lumbosacral epidural analgesic. Can. Vet. J. 1996, 37: 106–107.

Rohmann S., Erbel R., Darius H., Gorge G., Makowski T., Zotz R., Mohr-Kahaly S., Nixdorff U., Drexler M., Meyer J.: Prediction of rapid versus prolonged healing of infective endocarditis by monitoring vegetation size. J. Am. Soc. Echoc. 1991, 4: 465–474.

Sapico F. L., Keys T. F., Hewitt W. L.: Experimental enterococcal endocarditis. II. Study of in vivo synergism of penicillin and streptomycin. Am. J. Med. Sci. 1972, 263: 128–135.

Sisson D., Thomas W. P.: Endocarditis of the aortic valve in the dog. J. Am. Vet. Med. Assoc. 1984, 184: 570–578.

Sisson D. D.: Bacterial endocarditis. Proceedings, 18th Annual Kal Kan/OSU Symposium. 1994, 79.

Smith G. S.: Neutrophils. In: Schalm's Veterinary hematology. Eds. B. F. Feldman, J. G. Zinkl and N. C. Jain, Lea and Febiger, Philadelphia, 2000, 281-296.

Vilacosta I., Graupner C., Sanroman J., Sarria C., Ronderos R., Fernandez C., Mancini L., Sanz O., Sanmartin J., Stoermann W.: Risk of embolization after institution of antibiotic therapy for infective endocarditis. J. Am. Coll. Cardiol. 2002, 39: 1489–1495.

Woodfield J. A., Sisson D.: Infective endocarditis. In: Textbook of Veterinary Internal Medicine. Eds. W. B. Saunders, Ettinger S. J., Philadelphia, 1989, 1151–1162.

Corresponding author

Valérie Chetboul, DVM, PhD, Dipl. ECVIM-CA, Unité de Cardiologie d'Alfort, Ecole Nationale Vétérinaire d'Alfort, 7 avenue du Général de Gaulle, F-94704 Maisons-Alfort Cedex, Fax: 00 33 1 43 96 70 78,
E-mail: vchetboul@vet-alfort.fr

Received for publication: 10 septembre 2002
Accepted in final form: 20 novembre 2002