Septicemia, atrial fibrillation, cardiomegaly, left atrial mass, and Rhodococcus equi septic osteoarthritis in a foal

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A 70-day-old 125-kg Thoroughbred colt was admitted to the teaching hospital for evaluation of a swollen left hind metatarsophalangeal joint that caused signs of pain. Lameness and swelling had been noticed one month earlier, at which time synovial fluid and radiographs of the affected joint were considered normal. Penicillin and gentamicin had been administered for 6 days, and the lameness had resolved. During the ensuing 3 weeks, the foal's activity was less than normal. One week prior to admission, lameness and swelling redeveloped. Although synovial fluid and radiographs of the left hind metatarsophalangeal joint again were normal, the foal was febrile (39.7°C), and hematologic evaluation revealed leukocytosis (16,000 cells/µl). Treatment with trimethoprim-sulfa, orally, at an unspecified dosage, was instituted.

At admission, the colt was bright and alert, but spent an excessive amount of time lying down. The heart rate was 60 to 80 beats/min, respiratory rate was 36 breaths/min, and temperature was 38.4°C. The foal was III/IV degrees lame on its left hind limb. Moderate synovial effusion and periarticular swelling were palpable in the metatarsophalangeal region, and signs of pain were elicited on manipulation of the joint. Cardiac auscultation revealed an irregular cardiac rhythm, and a grade V/VI holosystolic crescendo murmur (point of maximal intensity over the mitral valve region). Peripheral pulses of variable intensity were palpable. Results of auscultation of the lung fields were normal.

The foal had mild leukocytosis (12,600 cells/µl, with 9,150 mature neutrophils and 2,806 lymphocytes) and hyperfibrinogenemia (700 mg/dl). Packed cell volume and serum electrolyte and serum creatinine concentrations were normal. Radiography of the left hind metatarsophalangeal region revealed an oval radiolucency surrounded by sclerotic bone in the distal physis of the third metatarsal bone. Multiple attempts to obtain synovial fluid were unsuccessful.

Electrocardiography revealed atrial fibrillation, with coarse fibrillation waves, no P waves, and irregular R-R intervals. Two-dimensional real-time echocardiography revealed changes consistent with mitral insufficiency, including enlargement of the left side of the heart and reduced wall motion (Table 1). A vegetative mass was visualized on the septal wall of the left atrium at the base of the mitral valve (Fig 1). Blood concentrations of cardiac isoenzymes of creatine kinase and lactate dehydrogenase, as well as blood selenium concentrations, were within normal limits. The umbilicus appeared normal on ultrasonographic examination. Thoracic radiography revealed moderate bronchointerstitial opacity in the caudodorsal lung fields and bronchoalveolar disease ventral to the caudal vena cava.

At this time, differential diagnoses included lameness, with radiographic signs most consistent with P-type osteomyelitis, pneumonia, and cardiac disease. The history of recurrent fevers, the

Figure 1—Echocardiogram of a colt with cardiomegaly, mitral insufficiency, and a vegetative mass. Notice hyperechoic region in atrial wall (LA = left atrium; LV = left ventricle).

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apparent focus of infection in the metatarsal phy-
sis, and the visualization of an endocardial mass
made bacterial endocarditis the most likely diag-
nosis. Extension of endocardial disease into the
myocardium, causing abnormal contractility with
subsequent chamber enlargement, mitral insuffi-
ciency, and atrial fibrillation, was likely.

