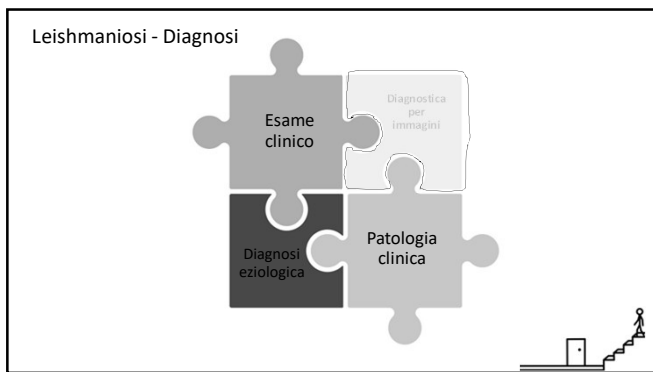
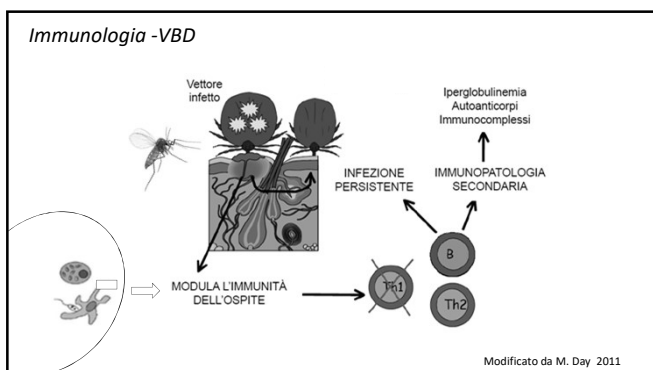


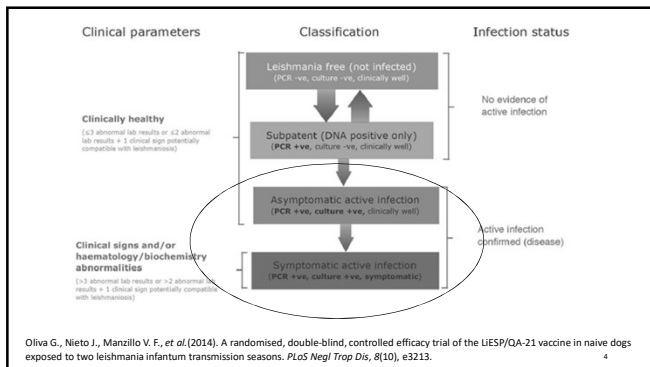
Quadri clinici comuni e atipici della leishmaniosi canina

Francesco Dondi
DVM PhD Ricercatore
Dipartimento di Scienze Mediche Veterinarie
Alma Mater Studiorum - Università di Bologna

Consulente Laboratorio «La Vallonée»
Nefrologia e Urologia







LEISHMANIOSI CANINA
SEGNI CLINICI

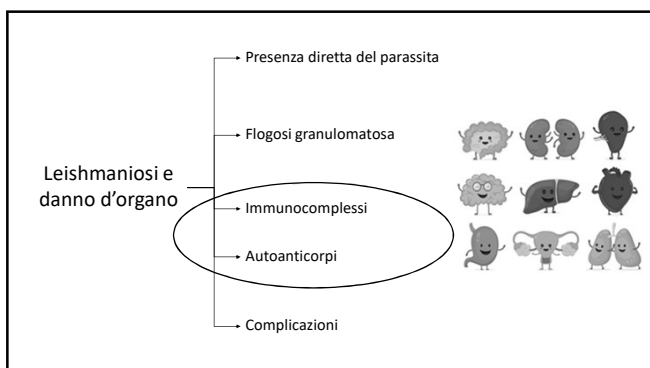
Tabella 1. Segni clinici e alterazioni clinicopatologiche riscontrabili nella Cani, causata da L. infantum.

SEGNI CLINICI	ALTERAZIONI DI LABORATORIO
Sistemi	CBC/Emiscat
<ul style="list-style-type: none"> ① Aumento di volume dei linfonodi splenici ② Febbre di punto ③ Diminuzione o aumento dell'appetito ④ Letargia ⑤ Punture della mucosa ⑥ Spontanea ⑦ Polmonite e polipneumonia ⑧ Anemia ⑨ Diarrea 	<ul style="list-style-type: none"> ① Anemia regenerative linea o moderata ② Leucopenia o leucopenia relativa, neutrofilia, monocitosi ③ Trombocitopenia ④ Trombocitopenia ⑤ Anemia differenziale secondaria a trombociti
Cutanei	Profilo ematologico ed elettrolitico delle proteine sieriche
<ul style="list-style-type: none"> ① Dermatite eruttiva non pruriginosa con o senza alopecia ② Dermatite eruttiva alopetica ③ Dermatite nodulare ④ Dermatite pustolosa ⑤ Dermatite pustolosa ⑥ Dermatite pustolosa ⑦ Dermatite pustolosa ⑧ Dermatite pustolosa ⑨ Dermatite pustolosa 	<ul style="list-style-type: none"> ① Spontanea ② Spontanea ③ Spontanea ④ Spontanea ⑤ Spontanea ⑥ Spontanea ⑦ Spontanea ⑧ Spontanea ⑨ Spontanea
Organi	** CBC - complete blood count (serie ematologica)
<ul style="list-style-type: none"> ① Binfite (infestazione, ulcera o noduli) ② Chondrodisplasia, ulcera o noduli ③ Chondrodisplasia, ulcera o noduli ④ Chondrodisplasia 	
Altri	
<ul style="list-style-type: none"> ① Lesioni mucocutanee e mucocutanee a noduli (nodi, gonfiori e noduli) ② Lesioni ③ Lesioni ④ Lesioni ⑤ Lesioni ⑥ Lesioni ⑦ Lesioni ⑧ Lesioni ⑨ Lesioni 	

“Segni clinici” di leishmaniosi

↓

segni clinici e/o alterazioni di laboratorio !



Leishmaniosi e Immunocomplessi



Ricorda:

i cani che hanno forme cliniche caratterizzate da lesioni riferibili a immunocomplessi hanno prognosi peggiore !

