APPARENT ATRIAL PARASYSTOLE ASSOCIATED WITH *EHRLICHIA CANIS* INFECTION IN A DOG. A CLINICAL CASE REPORT

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ABSTRACT

To date no clinical cardiac related changes have been documented or associated with canine monocytic ehrlichiosis (CME) caused by *Ehrlichia canis*. Evidence of increased activity of cardiac isoenzymes creatinine kinase and lactate dehydrogenase has been documented in dogs in the acute stage of the disease. In a recent study of serum cardiac Troponin I concentration in dogs with naturally acquired ehrlichiosis, acute infection with *E. canis* has been established to be a risk factor for myocardial injury. In a number of human cases of ehrlichiosis cardiac involvement has been reported. This communication presents for the first time a clinical case of CME associated with apparent electrocardiographic changes interpreted to be atrial parasystole. The electrocardiographic changes resolved following treatment for CME.

INTRODUCTION

Canine monocytic ehrlichiosis (CME) is a common worldwide tick borne disease caused by *Ehrlichia canis*. The principal vector of the rickettsia is the brown dog-tick *Rhipicephalus sanguineus*. After an incubation period of 8-20 days, signs of clinical disease appear characterized by fever, anorexia, weight loss, depression, lymphadenomegaly and splenomegaly. Dogs may present bleeding tendencies, mainly petechiae and ecchymoses of the skin and mucous membranes (1). After 1 to 4 weeks with no medical treatment (or after inadequate treatment) dogs may recover the acute disease and may enter the subclinical phase of CME (2). Dogs in this stage may remain persistent carriers of the rickettsia for months and years. Some dogs may subsequently develop the chronic pancytopenic form of the disease (3). Thrombocytopenia is the most common and consistent hematologic finding in all phases of CME. Mild leukopenia and mild anemia (usually non-regenerative normocytic normochromic) may occur in the acute stage of CME. The disease is a multi-systemic with clinical symptoms reflected mainly due to changes in the hematopoietic system. Besides the fever and hematological changes seen as a result of infection with *E. canis*, changes in liver enzymes indicative of liver involvement are commonly observed (4). There is a dearth of clinical reports of the effects of CME on specific organs, although ocular pathology is commonly reported (5-7). Until now, elctrocardiographic manifestations of heart disease in dogs with CME have not been described.

In this case presentation we describe for the first time an apparent association between potentially abnormal ECG findings, CME infection (presence of *E. canis* antibody and typical hematological findings) followed by therapy with Doxycycline and subsequent resolution of hematological changes, clinical signs and ECG findings.

CASE REPORT

A 10-year-old spayed female Maltese poodle-cross presented with symptoms of coughing. Her vaccination record was up to date. A full physical examination with a complete blood count (CBC) and blood chemistry examination were carried out. Auscultation of the lungs revealed fine crackles and a strong cough reflex which was readily elicited by tracheal palpation. Normal heart sounds were auscultated and no audible murmur was present. The clinical chemistry results were not indicative of any specific disease and a tentative diagnosis of low-grade bronchitis was made. A mild thrombocytopenia was noted (175 x 10^3 platelets/µL blood) (Table 1). The dog was treated with Ceforal (Cephalexin, Teva, Israel) (30 mg/kg PO q12). A month later after the owner reported no improvement treatment with enrofloxacin (Baytril, Bayer, Germany) (10 mg/kg q24) was initiated.

Four months after the initial examination, on account of the continuing cough, thoracic radiography was carried out, along with a repeat CBC. Two lateral (right and left) radiographs (Figure 1A & 1B) did not reveal any obvious pathological changes and there was no cardiomegaly of any kind (Vertebral

Heart Sum was 9.2v and 10.1v, respectively, while reference range in dogs is 9.7 ± 0.5v) (8) and pulmonary parenchyma appeared radiographically normal. No dorsoventral or ventro-dorsal radiographs were obtained. A tentative diagnosis was made of possible pulmonary fibrosis associated with aging. The CBC showed a mild decline in total leukocytes and a further drop in platelet numbers (117 x 10^3 platelets/μL blood). The mean corpuscular volume (MCV) was slightly decreased and the mean corpuscular hemoglobin concentration was slightly increased (Table 1). No treatment was instigated at that time.

