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Epistaxis and Its Clinical Reflection Among Dogs: 34 Cases Recorded Between 2007-2017

Epistaksis ve Köpeklerdeki Klinik Yansımaları: 2007-2017 Arasında Kaydedilmiş 34 Vaka

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ABSTRACT Objective: Epistaxis is a relatively remarkable clinical symptom in dogs that should be included in the differential diagnoses of diseases. **Material and Methods:** The present author's interest in this subject arose following receipt of several cases within the last 10 years. The purpose of the present article was to evaluate 34 dogs with epistaxis retrospectively. **Results:** There was bilateral (n=13) or unilateral (n=21) epistaxis, in which chronicity was evident in 13 dogs. Etiology deemed infectious (n=28), non-infectious (n=5) and unknown origin (n=1) causes. The infectious causes involved 13 cases with canine visceral leishmaniasis and other 9 with canine monocytic ehrlichiosis, followed by 6 co-infected dogs. Activated partial thromboplastin time was significantly ($p<0.001$) prolonged in coinfected groups. Regarding mean prothrombin time, a statistically important prolongation ($p<0.001$) was evident among leishmaniasis within other groups. Mean FIB values deemed elevated among all infected groups in contrast to healthy ones ($p<0.001$). Mean platelet values were decreased in *E. canis* mono and co-infected groups ($p<0.001$). Non-infectious diseases consisted of firearm injury (n=2), nasal malignant melanoma (n=1), lymphoma (n=1) and autoimmune hemolytic anemia (n=1). **Conclusion:** Taking into account review of this case series, it might be suggested that epistaxis should be on the list of clinical signs for infectious and non-infectious causes, which should be promptly treated based on probable tests and relevant findings.

Keywords: Coagulation; dog; epistaxis; vector-borne disease

ÖZET Amaç: Epistaksis, köpeklerde hastalıkların ayırıcı tanısında yer alması gereken nispeten dikkat çekici bir semptomdur. **Gereç ve Yöntemler:** Mevcut yazarların bu konuya ilgisi, çalışmanın amacını da içeren son 10 yıl içerisinde karşılaşılan çeşitli vakalar arasından 34 epistaksisli köpeğin değerlendirilmesi ile ortaya çıkmıştır. **Bulgular:** Mevcut olan iki taraflı (n=13) ya da tek taraflı (n=21) epistaksisli vakaların 13'ünde, kronik gelişim söz konusuydu. Enfeksiyöz (n=28), nonenfeksiyöz (n=5) ve sebebi bilinmeyen (n=1) etiyolojik faktörler ile karşılaşıldı. Enfeksiyöz nedenler arasında, 13 vakada kanin viseral layşmanyazis ve 9'unda kanin monositik erlişyoz teşhis edilmişken; bunların 6'sında koenfeksiyon belirlendi. Koenfekte grupta aktive edilmiş kısmi tromboplastin süresinin anlamlı şekilde uzadığı ($p<0,001$), ortalama protrombin zamanı değerinde ise diğer gruplara göre layşmanyazis ile enfekte olanlarda, istatistiksel olarak önemli uzama meydana geldiği görüldü ($p<0,001$). Sağlıklılara göre ortalama FIB değerleri, tüm enfekte gruplar arasında yüksek bulundu ($p<0,001$). Ortalama trombosit değerlerinin, *Ehrlichia canis* ile mono ve koenfekte gruplarda azaldığı görüldü ($p<0,001$). Non-enfeksiyöz hastalıklar arasında ateşli silah yaralanması (n=2), nazal malign melanom (n=1), lenfoma (n=1) ve otoimmün hemolitik anemi (n=1) yer almaktaydı. **Sonuç:** Birçok vakanın değerlendirilmesi göz önünde bulundurulduğunda epistaksisin, olası testler ve ilgili klinik bulgulara dayanan sağaltımının yer alması gereken enfeksiyöz ve non-enfeksiyöz nedenler için klinik bulgular arasında yer alması önerilmektedir.