STADIO III Malattia grave	Testi anticorpali da molti a elevati	Cani che, oltre ai segni clinici elencati negli Stadi I e II, presentano prominenti segni causati da lesioni da immunocomplessi (p.g. uveite o glomerulonefriti)	Alterazioni clinicopatologiche elencate negli Stadi I e II Insufficienza renale cronica (IRC) in stadio IRG con $SCr > 1.5$ e stadio II (proteinuria $1.0-2.0 \text{ mg/dl}^{***}$)	Allopiurismo + anemia di regimetro + insufficienza	Da riservare a infetti
------------------------------	-----------------------------------------	------------------------------------------------------------------------------------------------------------------------------------------------------------------------------	--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------	-------------------------------------------------------	---------------------------

LeishVet



Immunocomplessi e danno d'organo

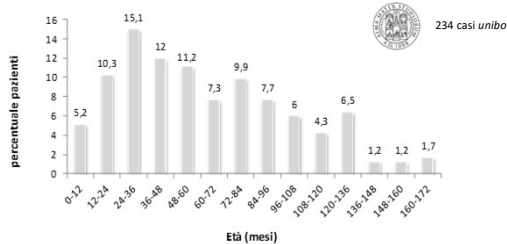


Distretti più sensibili al deposito di complessi immuni:

- | | |
|---------------|-----------------------------------------------|
| Vasi | → vasculite |
| Rene | → glomerulonefrite |
| Articolazioni | → poliartrite |
| Occhio | → uveite |
| Muscolo/cuore | → miosite, miocardite, versamento pericardico |
| Meningi | → meningoencefalite ... ? |
| Ossa | → osteo-periostiti e osteolisi ? |

Leishmaniosi – Segnalamento – età

Distribuzione dell'età nei pazienti con leishmaniosi
espressa in percentuale

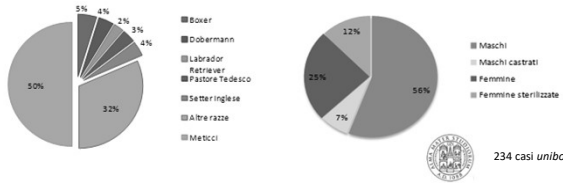


Leishmaniosi - Segnalamento

Razza: tutte le razze

Boxer e Pastore tedesco sono più rappresentate in letteratura

Sesso: alcuni studi riportano una prevalenza maggiore nei cani sesso maschile



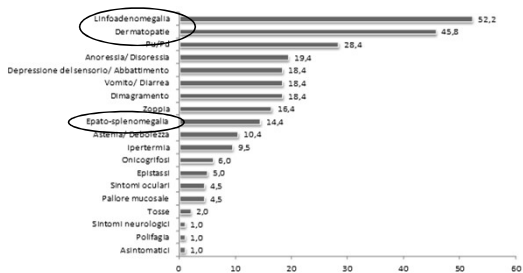
Leishmaniosi – Anamnesi !

Anamnesi ambientale è ancora fondamentale !



Leishmaniosi: segni clinici

234 casi unibo



Linfoadenomegalia generalizzata – diagnosi differenziali

- malattie infettive/infezioni disseminate
 - Virus/funghi/parassiti, malattie granulomatose
 - Ehrlichiosi, *Leishmaniosi*, Borreliosi ...
 - Dermatopatie diffuse
- malattie immunomediate/autoimmuni
 - Lupus eritematoso sistemico, poliartriti, cellulite giovanile
 - Reazione a farmaci (es. ciclosporina)
- neoplasie "emopoietiche"
 - linfoma, neoplasie istiocitarie (sarcoma istiocitario), leucemie ...
- metastasi ai linfonodi

Splenomegalia – diagnosi differenziali

Congestione
 Infarto splenico
 Iperplasia
 Emopoiesi extramidollare
 Ematoma
 Infiammazione/infezione
 Masse spleniche (neoplastiche e non neoplastiche)
 Neoplasie

Virali
 Epatite infettiva (adenovirus)
Rickettsial and Mycoplasmal
 Ehrlichiosi and anaplasmosi
 Rickettsiosi ?
Batteriche
 Batteriemia
 Bartonellosi
 Brucellosi
 Endotossemia
 Borreliosi (Lyme)
 Salmonellosi
 Tularemia
Micobatteri
Micosi
Protozoi
 Babesiosi
 Hepatozoonosi
Leishmaniosi
 Toxoplasmosi

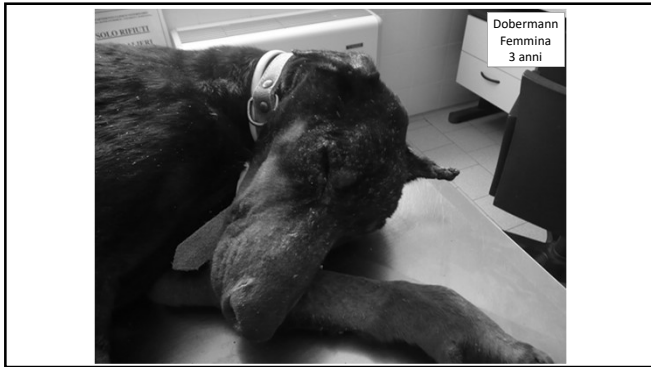
S.J.Ettinger, E.C.Feldman, E.Cote; Textbook of veterinary internal medicine: diseases of the dog and the cat, 8th edition, Elsevier, [2017]

Research Article
Prevalence of Dermatological Presentations of Canine Leishmaniasis in a Nonendemic Area: A Retrospective Study of 100 Dogs

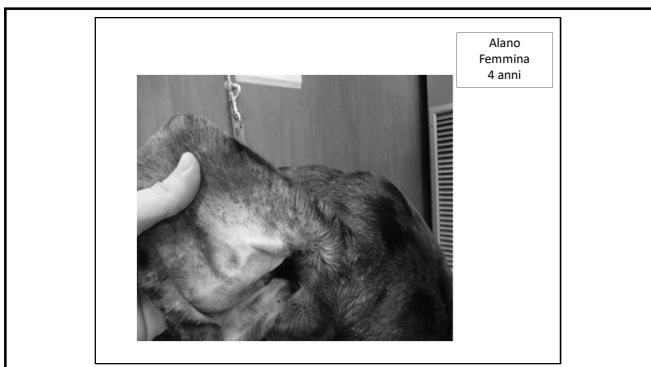
Roberta Pirog, Daniela Ferracini, Giada Ruggirelli De Giorgi, and Eva Spada
 Department of Clinical, Animal and Human Sciences, University of Bari, Italy
 J. Vet. Med. (2017) 2017, 1–5

TABLE 1: Distribution of dermatological manifestation of CanL in all 100 dogs and in 21 dogs in the group with only dermatological manifestations of CanL and no identifiable systemic signs.

Dermatological form or manifestation in 100 dogs	Number of subjects	Prevalence
Exfoliative dermatitis with or without alopecia	74	74%
Ulcerative dermatitis	18	18%
Nodular form	11	11%
Onychogryphosis	10	10%
Nasal and digital hyperkeratosis	9	9%
Nasal depigmentation	1	1%
Sterile pustular dermatitis	1	1%