Blood and a transtracheal aspirate were ob-
tained for bacterial culturing and sensitivity tests
prior to antimicrobial treatment. Potassium peni-
cillin G (22,000 IU/kg of body weight, q 6 h)
and gentamicin (3.3 mg/kg, q 12 h) were adminis-
tered IV. Digoxin treatment (10 μg/kg, PO, q 12 h) was
initiated for the myocardial dysfunction on day 2.
By day 4, myocardial function had improved
markedly, although the enlargement and mitral in-
sufficiency remained (Table 1). Peak and trough
culturing and sensitivity testing. A sterile, noncol-
lapsible, multipore drain was placed in the joint,
exiting laterally via a stab incision. A sterile
bandage was placed over the wound, and a support
bandage with a caudal splint was applied to the
distal portion of the limb.
The joint was lavaged with 500 ml of lactated
Ringer solution containing 1 g of amikacin every 6
hours for 4 days, at which time the drain was re-
moved. Culturing of synovial fluid, synovial mem-
brane, and bone obtained at surgery all yielded
pure growths of *Rhodococcus equi*, sensitive in vitro
to erythromycin and rifampin. Erythromycin (20
mg/kg, IV, q 6 h for 10 days, then 20 mg/kg, PO, q 6
h) and rifampin (5 mg/kg, PO, q 12 h) were added
to the antimicrobial regimen. After day 13, joint
effusion was minimal; periarticular swelling gradu-
ally subsided, and the foal’s soundness steadily
improved. By hospital day 27, the foal was consis-
tently II/IV degrees lame at the trot.

Blood and transtracheal aspirate culturing
yielded *Escherichia coli*, and *E coli* and *Klebsiella*
sp, respectively, all demonstrating in vitro sensitivity
to gentamicin. On the basis of these results, ceftax-
taxime administration was discontinued and treat-
ment with potassium penicillin and gentamicin
was resumed on day 9. However, within 48 hours,
the foal became persistently febrile (40 C for 6
hours); thus, treatment with ceftaxime was rein-
stituted. Cefotaxime administration was continued
through day 35, and the foal remained afebrile.
The foal’s condition steadily improved over
days 14 to 27. Atrial fibrillation persisted, but se-
rial echocardiography revealed a decrease in left
heart size to within normal limits, with normal
myocardial function despite reduction in digoxin
dosage (Table 1). Peak and trough serum digoxin
concentrations were 0.90 and 0.61 ng/ml, respec-
tively, on day 26, when digoxin was administered
at a dosage of 0.45 mg, PO, q 12 h. The left atrial
mass appeared unchanged. A precordial thrill was
no longer palpable, and the systolic murmur had
decreased in intensity to a grade II/VI by day 20.
The foal was increasingly active and steadily gain-
ing weight.

Oral administration of quinidine sulfate was
instituted on day 27. Quinidine was given at an
initial dosage of 12 mg/kg, q 6 h, for 5 doses.
The dosage was doubled after each 5-dose regimen
as long as the colt did not have signs of quinidine
toxicosis. Serum electrolytes were monitored daily,
electrocardiography was done every 6 hours, and
cardiac auscultation was performed hourly during
quinidine treatment. Normal sinus rhythm was
achieved on hospital day 33, after 5 doses of qui-
nidine sulfate were given (6 g, PO, q 6 h). Plasma
quinidine and digoxin concentrations at this time
were 4.2 μg/ml and 1.4 ng/ml, respectively. Digoxin

<table>
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<th>Hospital day</th>
<th>LVEDD (cm)</th>
<th>LVESD (cm)</th>
<th>Shortening fraction (%)</th>
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*Shortening fraction = [(LVEDD-LVESD)/LVEDD] × 100.
LVEDD = left ventricular end diastolic diameter; LVESD = left ventricular
end systolic diameter.

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4 Lanoxin Elixir, Coopers Animal Health, Kansas City, Mo.
5 Claforan, Hoechst-Roussel, Somerville, NJ.
6 Closed Wound Vacuum, Adler Instrument Co, Atlanta, Ga.
7 Rifadin, Merrell-Dow, Cincinnati, Ohio.
8 Sigma Corp, St Louis, Mo.
administration was discontinued on hospital day 33.

Cefotaxime and erythromycin administration was discontinued on day 35. Rifampin administration was continued, and chloramphenicol was administered (50 mg/kg, po, q 6 h). The foal was discharged from the hospital on day 40. Reexamination on day 54 revealed a heart rate of 52 beats/ min, a grade III/VI holosystolic murmur with maximal intensity over the left AV valve, normal sinus rhythm, and a grade II/IV lameness in the left hind limb at the trot. Antimicrobial treatment was continued for 5 weeks.