Three months later (7 months following initial presentation) the owner reported signs of exercise intolerance and weakness. It was decided to carry out a repeat CBC and an electrocardiographic (ECG) examination. The ECG was examined for lead II (Figure 2): Heart rate and rhythm were normal (sinus rhythm with an **R**-to-**R** interval of 605±10 milliseconds, which translates to a heart rate of 99±2 bpm). Measurable amplitudes and intervals were all within reference range, as follows: PR=100 milliseconds, QRS=50 milliseconds, QT=180 milliseconds, R=0.7 millivolts). The only suspected abnormal finding was an extra, low-amplitude, positive deflection preceding the P-wave that occurred frequently and consistently over several consecutive cardiac cycles, although it's morphology and time interval relative to the following P wave was not constant. The differential diagnosis list included an artifactual recording, atrial parasystole, or atrial dissociation. Of these differential diagnoses atrial parasystole seemed to be the most relevant choice. The ECG appeared to show evidence of two independent atrial rhythms, one of which triggered a QRS complex while the other did not. Each of these two rhythms appeared to have its own "internal" P-to-P interval, and they did not interfere with each other.

At the time when the extra P-like wave was recorded the hematological parameters showed mild anemia, leukopenia and thrombocytopenia (Table 1). On the basis of these results a tentative diagnosis of canine monocytic ehrlichiosis was made. An indirect immunofluoresence antibody (IFA) test revealed a titer of IgG *E. canis* antibodies of 1:1280, which is considered indicative to exposure to *E. canis* (9). Treatment was commenced with Doxycycline (Doxylin, Dexxon, Israel) at 10 mg/kg PO SID for three weeks. After 10 days of treatment the owner reported that although the cough had still not resolved the dog was perkier and had returned to her normal self. At this stage the hematological parameters had all returned to within normal limits and the platelet count was now 356 x 10^3 platelets/μL blood, an increase of 104% from the count performed before commencement of treatment (Table 1).

The ECG was repeated (Figure 3) and demonstrated normal sinus rhythm at a heart rate of ~120/minute, with normal intervals and amplitudes which were essentially identical to those recorded previously, except for the absence of an extra P-like wave.

A follow-up CBC preformed 3 weeks later showed that the hematological parameters remained in the normal range (Table 1).

Echocardiography was carried out 8.5 months following initial presentation, revealing only trivial mitral, tricuspid, and aortic valve insufficiencies, with no resultant hemodynamic effects such as measurable abnormalities in atrial or ventricular internal diameter, ventricular force of contraction, or wall thickness. None of these findings was considered, in retrospect, as related to the previously documented electrocardiographic, hematological or other findings.

DISCUSSION

In the case presented in this report an apparent association has been found between potentially abnormal ECG findings, CME infection (presence of *E. canis* antibody and typical hematological findings), and resolution of hematological changes, clinical signs and ECG findings following Doxycycline therapy. The stage of infection with *E. canis* in this case may have been at first subclinical, suggested by the persistently reduced platelet counts, the increased mean platelet volume and *E. canis* antibody titer (2). For no apparent reason this may have regressed to the mild pancytopenic form. The reductions in erythrocyte, leukocyte and platelet counts were mild with parameters falling below the normal range. The rapid clinical response to treatment with the antibiotic Doxycycline and the quick return of the hematological parameters to within the normal range is added evidence for active CME infection (10).

This case appeared to be a case of progression of CME from the subclinical form to the chronic state. The factors responsible for the transition from subclinical to chronic ehrlichiosis are unknown and in this case no specific initiating cause could be identified. Possibly if this dog had not been treated promptly it would have declined into the chronic severe pancytopenic state with a poor prognosis. Besides the consistent thrombocytopenia seen, no other hematological parameters gave a suggestion of the ongoing disease (2).

The exact etiology of the cough and exercise intolerance was not established. A subjective impression of age-related pulmonary fibrosis was made on radiology. No further diagnostic procedures were carried out at the request of the owners. The cough remains static to this day without any further deterioration.

Although the ECG findings are compatible with either pace making or conduction aberrancies the exact nature of organic or structural changes is not known. Of the three differential diagnoses, artifactual recording, atrial parasystole, or atrial dissociation, atrial parasystole seemed to be the most applicable choice. The origin of this independent pacemaker appeared to be atrial as there was no inscription of a repolarization event, which would have been expected to follow ventricular depolarization. There appears to be two independent atrial

pacemaker sites remote from each other, one at the SA node that "fired" normally and the other elsewhere in one of the atria.