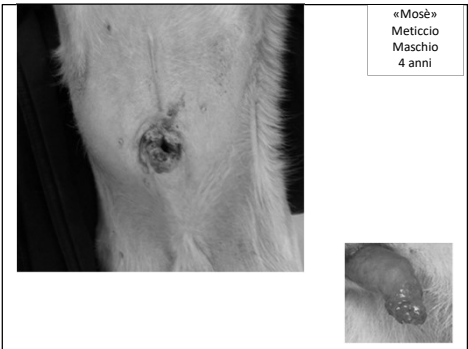




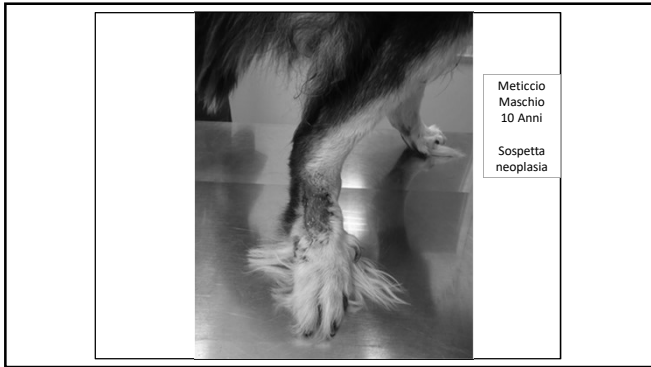
«Mosè»
Meticcio
Maschio
4 anni

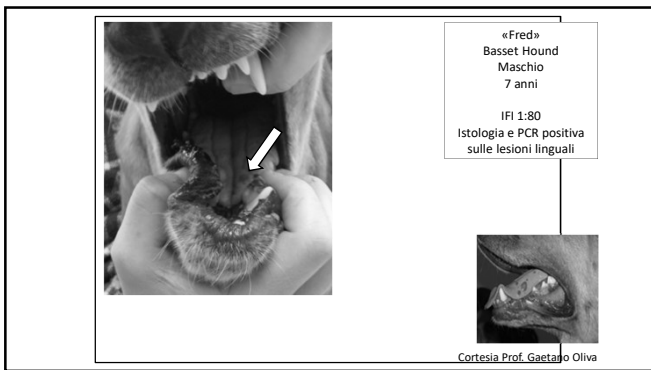


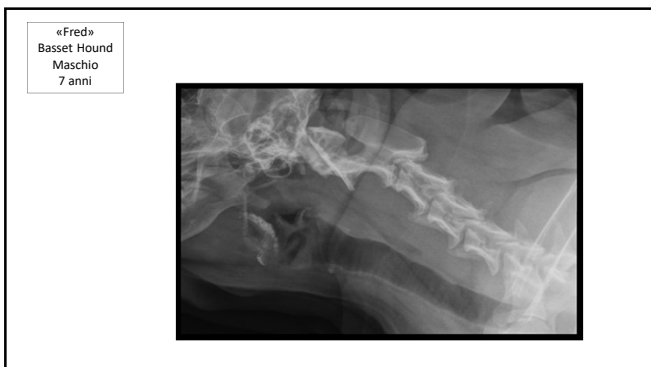
Meticcio
Maschio
4 anni

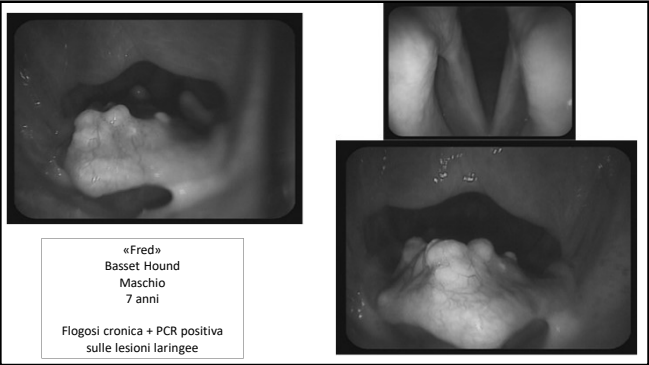


«Mosè»
Meticcio
Maschio
4 anni









Available online at www.sciencedirect.com
ScienceDirect

INFECTIOUS DISEASE

Laryngeal Granuloma due to *Leishmania* spp. Infection in a Dog

E. Torrent^{a,*}, J. Pastor^a, L. Fresno^a, I. Viguera^a, M. I. Casanova^a, A. Ramis^a and L. Solano-Gallego^b

^a Fundació Hospital Clínic Veterinari, ^b Departament de Medicina i Ciències Animals, Facultat de Veterinària i ^c Departament de Sanitat i Anatomia Animal, Servei de Diagnòstic de Patologies Veterinàries, Universitat Autònoma de Barcelona, Edifici V, Campus UAB, Bellaterra, Spain

Summary

A French bulldog with a previous history of leishmaniasis was presented due to respiratory distress associated with a laryngeal mass. The mass was resected and cytological and histopathological examinations revealed pyogranulomatous inflammation with *Leishmania* spp. amastigotes. After surgery, the respiratory condition resolved; however, 3 months later the dog developed clinical-pathological signs of leishmaniasis, which improved with systemic treatment. This case shows an atypical presentation of leishmaniasis with a local tumour-like mass in the vocal folds as the only clinical sign.

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Fig. 1. Laryngoscopic examination showing an erythematous mass (D) dorsal to the everted left laryngeal sacule (L). R, right arytenoid cartilage; L, left arytenoid cartilage.

Experimental Ophthalmology (2009) 8, 27–40

Ocular and periocular manifestations (1993–1998)

M. T. Peña^a, X. Roura^a and M. G. Davidson^b
^a Vets of Veterinary Medicine, Autonomous University of Barcelona, Bellaterra, Spain; ^b Vets of Veterinary Medicine, State University, Raleigh, NC 27606, USA

Table 1 Distribution of ocular lesions in 105 dogs (210 eyes) with leishmaniasis

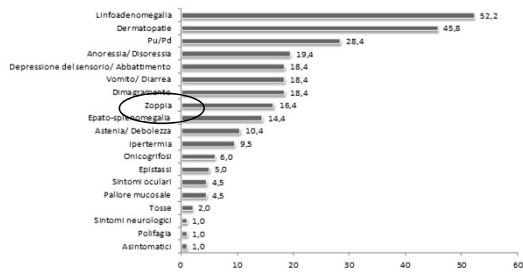
Ocular sign	Affected eyes (%)	Prevalence
Anterior uveitis	90	42.8%
Periocular alopecia	56	26.7%
Diffuse blepharitis	54	25.7%
Ulcerative blepharitis	8	3.8%
Solitary eyelid nodule	2	0.09%
Conjunctivitis	66	31.4%
Uveitis	66	31.4%
Uveitis sicca	6	2.8%
Retinitis	8	3.8%
Chorioretinitis	4	1.9%

Figure 1. Ocular lesion in a dog with leishmaniasis.

Leishmaniosi: segni clinici



234 casi unibo



Zoppia e Leishmaniosi – diagnosi differenziale

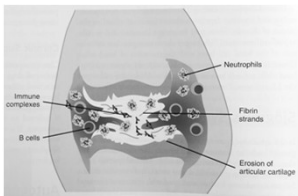
Poliartrite

Coinvolgimento osseo

Miosite

Leishmaniosi e Poliartriti immunomediate

Infiammazione della sinovia secondaria alla «deposizione» di immunocomplessi

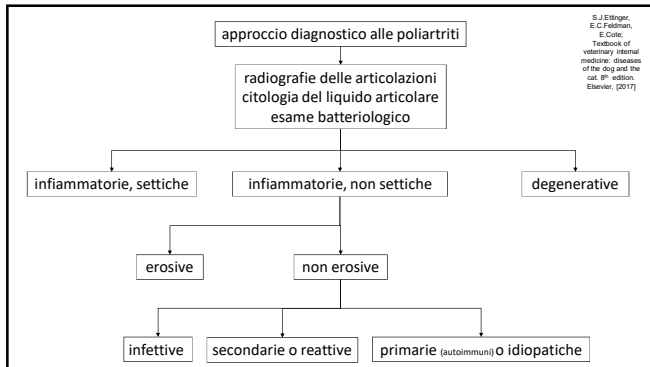


Ipersensibilità di III tipo

Ipersensibilità di II tipo in alcuni casi ?