Anahtar Kelimeler: Koagülasyon; köpek; epistaksis; vektör kökenli hastalıklar

Epistaxis is a well-recognized and unfrequent clinical sign to those of dogs with a probable systemic disorder or selected nasal disease.[1-4] It has been established that entire clinical/physical interpretation deemed necessary, because of extra unique local (i.e., tumors or mycotic infestation) or systemic (i.e., bleeding tendency, hyperviscosity syndrome) disorders affecting in partial prognosis and therapeutical applications.[5]

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Conducting a search on the occurrence of epistaxis and its spatial distribution among dogs with vector-borne diseases, some selected studies were analyzed in which there is a lack of sufficient data. Furthermore, given the possibility that in geographic areas highly endemic for vectorborne diseases, similar to the present authors' residing area, the incidence of the disorders eventually leading to epistaxis in dogs could be somewhat different.[6,7] Therefore the purposes of this study were to detect a) the incidence of underlying diseases associated with epistaxis in dogs b) the roles of vector-borne diseases and c) to highlight the homeostasis and coagulative alterations among selected diseases.

MATERIAL AND METHODS

DIAGNOSTIC PROCEDURES

Official records for enrolled cases presenting nasal bleeding in the present research were reviewed, and data regarding signalment, clinical signs, laboratory alterations, and presumptive diagnosis were achieved. The diagnostic tree in an attempt to detect underlying probabilities were detected as follows: (i) canine monocytic ehrlichiosis (CME) was diagnosed based on rapid diagnostic test kits (Snap 4Dx plus, IDEXX, USA) and/or conventional polymerase chain reaction in blood and/or the microscopical visualization of *Ehrlichia canis* morulae as detected via Giemsa staining through lymph node aspiration; (ii) canine leishmaniasis (CanL) as determined via rapid diagnostic ELISA test kits (Snap Leishmania, IDEXX, USA) and immunofluorescent antibody test analysis and if amastigote detection via lymph node aspiration; (iii) anticoagulant toxication by insecticides or pesticides via coagulation monitorization (prolonged partial thromboplastin time and prothrombin time) inclusive of history of restoration of hemostatic function subsequent therapy with vitamin K; (iv) immune-mediated thrombocytopenia according to disease severity, (v) tumoral changes were detected via surgery and/or histopathologic investigation.[8,9] Healthy dogs were selected from clinic for vaccination and general control purposes. Anemia were classified as mild (HCT >30%), moderate (HCT 15-30%) severe (HCT <15%) and very severe (HCT <%10) according to routine hemogram analysis.

STATISTICAL ANALYSES

The mean and standard error values of the activated partial thromboplastin time (aPTT), prothrombin time (PT), fibrinogen (FIB) and platelet (PLT) values obtained from the study were tabulated. ANOVA test was used to determine the differences between groups in the data with normal distribution. Spearman correlation analysis was used to perform the correlation analysis. In all analyzes, using the SPPS 21.0 (IBM) program, cases where the p value was below 0.05 was considered statistically significant.

RESULTS

CLINICAL FINDINGS AND RELEVANT DATA

Thirty-four dogs were enrolled in the present study. Out of those, 15 (44%) were intact males and 19 (56%) females with a mean age of 5.7 (±3.5) years (range 1 to 13 years). Twenty-one (62%) of these dogs were purebreds representing a total of 12 breeds and 13 (38%) crossbreds. In 13 (38%) dogs; epistaxis was detected at initial referral and/or during hospitalization and in 21 (62%) dogs at least for 2 weeks duration. Epistaxis was secondary to infectious diseases in 28 (82%) dogs, non-infectious diseases in 5 (15%) dogs and there was a case with unknown etiology (3%). Epistaxis was bilateral in 13 (38.2%) dogs and unilateral in 21 (62%) dogs.

Infectious diseases included mono infection of canine visceral leishmaniasis (CVL) (n=13), CME (n=9) and co-infection of CME with CVL (n=3), canine granulocytic anaplasmosis (CGA) (n=1) and dirofilariasis (n=1) as well as a case with triple co-infection of CME, CVL and CGA. Clinical findings included lymphadenopathy (n=11), weight loss (n=7), alopecia (n=6), skin lesions (n=6), pale mucous membrane (n=5), onychogryphosis (n=4), depression (n=3), keratoconjunctivitis (n=3), anorexia (n=2), polyphagia (n=1), abdominal pain (n=1), edema (n=1), arrhythmia (n=1), tracheitis (n=1), pharyngitis (n=1) and uveitis (n=1) whereas severe anemia (n=10), moderate anemia (n=7), mild anemia (n=6), very severe anemia (n=3) and

thrombocytopenia (n=8) were detected as abnormal laboratory findings.