The possibility that this finding was artifact must also be considered (11). Although this is a possibility, its likelihood is considered low: the association of the additional P-wave during the pinnacle of the disease and its disappearance after treatment with resolution of the clinical signs may add some credibility to ECG recordings, both at the time of the disease and at recovery. The diagnosis of atrial dissociation has also been rejected due to its being very rare and typical of advanced heart disease (unlike the presently reported patient) and due to the fact that, as opposed to the trace in the presently reported patient, its P-like wave is typically smaller than the one resulting from sinus rhythm. (11, 12)

To the authors' knowledge no association between CME and electrocardiographic changes has yet been made in dogs. Evidence of possible cardiologic effects of CME may be based on post mortem and histological findings, as well as on biochemical studies. Epicardial and endocardial hemorrhages have been observed in 84% of dogs dying from CME (13). Histologically, hemorrhage was seen to extend between myocardial fibers but did not appear to originate from myocardial blood vessels. In addition, the blood vessels in the myocardial fat were often surrounded with both plasma cells and reticuloendothelial cells. Small foci of mononuclear cells were observed in close proximity to small vessels in the myocardium and only one dog had a focus of non-suppurative myocarditis (13). Further evidence of CME-related cardiac injury was seen in a study carried out on dogs artificially infected with *E. canis*. This study showed an increase in the activities of the serum cardiac isoenzymes creatinine kinase and lactate dehydrogenase during the acute phase of the disease (14). In a recent study of serum cardiac Troponin I concentration in dogs with ehrlichiosis, acute infection with *E. canis* was found to be a risk factor for myocardial injury in naturally infected **B**razilian dogs. The authors were however not able to evaluate the contribution of the severity of anemia and systemic inflammatory response syndrome which might have also contributed to the pathophysiology of myocardial damage in these dogs (15).

Human monocytic ehrlichiosis (HME) is caused by the monocytotrophic ehrlichial agent *Ehrlichia chaffeensis* that is closely related to *E. canis* (16). Although considered rare, a number of clinical cases of HME associated with myocardial changes have been described in humans (17-20). A recent case report has documented severe myocarditis and congestive heart failure in a human patient diagnosed with human monocytic ehrlichiosis. The patient recovered promptly after the initiation of treatment with doxycycline (19). Myocardial cell infiltrates with edema have been observed with *E. chaffeensis* infections in man (21). It has been suggested that macrophages activated by Ehrlichia species through the effects of interferon-γ may infiltrate the myocardium and produce pro-inflammatory cytokines or induce their production by other cells (22, 23). Whether similar myocardial pathophysiology occurs in canine patients with CME remains to be investigated.

In conclusion, this report presents a case of chronic CME associated with suspected electrocardiographic changes. To the best knowledge of the authors this is the first clinical report of a possible relationship between infection with *E. canis* and abnormal electrocardiographic findings in a dog. Further research is warranted to clarify the association between CME and its potential cardiac effects.

Legends to figures

Figure 1A
Thoracic radiograph in right lateral recumbency in a 10 year old female spayed dog with CME, 4 months following initial presentation with a chronic cough.

Figure 1B
Thoracic radiograph in left lateral recumbency of the same dog as in Figure 1A.

Figure 2
ECG lead II rhythm strip (10 mm/mV, 50 mm/sec) recorded during the chronic phase of CME from the same dog as in Figure 1, 7 months following initial presentation. Note the suspected extra P-wave.

Figure 3
ECG lead II (10 mm/mV, 50 mm/sec) recorded from the same dog as in Figure 1, 10 days after treatment with Doxycycline and recovery from symptoms and clinical signs. Note the disappearance of the extra P-wave.