+ presenza del parassita a livello articolare !

Tizard, Veterinary Immunology 2013



Poliartriti immunomediate - dati clinici

Storia clinica con segni clinici tipicamente intermittenti

Rigidità
Difficoltà ad alzarsi
Zoppia
Articolazioni tumefatte, calde e dolenti


Letargia
Depressione
Anoressia

Linfoadenomegalia

Pu/Pd

Febbre

Segni clinici riferibili alla malattia primaria (quando presente)



Poliartriti immunomediate - dati clinici

Articolazioni tumefatte, calde e dolenti

Maggiormente colpite la **articolazioni distali**

Carpio
Tarso
Interdigitali
Ginocchio e gomito

Possibile coinvolgimento solo del gomito

Possibile dolore al rachide come unico segno

→ Dolore maggiore a livello della coda → coda tenuta flessa e dolore alla manipolazione



Poliartriti immunomediate - infettive

Lo stimolo immunogeno è nell'articolazione !!

- Batteri (Gram positivi, raramente + articolazioni)
- Rickettsie
- *Anaplasma/Ehrlichia spp.*
- *Borrelia burgdorferi*
- Micoplasmi
- *Leishmania spp.*
- Funghi
- Virus



Retrospective study of 14 cases
of canine arthritis secondary
to *Leishmania* infection

Journal of Small Animal Practice (2014) 55, 309–313
DOI: 10.1111/jsap.12204
Accepted: 30 January 2014; Published online: 3 April 2014

S. SBRANA*, V. MARCHETTI*, E. MANGIANTE†, G. GUIDI* and D. BENNETT‡

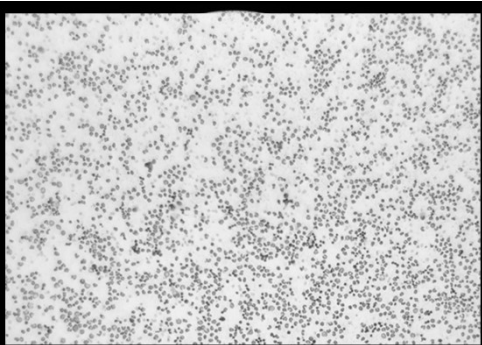
Table 2. Breed, age, sex, weight, general clinical signs and orthopaedic findings in the dogs in the study						
Case	Breed	Age (months)	Sex	Weight (kg)	General clinical signs	Orthopaedic complaint
1	Schnauzer	84	F	33	Lymphadenomegaly, Splenomegaly	Generalised stiffness and pain
2	Epigriul Briton	74	M	13	None	Generalised stiffness and pain
3	Crossbreed	48	F	21	Weakness, Lymphadenomegaly, Dermatitis	Generalised stiffness and pain
4	Crossbreed	60	F	38	Lymphadenomegaly, Splenomegaly, Dermatitis, Weakness	Generalised stiffness and pain
5	Crossbreed	32	M	34	Hyperthermia, Lymphadenomegaly	Generalised stiffness and pain
6	Crossbreed	72	M	7	Alopecia, Severe diffuse pain, Weakness	Generalised stiffness and pain
7	Crossbreed	62	F	10	None	Generalised stiffness and pain
8	Labrador retriever	120	M	38	None	Bilateral hindlimb lameness
9	Crossbreed	65	M	46	None	R hindlimb lameness
10	Crossbreed	15	F	21	Lymphadenomegaly, Splenomegaly, Dermatitis	Bilateral fore limb lameness
11	Retriever	60	M	45	Lymphadenomegaly	Bilateral hindlimb lameness
12	Crossbreed	72	M	42	None	Bilateral hindlimb lameness
13	Crossbreed	60	F	25	Lymphadenomegaly, Dermatitis	L fore limb lameness
14	Crossbreed	72	M	45	None	R fore limb lameness

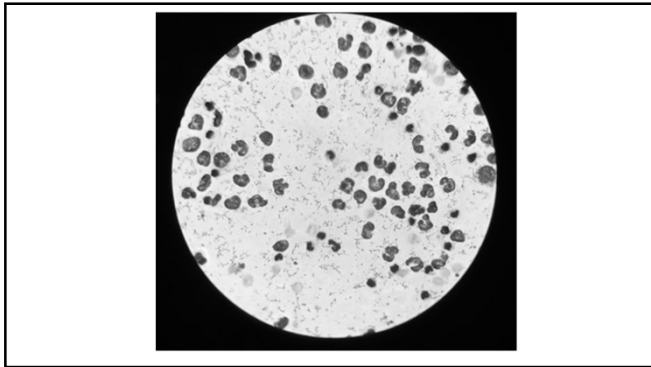
*M MSc, FRCV, C. L. R. R. R. R.

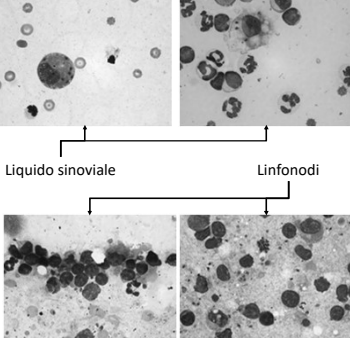
Poliartriti - Protocollo diagnostico

- Esame emocromocitometrico
- Profilo chimico + CRP
- Analisi urinaria
- Artrocentesi + citologia del liquido sinoviale (+ batteriologico)
→ almeno 4 articolazioni a prescindere dai segni clinici
- Radiografie arti
- Rx torace e ecografia addominale
- Test eziologici ...










Liquido sinoviale Linfonodi

Liz
Beauceron
FS
Anni 4

Zoppia
Febbre
Iperproteinemia

Provenienza: Ravenna




Leishmaniosi e Miopatie

Danno diretto → presenza di amastigoti

Deposizione di immuno-complessi
correlato a vasculiti e anticorpi anti-miofibrociti

Istologia:
infiammazione linfoplasmocellulare e/o granulomatosa → fibrosi



macro cell

Review

Pathologic Mechanisms Underlying the Clinical Findings in Canine Leishmaniosis due to *Leishmania infantum/chagasi*

A. P. Koutinas¹ and C. R. Koutinas²

Clinical and radiographic study of bone and joint lesions in 26 dogs with leishmaniasis

A. AGUT, N. CORZO, J. MURCIANO, F. G. LAREDO, M. SOLER

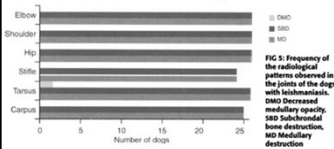


FIG 5. Frequency of the radiological patterns observed in the joints of the dogs with leishmaniasis. DAO Decreased articular space, SBO Subchondral bone destruction, MO Medullary opacity.