Non-infectious diseases consisted of firearm injury (n=2), nasal malignant melanoma (n=1), lymphoma (n=1) and autoimmune hemolytic anemia (n=1). Weight loss was presented solely in 1 case whereas mild anemia (n=2), moderate anemia (n=1), severe anemia (n=1) and thrombocytopenia (n=2) were detected as abnormal laboratory findings (Table 1).

In comparison to the healthy group, aPTT was significantly ($p<0.001$) prolonged in leishmaniasis and *E. canis* coinfected groups. Regarding mean PT, statistically important prolongation ($p<0.001$) was evident among Leishmaniasis within other groups. Mean fibrinogen values deemed elevated ($p<0.001$) among all infected groups in contrast to healthy ones. Mean PLT values were decreased in *E. canis* mono and co-infected groups ($p<0.001$) (Table 2). There was positive and mild ($p<0.05$, $r=0.341$) correlation among FIB and aPTT values as shown in Table 3.

DISCUSSION

In a prior research in the USA emergency veterinary clinics, 176 dogs were enrolled, and 32 animals (75%) were examined at admission with a prevalence of 0.3% epistaxis. Dogs with epistaxis admitted to the clinics were at older ages (≥6 years), male, and large breed (≥26 kg). Out of 176 dogs, 109 (62%) with epistaxis, were achieved a precise diagnosis with local causes (trauma, rhinitis with unknown etiology, nasal tumor, and abscess formation) or systemic etiology (vasculitis, thrombocyte, and coagulation disorders and hypertension).[10] Cases presenting local etiology were more prone to show unilateral in contrast to bilateral epistaxis, whereas eleven out of twenty-one (52%) dogs with systemic disorders also had unilateral epistaxis.[11] Epistaxis was retrospectively evaluated previously among 35 dogs, of which 7 (mean 5.6 years) showed systemic disease and other relevant 29 cases with an intranasal disease. Those of dogs at an older age (mean 10.0 years) with intranasal disease, 19 presented neoplasia. In dogs with intranasal disease, epistaxis was persisting for >1 month. According to the latter researchers' unilateral epistaxis was not associated with intranasal or systemic disorder, on the other hand, cases presenting systemic disorder presented declined packed cell volume (mean 31.8%) in contrast to cases showing nasal pathology (mean 42.7%).[12] In the present study, spatial distribution of epistaxis was acute (n=21) or chronic (n=13), unilateral (n=21) or bilateral (n=13). Regarding etiological examination, 5 of them were non-, and 28 of the dogs presented infectious disease. To those of infectious diseases, CVL (n=13) and CME (n=9) were frequently observed. Similarly, a previous paper indicated that CVL and CME are the major reasons for canine epistaxis in Greece.[13] Epistaxis exists in 10-27% percent of CME affected dogs frequently associated with thrombocytopenia and/or thrombocytopathy.[6,14-20] Besides, it may be related to the chronic myelosuppressive phase of CME.[6,14,15] On the other hand, about 10-15% of dogs with CanL might present epistaxis.[9,21-23] The proposed pathogenesis of CanL-induced epistaxis composed of chronic rhinitis and defective hemostasis.[24-26]

In a prior research, 30 dogs were naturally infected with CVL (subclassified into-oligo-symptomatic, symptomatic, and markedly symptomatic dogs) as described by Ciaramella et al. and those of 10 dogs (healthy group) were analyzed for homeostasis.[22] In that study, the authors proposed that in dogs with severe clinical signs involvement of the intrinsic pathway has been elucidated based on prolonged APTT levels. The latter authors claimed that declined synthesis along with an elevated consumption of clotting factors might be due to chronic inflammatory conditions.[11] Similar findings were also suggested previously by Moreno.[25] The latter study suggested that in naturally existing CVL primary and secondary hemostasis and related changes exist due to the severity of clinical signs.[11] In the present study, APTT was significantly ($p<0.001$) prolonged in *CVL* and *CME* coinfected groups. On the other hand, PT was significantly prolonged ($p<0.001$) among *CVL* infected dogs, suggesting coagulation alterations among selected vector-borne diseases in this study.

In-depth researches have been performed on PT derived fibrinogen, APTT derived fibrinogen has

TABLE 1: Evaluation of 34 cases with epistaxis between the years 2007-2016.