On reexamination on day 118, the foal was sound in the left hind limb, with no joint effusion; however, the foal’s attitude was dull, it had a rough coat, a pot-bellied appearance, and a mucopurulent nasal discharge. Temperature was normal, and respiratory rate was mildly higher than normal (24 breaths/min). The foal was re-admitted to the hospital.

Cardiac auscultation and ECG revealed atrial fibrillation, with a heart rate of 60 to 70 beats/min. A grade II/VI holosystolic murmur with point of maximal intensity over the mitral valve region was audible. Echocardiographically, the left atrium was large, but myocardial function, left ventricular size, and mitral valve leaflets appeared normal. The left atrial mass was still evident, but smaller and more echogenic.

Harsh pulmonary bronchovesicular sounds were auscultated. Thoracic radiography revealed persistent bronchoalveolar disease over the heart base. High numbers of degenerative neutrophils, gram-positive cocccobacillary organisms, and some gram-negative rods were seen on microscopic examination of a transtracheal aspirate. Culturing of the aspirate produced an E coli-sensitive in vitro to cephalothin and amikacin. The morphologic characteristics of the gram-positive organisms and previous culture of R equi from synovial membrane made this an additional likely pathogen in the foal’s pulmonary disease.

Administration of erythromycin (30 mg/kg, po, q 6 h) and rifampin (10 mg/kg, po, q 12 h) was begun. Cephradine (22 mg/kg, po, q 6 h) was added to the treatment regimen 6 days later on the basis of culture and sensitivity of the E coli isolate. Quinidine sulfate was given on day 123 (6 g, po, q 6 h). Normal sinus rhythm was achieved 2 hours after the second dose of quinidine was given. Serum quinidine concentration at the time of conversion was 2.4 μg/ml. A distinct improvement in attitude was noticed on day 125. On day 129, the foal was discharged with instructions to the owners to continue the antimicrobial administration for 4 weeks.

On reexamination on day 179, the foal had gained weight, had an improved coat, and was active. Vital signs were normal. Cardiac and pulmonary auscultation were unchanged since its discharge from the hospital. Microscopic examination of a transtracheal aspirate revealed persistence of high numbers of a uniform population of coccobacillary gram-positive organisms, both intra- and extracellularly. Because of economic considerations, further treatment with erythromycin and rifampin was not pursued. The foal received trimethoprim-sulfadiazine (4 mg trimethoprim/kg, po, q 12 h) for an additional 5 weeks.

When it was 20 months old, the foal was re-admitted to the hospital for evaluation of left hind limb lameness that developed after initiation of race training, which began 2 weeks prior to readmittance. The foal was in excellent body condition, with normal vital signs. Pulmonary auscultation was unremarkable; cardiac auscultation revealed a grade III/VI holosystolic murmur, with point of maximal intensity over the mitral valve. Echocardiography revealed normal myocardial contractility, with a mildly enlarged left atrium. The atrial mural mass was still evident, but greatly reduced in size. Cardiac function was considered normal.

Radiography of the left metatarsophalangeal joint revealed degenerative joint disease with no joint effusion. The foal was responsive to stall rest and phenylbutazone (4 mg/kg, po, q 12 h, for 5 days). The colt returned to training 4 weeks later. At the time of this publication, the colt is sound.

Focal infections in foals are typically hematogenous in origin and are seen as sequelae to neonatal septicemia. Whereas osteomyelitis/arthritis is one of the most commonly reported complications of this kind, vegetative bacterial endocarditis is rare in a foal this age. Ruptured chordae tendineae with mitral valvular insufficiency secondary to bacterial endocarditis has been reported in one foal.4

Vegetative endocardial lesions are seen most commonly on the aortic and mitral valve leaflets in horses.3 In addition, mural atrial vegetative lesions have been reported in dogs and adult horses.6 Disruption of the atrial endocardium secondary to turbulent blood flow initiates the adherence of platelets and fibrin. This site then is predisposed to bacterial invasion and colonization during a subsequent bacteremia.7 A primary mitral valve insufficiency in this foal may have been responsible for abnormal blood flow in the left atrium. Thickening of the free edge of the mitral valve leaflets was revealed on echocardiography in this foal.