1. Reazione granulomatosa legata alla presenza del parassita → ossa lunghe
2. Deposito di immuno-complessi a livello sinoviale & reazione di ipersensibilità di III tipo → neutrofili
Alterazione articolazioni
Vasculiti
Aumento della permeabilità vascolare





Cortesía Dr. Vezzani ENHCO

Table 1. Tick-borne and nontick-borne infectious agents associated with glomerulonephritis.

Infectious Agent	Class of Infection	Type of Infected Cell	Major Vector	Tests	Need Paired Tests	Bite or Blood-borne	Rx	Carrier Status
<i>Anaplasma phagocytophilum</i>	Rickettsial	Granulocyte	Ixodes	ELISA, PCR	X	X	D	X
<i>Anaplasma platys</i>	Rickettsial	Platelet	Rhipi	ELISA, PCR	X	X	D	X
<i>Bartonella</i> spp.	Bacterial	Endothelial cells, Epi-ecb, Macrophages	Ixodes, fleas, other ticks	PCR, WB, IFA, culture	?	X	DF, DR, Z	X
<i>Borrelia burgdorferi</i> (Lyme disease)	Spirochete	Extracellular near fibroblasts	Ixodes	ELISA, Co*, WB, IFA	No	Unlikely	D (AEZ)	X
<i>Babesia canis, sensu lato</i> , large B.	Protozoan	Rbc	Rhipi	PCR, IFA	X	X	Im	X
<i>Babesia gibsoni</i>	Protozoan	Rbc	Rhipi	PCR, IFA	X	X	Z-Q (Cba)	X
<i>Babesia microti</i>	Protozoan	Rbc	Ixodes	PCR, IFA	X	X	Z-Q	X
<i>Brucella canis</i>	Bacterial	Lymphocyte	Varied	RSAT, ELISA, PCR	X	X	MD	X
<i>Cyranosom felis</i>	Protozoan	Rbc, schizonts in mar	Ambly	PCR	No	X	Z-Q	X
<i>Ehrlichia canis</i>	Rickettsial	Monocyte wbc	Duma	ELISA, IFA, PCR	X	X	Im	X
<i>Ehrlichia chaffeensis</i>	Rickettsial	Monocyte wbc	Ambly	ELISA, PCR	X	X	D	X
<i>Ehrlichia ewingii</i>	Rickettsial	Granulocyte	Ambly	PCR	X	X	D	X

GOLDSTEIN, R. E., et al. Consensus recommendations for treatment for dogs with serology positive glomerular disease. *Journal of veterinary internal medicine*, 2013, 27, 11.

Table 1. Tick-borne and nontick-borne infectious agents associated with glomerulonephritis.

Infectious Agent	Class of Infection	Type of Infected Cell	Major Vector	Tests	Need Paired Tests	Bite or Blood-borne	Rx	Carrier Status
<i>Hepatozoon americanum</i>	Protozoan	Myocyte, Lymphoid, Liver, Wbc	Ambly (dog ants tick)	PCR, Muscle biopsy, IFA	No		spc	X
<i>Leishmaniasis</i>	Protozoan	Extracellular Macrophages	Sandfly, Vertical	ELISA, HISTOLOGY, PCR, MAT	No	X	PA	X
Leptospirosis	Spirochete	Extracellular	Urine	PCR, MAT	X	Unlikely	D (A)	X
<i>Mycoplasma</i> spp.	Bacterial	Epi-ecb	Fleas, Ticks	PCR, ELISA	?	X (future)	DF	X
<i>Rickettsia rickettsii</i> (Rocky Mountain Spotted Fever, RMSF)	Rickettsial	Endothelial cells	Duma	IFA, DFA	X	Unlikely	D	No

A, amoxicillin; Co*, C6 peptide antigen in SNAP-3Dx, SNAP-4Dx, SNAP-4DxPLUS or Lyme Quant C6 (IDEXX)*Or other Lyme antibody tests: Abaxis, AccuPlex4, Multiplex4, opA, opC, opF tests; Clin, clindamycin; D, doxycycline; Dma, Demarecort; E, erythromycin; F, fluoroquinolone; Im, immunosuppressive; MAT, microagglutination test; MD, minocycline and dithyostreptomycin; PA, pentostam (sodium stibogluconate); amphotericin B, allopurinol; Q, atovaquone; R, rifampin; Rhipi, Rhipicephalus; RSAT, rapid slide agglutination test; Rx, treatment; spc, saliva; pyrimethamine and clindamycin; deoxyquinase; UPC, urine protein:creatinine ratio; X, yes; Z, azithromycin (Zithromax).

Adapted from Littman³ and Littman MP. Cystopenia, Vasculitis, Polyarthropathy, and Proteinuria. *Atlantic Coast Veterinary Conference Proceedings*, April 2011.

GOLDSTEIN, R. E., et al. Consensus recommendations for treatment for dogs with serology positive glomerular disease. *Journal of veterinary internal medicine*, 2013, 27, 11.

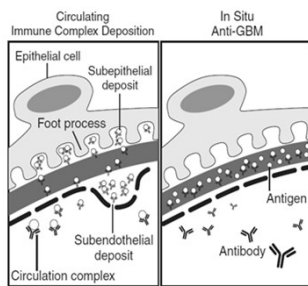
Principali cause di glomerulopatia glomerulonefrite nel cane

- Neoplastiche**
- Leucemie
 - Linfoma
 - Mastocitoma
 - Eritrocitosi primaria (politemia)
 - Istocitosi sistemica/sarcoma sinocitario
 - Altre neoplasie
- Infezioni infiammatorie**
- Borreliosi (malattia di Lyme)
 - Bartonellosi
 - Brucellosi
 - Endocarditi
 - Pneumia
 - Prostatite/accesso prostatico
 - Pielonefrite
 - Piodermite
 - Infezioni batteriche croniche
 - Babesiosi
 - Leishmaniosi
 - Filariosi
 - Ehrlichiosi/Anaplasmosi
 - Adenovirus canino tipo 1 (epatite di Rubarth)
 - Micosi sistemiche



- Infiammatorie non-infettive**
- Dermatopatie croniche
 - IBD
 - Pancreatite
 - Poliartriti immuno-mediate
 - Lupus eritematoso sistemico
 - Patologie immuno-mediate/autoimmuni in generale
 - anemia emolitica trombocitopenia (IMHA, IMT)
- Altro**
- Sindrome di Cushing/somministrazione di steroidi
 - Iddiopatico

Patogenesi del danno renale



+ Formazione di autoanticorpi?
(anticorpi anti-istone)