No	Year	Breed	Age	Sex	Epistaxis	Acute/Chronic	Clinical findings	Diagnosis	HCT	RBC	Hb	PLT	WBC
1	2007	Terrier	13	F	UL	A	Weight, loss melanoma	Nasal malignant	34.84	5.7	11.8	136	24
2	2008	Pointer	9	F	UL	A		Firearm injury	47	5.86	16	420	33.1
3	2008	Doberman	10	F	UL	A	Pale mucous membrane, alopecia, onychogryphosis	CVL	18.13	3.09	5.8	753	10.7
4	2008	Doberman	1.5	F	BLT	A	Pale mucous membrane, lymphadenopathy	CME	13.06	1.83	3.1	8	8.6
5	2008	Kangal	3	M	BLT	C	Skin lesions, lymphadenopathy	CVL	16.94	2.81	5.3	202	5.4
6	2008	German shepherd	3	M	UL	C		CVL+CME	25.6		8	146	9.7
7	2009	English Setter	12	F	UL	A	Keratoconjunctivitis, lymphadenopathy	CVL	31.9	4.07	9.8	159	3.9
8	2008	Pekinese	8	M	UL	A		CME	14.68	2.3	4.2	10	5.94
9	2009	Mix	3	M	BLT	C	Alopecia, crusting of the skin, lymphadenopathy, weight loss, keratoconjunctivitis, anorexia	CVL	14.87	2.8	4.5	NA	15.4
10	2009	Mix	2.5	F	UL	A		CVL	33	NA	12.1	NA	9.3
11	2010	Mix	10	F	UL	C	More than 1 year	Firearm injury	36.28	4.61	12.9	NA	28.7
12	2010	German shepherd	7	M	UL	A	Depression, abdominal pain	CME	30	NA	NA	NA	20.6
13	2010	Samoyed	4	M	BLT	C		CME	45.77	7.05	15.3	314	8
14	2010	Mix	10	F	BLT	C	Weight loss, skin lesions, conjunctivitis, onychogryphosis	CVL	22.36	3.62	8.3	412	10.8
15	2010	Mix	4	F	UL	A	Lymphadenopathy, skin lesions, onychogryphosis	CVL	27.17	4.04	8.9	222	7.4
16	2012	Mix	3	F	BLT	C	Alopecia, scaling of the skin, weight loss, onychogryphosis	CVL	32.86	5.66	10.5	253	10.6
17	2012	Golden retriever	5	F	UL	C		CME	17.46	2.93	6	12	9.4
18	2012	Boxer	10	M	UL	C		CME	47.22	6.74	17.2	455	30.7
19	2012	Mix	7	F	UL	C	Anorexia, fatigue	CME	22	2.71	6.8	36	33.1
20	2013	Mix	2.5	M	UL	A		CVL	13.46	2.83	4	532	14.4
21	2014	Sharpie	6	M	BLT	C		Unknown	15.27	2.44	5.4	256	35.1
22	2014	Mix	3.5	F	UL	A	Alopecia, scaling of the skin, lymphadenopathy	CVL	41.64	5.32	13.2	307	11
23	2014	Golden retriever	3.5	M	UL	A	Polyphagia, weight loss, lymphadenopathy, pale mucous membrane	CVL	15.27	2.44	5.4	256	11
24	2014	Mix	13	F	UL	A	Lymphadenopathy, edema, abdomen mass, the cysts in ultrasonography	CME	38.44	5.94	13.1	278	16.6
25	2014	Kangal	7	M	BLT	A		Lymphoma	19.57	2.71	6.4	175	10
26	2015	Terrier	8	F	BLT	A	Autoimmune hemolytic anemia		23.6	3.41	9.3	1	20.4
27	2015	Kangal	1.5	M	BLT	A	Weight loss, alopecia	CVL	35.9	5.22	13.5	275	16.4
28	2015	German shepherd	6	M	UL	A	Lymphadenopathy, weight loss	Anaplasmosis+CME+CVL	20.4	3.01	7.3	300	7.8
29	2015	Mix	8	M	BLT	C	Arrhythmia, tracheitis, pharyngitis, lymphadenopathy	CME+Dirofilariasis	31.79	4.73	11.6	148	9.4
30	2015	Pointer	2.5	F	BLT	A	Pale mucous membrane, lymphadenopathy	CME	18.24	2.96	5.7	4	0.7
31	2015	Rottweiler	1	M	UL	A	Tick infestation	CME+Anaplasmosis	23.22	3.67	7.9	61	12.9
32	2016	Mix	2	F	BLT	A	Pale mucous membrane, weight loss, alopecia, depression, uveitis	CME+CVL	10.2	1.41	4.3	156	4.7
33	2008	Mix	1.5	F	UL	C	Systemic findings	CME+CVL	7.9	NA	2.3	NA	
34	2015	Pointer	5	F	UL	A		CVL	20.2	3.5	7.5	320	