Mitral valve abnormalities have been reported as the most common pathologic finding in horses with atrial fibrillation.5 Atrial enlargement or myocardial dysfunction causing conduction abnormalities may have contributed to the pathogenesis of atrial fibrillation in this foal. Persistent left atrial enlargement may have contributed to the redevelopment of the arrhythmia. Arrhythmias in human patients with bacterial vegetative endocarditis may result from direct extension of the bacterial lesion into the myocardium (myocarditis) or may be sec-
ondary to thromboembolic myocardial ischemia. In one study, 28% of human patients that died with bacterial endocarditis had myocardial absces-
sation at postmortem examination.

Bacteriologic cure is the goal of treatment for bacterial endocarditis. Poor penetration of antimicrobials into vegetations, high numbers of bacteria at the site of infection (inoculum effect), and slow growth of deep-seated bacterial colonies all hinder the effectiveness of antimicrobial treatment and complicate the interpretation of in vitro susceptibilities. Any of these conditions may have been responsible for the poor clinical response to gentamicin in this foal despite in vitro sensitivity of the isolated organism to gentamicin. Cefotaxime is a third-generation cephalosporin, with a broad gram-negative spectrum and excellent tissue penet-
ration. When tested in vitro against cefotaxime, most E. coli isolates have minimal inhibitory concentrations of 0.12 to 0.5 μg/ml.

Treatment with quinidine sulfate of atrial fibrillation and serious underlying cardiac disease usually is contraindicated in horses, because quini-
dine is a negative inotrope and a positive chrono-
trope. Quinidine sulfate treatment was not in-
stituted in this foal until the myocardial function and the size of the left side of the heart had returned to normal. Each dose of quinidine was adminis-
tered for 5 half-lives (t½ = 6 hours) to gradually achieve steady-state serum concentration. Digoxin treatment was continued during the quinidine sul-
fate treatment to counteract the negative inotropic and positive chronotropic effects of quinidine sul-
fate.

A narrow margin exists between the therapeu-
tic (3 to 5 μg/ml) and toxic (6 μg/ml) concentrations of quinidine sulfate. This is further comp-
licated in the digitalized horse by the interaction of these 2 drugs. Ninety percent of digitalized human patients receiving concurrent quinidine treatment have a 2- to 4-fold increase in serum digoxin concentrations. The digoxin dosage in this foal was decreased by 50%, and serum digoxin concentra-
tion in the low therapeutic range (0.5 to 2 ng/ml) was measured prior to beginning quinidine treatment. When the serum quinidine concentra-
tion increased to the therapeutic range, the serum digoxin concentration increased 100%.

Firth has described 3 types of lesions associ-
ated with osteomyelitis/arthritis in foals. Although R. equi is not commonly associated with os-
teomyelitis/arthritis in foals, Firth reports a higher incidence of R. equi isolates from P-type lesions (such as the one in this foal) than from either S- or E-type.

The use of aggressive surgical debridement or local antibiotic treatment in osteomyelitis/arthritis remains controversial in all species. Goals of surgical debridement include the physical removal of necrotic tissue, purulent material, and inflam-
matory products, as well as the establishment of drainage adequate to ensure continued evacuation of these substances. Bertone reported a reduction in synovitis and articular fibrin formation in horses with experimental tarsocrural septic arthritis treated with arthrolysis and lavage. Local antimicrobial treatment for osteoarthritis was used in the foal of this report because physiologic alterations that accompany inflammation and the aforementioned inoculum effect may alter the clinical response to systemically administered anti-
microbials. The potential benefits of high local concentrations of antimicrobials were deemed to outweigh the effects of synovial irritation that might result.

The acute stages of bacterial endocarditis with underlying cardiac disease and septic osteoarthri-
tis were treated successfully in this foal. Other horses treated successfully for bacterial endocardi-
tis have succumbed to late complications related to persistent mitral insufficiency. This foal's return to normal cardiac function is most likely attribut-
able to the mural location of the vegetation. Scar-
ring of the mitral valve leaflets did not develop with resolution of the cardiac disease; thus, no considerable mitral insufficiency developed.

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