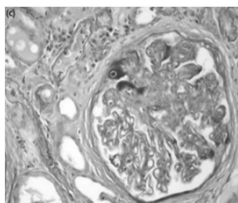


Leishmaniosi e danno renale

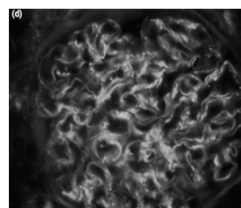
Danno renale caratterizzato da:

- coinvolgimento glomerulare → Glomerulonefrite
 associata a deposito glomerulare di immunocomplessi
GN membrano-proliferativa
GN membranosa
GN mesangioproliferativa
Glomerulo-sclerosi focale segmentale (FSGS) (non associata a IMC)
- danno tubulo-interstiziale → Nefropatia tubulo-interstiziale ?
 infiltrazione linfoplasmacellulare + macrofagi

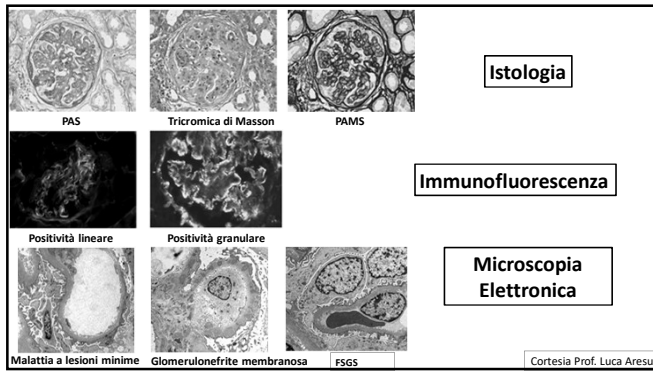
Kautinas et al., 1994; Costa et al., 2003; Zatelli et al., 2003; Aresu et al., 2012



**Glomerulonefrite
MEMBRANOPROLIFERATIVA**



Aresu et al., 2008, Veterinary Record



Leishmaniosi e Glomerulopatie

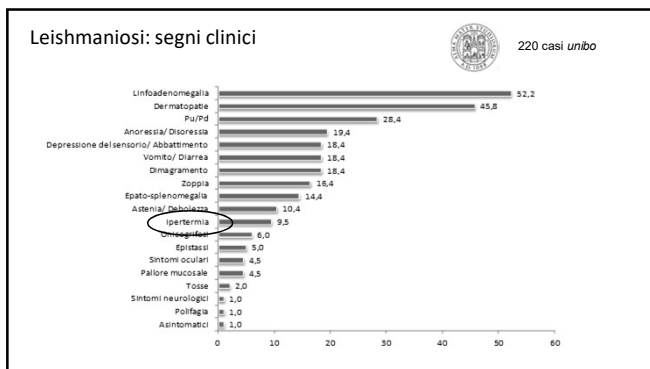
Proteinuria come unico reperto clinicopatologico in molti pazienti !

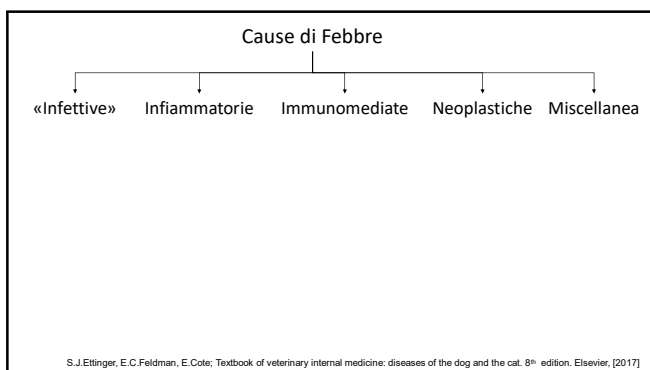
Quadri clinici legati a:

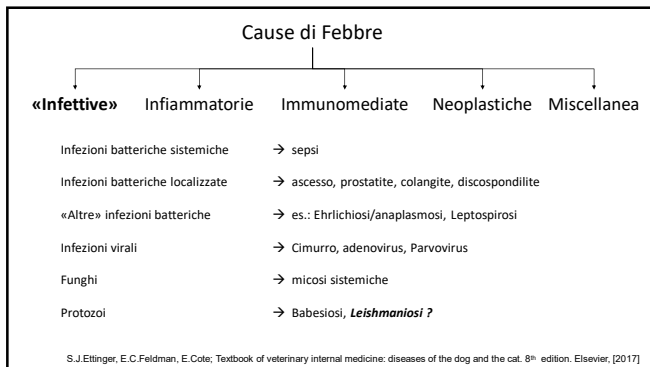
- glomerulonefrite e **proteinuria**
- CKD
- sindrome nefrosica (proteinuria+edemi)

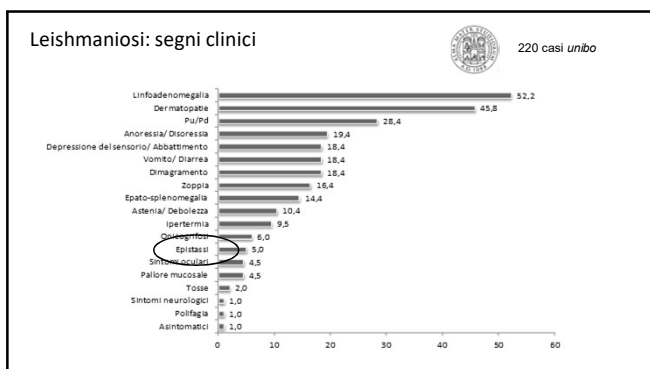




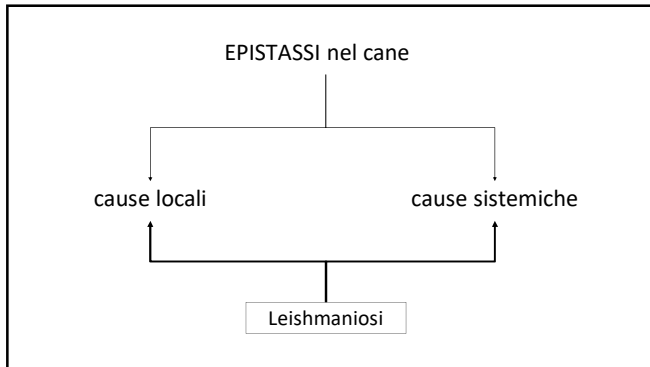












Ringraziamenti:

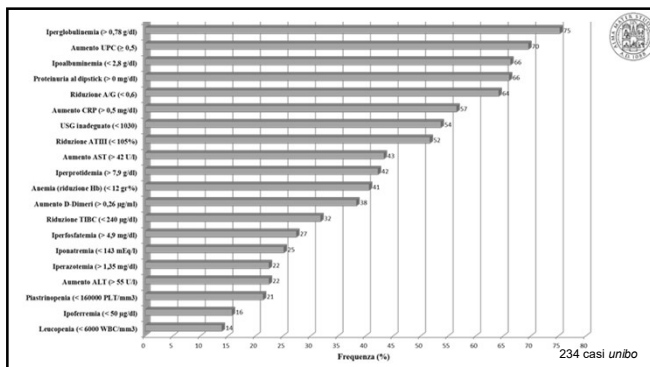
Sofia Segatore

Roberta Troia
Chiara Grisetti
Erika Monari
Kateryna Vasylyeva
Silvia Zamagni
Alessandro Tirolo
Linda Perissinotto