HCT: Hematocrit; RBC: Red blood cell; Hb: Hemoglobin; PLT: Platelet; WBC: White blood cell; UL: Unilateral, BLT: Bilateral; CVL: Canine visceral leishmaniasis; CME: Canine monocytic ehrlichiosis.

TABLE 2: Coagulation parameters and relevant data among groups.

	aPTT (X ±SE)	PT (X 0±SE)	FIB (X ±SE)	PLT (X ±SE)
Healthy	11.1±0.6[a]	7.5±0.6[a]	140.7±41.5[a]	330±108[a]
Ehrlichia canis	15.0±9.8[ab]	8.2±1.6[a]	324.7±212.4[b]	139±169[b]
Ehrlichia canis coinfection	19.3±8.8[bc]	8.6±1.3[a]	401.5±222.5[b]	150.2±82.5[b]
Leishmaniasis	20.6±8.3[c]	15.6±8.8[b]	341.1±155[b]	309±169[a]

APTT: Activated partial thromboplastin time; PT: Prothrombin time; FIB: Fibrinogen, PLT: Platelet; SE: ; a,b,cValues expressed with different letters in the same column are statistically different.

been rarely suggested.[27] In some cases, i.e., monitorization of heparin treatment, PT could not be available. Hence APTT could easily be used as a replacement for estimating the fibrinogen levels for tracking the alterations among fibrinogen levels during selected disorders (i.e., disseminated intravascular coagulation, hyper/hypo-fibrinogen).[28] In the present study a positive ($p<0.05$, $r=0.341$) correlation among FIB and APTT values were detected. This might be briefly explained with the relationship among inflammation and coagulation (change), or it may be suggested that during clinical disease state in CVL, hemorrhagic diathesis might occur, not only due to the existence of the parasite but also related to inflammation, immunocompetence and probably because of hepatic/renal failure.[29]

CONCLUSION

In conclusion, our research suggesting that CanL and CME are the foremost etiological disorders for epistaxis among dogs, enrolled in present study, in Turkey. From an etiological point of view, palled mucosae, coagulation disorders and pancytopenia in a relationship with CME and peripheral lymphadenomegaly and hyperproteinaemia related to CanL, have all been observed as the vast majority of cases leading to epistaxis. Taking into account review of case series, it might be suggested that epistaxis should be on the list of clinical signs for infectious and non-infectious causes, which should be promptly treated based on probable tests and relevant findings.

TABLE 3: Correlation among coagulation parameters.

	aPTT	PT	FIB	PLT
aPTT				
PT	0.326			
FIB	0.341*	0.118		
PLT	-0.299	0.127	0.298	

APTT: Activated partial thromboplastin time; PT: Prothrombin time; FIB: Fibrinogen, PLT: Platelet.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Serdar Paşa, Kerem Ural, Hasan Erdoğan;* ***Design:*** *Serdar Paşa, Kerem Ural, Hasan Erdoğan;* ***Control/Supervision:*** *Serdar Paşa, Kerem Ural, Mehmet Gültekin, Hasan Erdoğan, Songül Erdoğan;* ***Data Collection and/or Processing:*** *Serdar Paşa, Hasan Erdoğan, Mehmet Gültekin, Songül Erdoğan;* ***Analysis and/or Interpretation:*** *Serdar Paşa, Kerem Ural;* ***Literature Review:*** *Hasan Erdoğan, Serdar Paşa;* ***Writing the Article:*** *Serdar Paşa, Kerem Ural, Hasan Erdoğan, Mehmet Gültekin, Songül Erdoğan;* ***Critical Review:*** *Serdar Paşa, Kerem Ural, Hasan Erdoğan;* ***References and Fundings:*** *Serdar Paşa, Kerem Ural, Mehmet Gültekin, Songül Erdoğan;* ***Materials:*** *Mehmet Gültekin, Hasan Erdoğan, Songül Erdoğan.*

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