Figure 1A

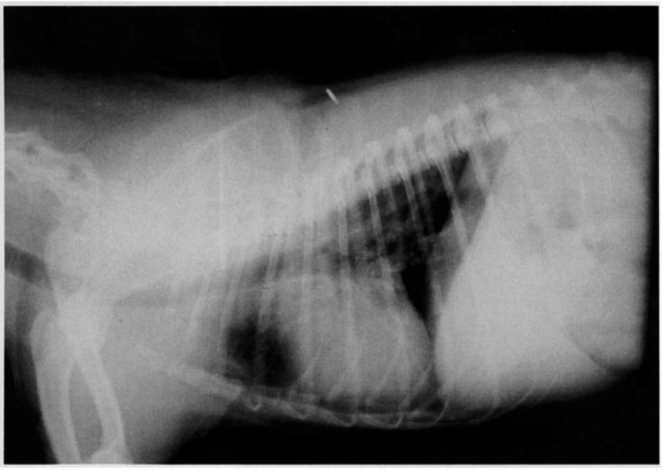

Figure 1B

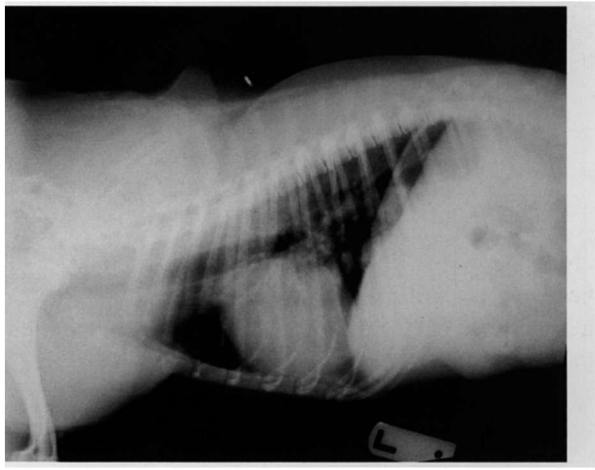

Figure 2

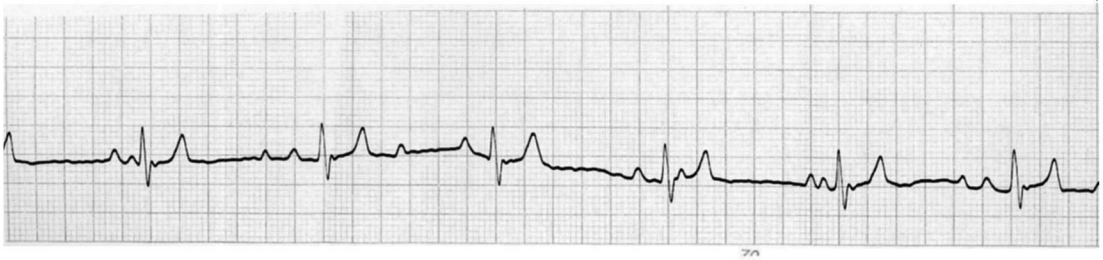

Figure 3

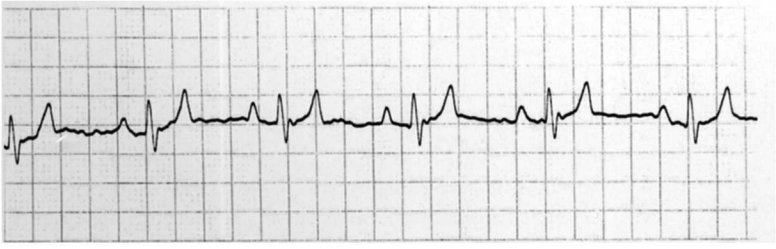

Table 1. Hematological results
Sequential hematological findings documenting the subclinical stage of CME, the chronic pancytopenic disease and the recovery phase after treatment with Doxycycline.

Date/Parameter	*Units*	*17 Mar 06*	*7 Jul 06*	*13 Oct 06*	*24 Oct 06*	*2 Nov 06*	*Normal ange*
Hematocrit	%	45.8	37.4	29.2	40.4	48.7	*37-55*
Erythrocytes	x 10^6/µl	6.93	6.82	5.27	6.56	7.53	*5.5-8.5*
Hemoglobin	g/Dl	13.9	13.8	11.3	13.2	14.9	*12.0-18.0*
MCV	μ^3	66.1	54.8	55.2	61.6	64.7	*60-77*
MCH	ρg	20.1	20.2	21.4	20.1	19.8	*19.5-24.5*
MCHC	%	30.4	36.9	38.7	32.7	30.6	*32-36*
Reticulocytes	%	nr	0.19	1.45	0.68	0.19	*0.0-1.5*
Platelets	x 10^3/µl	175	117	174	356	393	*200-500*
MPV	μ^3	7.5	19.5	16.3	11.5	11.5	*5-15*
Leukocytes	x 10^3/µl	6.24	5.62	4.50	7.70	6.02	*6-17*
Neutrophils	x 10^3/µ	4.54	4.22	2.22	5.56	5.04	*3-11.5*
Lymphocytes	x 10^3/µ	0.95	1.05	1.57	1.17	0.51	*1.0-4.8*
Monocytes	x 10^3/µ	0.56	0.17	0.62	0.52	0.19	*0.15-1.35*
Eosinophils	x 10^3/µ	0.28	0.16	0.07	0.35	0.24	*0.01-1.25*
Basophils	x 10^3/µ	0.03	0.02	0.02	0.01	0.04	*0-0.5*

nr = no result

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ERRATUM

*Histophil*us somi in Israel

In a recently published abstract (1) we stated that "*H. somni* was first described in Israel in 1991, from a case of bovine mastitis. Further cases were not reported until 2002". In fact, as pointed out by Dr. A. Grinberg, who isolated and published the abovementioned case, the microorganism was isolated in 1993 from cases of calf pneumonia and semen of clinically healthy bulls (2). Moreover, the microorganism was isolated from the lungs of a calf diagnosed histo-pathologically as being afflicted by Trombotic Meningoencephalitis, in 1994 (3). All these cases occurred in the northern region of Israel. Unfortunately these reports were overlooked due to the limitations of electronic bibliographic searches.

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