Tutti i colleghi della UO di Nefrologia e Urologia

f.dondi@unibo.it

62



EPISTASSI nel cane – cause locali



- trauma/CE
- neoplasie (carcinomi/adenocarcinomi, sarcomi, cellule rotonde)
- patologie dentali (ascessi radicali, fistole odontopatiche)
- “infiammatorio-infettivo” (MICOSI, riniti croniche, rinite ulcerativa)

EPISTASSI nel cane – cause sistemiche



CAUSE SISTEMICHE

- | | |
|------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------|
| <ul style="list-style-type: none"> • trombocitopenie • trombocitopatie • coagulopatie | <div style="border: 1px solid black; padding: 5px; text-align: center;">Alterazioni emostatiche</div> |
| <ul style="list-style-type: none"> • “vasculiti” • ipertensione arteriosa | <div style="border: 1px solid black; padding: 5px; text-align: center;">Aumentata “fragilità” capillare</div> |

EPISTASSI nel cane – cause sistemiche

Vasculiti/aumentata fragilità capillare
 Sindrome da iperviscosità
 Mieloma multiplo/plasmocitoma
 Ehrlichiosi, Leishmaniosi
 Eritrocitosi
 Leucemie
 Iperlipidemia
 Trombosi
 Neoplasie

PAPER

A retrospective study of 61 cases of spontaneous canine epistaxis (1998 to 2001)

M. E. MYLONAKIS, M. N. SARIDOMICHELAKIS*, V. LAZARIDIS, L. S. LEONTIDES†, P. KOSTOULAS† AND A. F. KOUTINAS

Companion Animal Clinic, Faculty of Veterinary Medicine, Aristotle University of Thessaloniki, 11 Stavrou Vouyrya Str., 54627 Thessaloniki, Greece

*Clinic of Animal Medicine †Laboratory of Epidemiology, Biostatistics and Economics of Animal Production, School of Veterinary Medicine, University of Thessaly, 224 Trikolon Str., 43100 Karditsa, Greece

Journal of Small Animal Practice (2008) **49**, 191–196
DOI: 10.1111/j.1748-5827.2007.00441.x

PAPER

A retrospective study of 61 cases of spontaneous canine epistaxis (1998 to 2001)

Table 1. Diagnoses established in 61 canine patients with spontaneous epistaxis

Diagnosis	Number of cases (%)
Systemic diseases (n=56)	
Leishmaniasis (<i>Leishmania infantum</i>)*	29 (48)
Monocytic ehrlichiosis (<i>Ehrlichia canis</i>)*	28 (46)†
Rodenticide toxicity	2 (3)
Immune-mediated thrombocytopenia	1 (2)
Suspected oestrogen toxicity	1 (2)
Systemic arterial hypertension	1 (2)
Intranasal diseases (n=5)	
Transmissible venereal tumour	3 (5)
Nasal adenocarcinoma	1 (2)
Nasal aspergillosis	1 (2)

*Six dogs (11 per cent) had concurrent leishmaniasis and monocytic ehrlichiosis

†Thirteen of the 28 dogs (46 per cent) were German shepherd dogs

Journal of Small Animal Practice • Vol 49 • April 2008 • © 2007 British Small Animal Veterinary Association

J Vet Intern Med 2008;22:866–872

Factors Associated with the Occurrence of Epistaxis in Natural Canine Leishmaniasis (*Leishmania infantum*)

T.A. Petanides, A.F. Koutinas, M.E. Mylonakis, M.J. Day, M.N. Saridomichelakis, L.S. Leontides, R. Mischke, P. Diniz, E.B. Breitshwerdt, M. Kritsepi, V.A. Garipidou, C.K. Koutinas, and S. Lekkas

Background: Canine leishmaniasis (CanL) is a common cause of epistaxis in dogs residing in endemic areas. The pathogenesis of CanL-associated epistaxis has not been fully explored because of the limited number of cases reported so far.

Hypothesis: Epistaxis in CanL could be attributed to more than 1 pathomechanism such as haemostatic dysfunction, biochemical abnormalities, or a combination of factors. In conclusion, the results of this study indicate that a single pathogenetic mechanism cannot invariably be incriminated for epistaxis in natural CanL, but rather the interaction of various internal factors such as thrombocytopathy, hyperglobulinemia-induced serum hyperviscosity, and ulcerative or nonulcerative rhinitis most likely is responsible.

Key words: Dysproteinemia; Rhinitis; Thrombocytopathy.

(n = 27) of *Aspergillus* regation re-axis than in = .029) and h was lower
tors such as

Myocarditis and generalised vasculitis associated with leishmaniosis in a dog

A three-year-old, female bulldog was presented with bilateral uveitis, apathy, lethargy, generalised lymphadenopathy and paravertebral haematomas. The initial laboratory studies showed non-regenerative anaemia, polyclonal gammopathy and a high urine protein:creatinine ratio. Serology for leishmaniosis was positive and treatment with allopurinol and meglumine antimonate was started. Despite treatment, the dog's clinical condition deteriorated. Signs included cutaneous ecchymosis, respiratory distress and finally cardiovascular arrest. Histopathological studies of postmortem tissue samples revealed a generalised vasculitis of several internal organs and severe myocarditis. *Leishmania* species organisms were identified in affected tissues using immunoperoxidase labelling and PCR techniques.

E. Toranzo, M. Lina, J. Sotillo*, J. Fariña, T. Peña, B. Castiella* and J. Durán
Journal of Small Animal Practice (2005) 46, 549–552

INTRODUCTION

Canine leishmaniosis is an infectious disease, caused by a protozoan of the genus *Leishmania*, that affects people and wild and domestic animals (Simpson and Fayer 1998). The disease is endemic in

CASE HISTORY

A three-year-old, entire female bulldog with chronic keratoconjunctivitis sicca was treated surgically for entropion and dystrichiasis. After surgery and resolution of the keratitis, a bilateral nuchal mass

Clinical signs of leishmaniosis are caused by the parasite itself and by an immune B cell activity that generates large numbers of circulating immune complexes, the deposition of which may lead to polyarthralgia, uveitis, glomerulonephritis and vasculitis (Laper and others 1996). In canine leishmaniosis, some common skin lesions are attributed to vasculitis (Mikolaj 1997). However, the presence of generalised internal vascular lesions has been less commonly recognised (Panatier and others 1991). Leishmaniosis involving myocarditis has only rarely been reported (Boggs and Mikolaj 1977; Fayer and others 1998). This case report describes an unusual presentation of leishmaniosis that included generalised vasculitis and myocarditis in a dog.

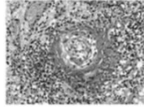
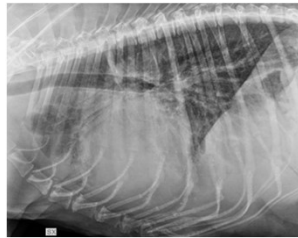
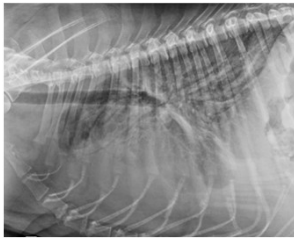


Fig 1. Myocarditis and vasculitis in a dog with leishmaniosis. (H&E, 100x magnification.)

Rodi
 Pastore tedesco
 MC
 10 anni

Pregressa positività a Leishmania IFI: 1:320
 Trattato anni prima con :
 antimoniali+allopurinolo



Journal of Veterinary Cardiology (2019) 23, 32–37



Case Report

Canine leish pericardial

P. Sebastián-Mar S. Gómez, DVM, PhD^{a,c}

^aDivision of Veterinary Medicine, Veterinary Faculty, Univ
^bDepartment of Compa University of Murcia, Ca
^cDepartment of Animal Campus Espinardo, 3010

Received 4 February 2018;

Journal of Veterinary Cardiology

www.elsevier.com/locate/jvc

Abstract A 4-year-old crossbreed dog presented with a two-day history of lethargy and abdominal effusion. Physical examination and echocardiography revealed pericardial effusion with cardiac tamponade. Pericardiocentesis was performed. Intracytoplasmic *Leishmania* amastigotes were found on cytological examination of the pericardial fluid. The animal was treated with N-methylglucamine antimonate and allopurinol. After an initial favorable response, cardiac tamponade reoccurred one month later. The dog died during a pericardiectomy four months after the initial diagnosis. Histology confirmed the presence of chronic pericarditis. The presence of *Leishmania* amastigotes on cytological examination of pericardial effusion suggests a possible association between canine leishmaniasis and chronic pericarditis. This finding also supports the importance of cytological examination of pericardial fluid in areas endemic for canine leishmaniasis.

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REVIEW

Neurological manifestations in dogs naturally infected by *Leishmania infantum*: descriptions of 10 cases and a review of the literature

A. P. GIANNUZZI, M. RICCIARDI, A. DE SIMONE AND E. GERSONI

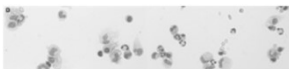
*Corresponding author email: fiperguene@gmail.com

In order to evaluate possible nervous system involvement in canine leishmaniasis, retrospective evaluation of 5 medical records of leishmaninergic drugs affected neurological signs referred to our hospital was performed. The study included 10 dogs of 10 dogs of 10 dogs. Depending on the anatomical location of the drug under affected areas of imaging, cerebrospinal fluid analysis, electroencephalographic testing and histopathologic evaluation. The final neurological diagnosis was: meningoencephalitis (n=2), brain haemorrhagic stroke (n=1), haemorrhagic chorioiditis (n=1), meningomyelitis (n=2), ischaemic myelopathy (n=1), polymyositis (n=2) and peripheral neuropathy (n=1). This study confirms that both central and peripheral nervous systems can be affected by leishmaniasis and provides an overview on the possible etiopathogenic mechanisms. In addition, ethical and diagnostic findings, therapy and follow-up of affected dogs are described.

Journal of Small Animal Practice (2017) **58**, 125–130
DOI: 10.1111/jcpp.12400
Accepted: 14 October 2016

Meccanismi patogenetici proposti:

- 1) **effetto diretto del parassita**
- 2) **lesioni immunomediate**
- 3) **vaskulite** o altre lesioni vascolari
- 4) complicazioni legate a immunosoppressione
- 5) altre complicazioni



Immunopatologia e segni clinici – “casi atipici”

permanenza dell'antigene + «mimica molecolare» e liberazione antigeni criptici

produzione di autoanticorpi

- anti-globuli rossi → IMHA
- anti-piastrine → IMT
- anti-granulociti → IMN ?

- anti-nucleari → ANA test +
- anti-Ag cutanei → dermatopatie immunomediate ?
- anti-istone → glomerulonefrite ?

Reazioni di ipersensibilità di tipo II

Autoimmune manifestations in patients with visceral leishmaniasis

Journal of Microbiology, Immunology and Infection (2013) **46**, 302–305

Evangelos Liberopoulos*, Anastazia Kei, Fotini Apostolou,
Moses Elisaf

Table 2 Immune laboratory findings on admission

Parameter (reference range)	
ANA (1:160)	Elevated in 14 patients (88%); 1/480 (1/160–1/2560)
RF	Decreased in 10 patients (63%); 42.7 ± 35.9 U/mL
C3 factor of complement (88–201 mg/dL)	Decreased in 2 patients (13%) 1 st patient: 38 mg/dL 2 nd patient: 44 mg/dL
C4 factor of complement (16–47 mg/dL)	Decreased in 8 patients (50%); 11.2 ± 4.5 mg/dL
Anti-cardiolipin antibodies (g/L)	1 st patient: 35 U/mL 2 nd patient: 40 U/mL
Coombs' test	Detected in 8 patients (50%) • Direct: positive in 2 patients (13%) • Indirect: positive in 1 patient (6%)
Anti-microglobulin (0–1900 µg/L)	Elevated in 4 patients (25%); 37,900 ± 23,800 µg/L
Hyperimmunoglobulinemia	• Polyclonal: 3 patients (19%) • Biconal: 1 patient (6%) • Monoclonal: 6 patients (38%)
ANA	Detected in 4 patients (25%); 1/160 (1/80–1/240)
Anti-TRF/anti-TBGG	Detected in 4 patients (25%) 1/40 (1/20–1/80)
Anti-ENA	Detected in 1 patient (6%)
Anti-MPO	Detected in 2 patients (13%)
Anti-Ro	Detected in 1 patient (6%)
Anti-Sm	Not detected (0%)
Anti-ds-DNA	Not detected (0%)

* Values are expressed as mean \pm standard deviation, except for ANA, ASMA and p-ANCA, which are expressed as median (range). ANA = anti-nuclear antibody; anti-ds-DNA = anti-double-stranded DNA antibody; anti-ENA = anti-extractable nuclear antigen antibody; anti-MPO = anti-mielyeloperoxidase antibody; anti-PR3 = anti-proteinase 3 antibody; anti-Sm = anti-SmRt antibody; anti-TBG = anti-thyroxine binding globulin antibody; anti-TPO = anti-thyroid peroxidase antibody; ASMA = anti-smooth muscle cell antibody.

Perinuclear antineutrophil cytoplasmic autoantibodies in dogs infected with various vector-borne pathogens and in dogs with immune-mediated hemolytic anemia

Anna E. Karagianni, DVM, MRes; Laia Solano-Gallego, DVM, PhD; Edward B. Breitschwerdt, DVM; Frédéric P. Gaschen, Dr med vet, Dr habil; Michael J. Day, BVMS, PhD, DSc; Michele Trotta, DVM, PhD; Barbara Wiedand, Dr med vet, PhD; Karin Allenspach, Dr med vet, PhD

Group	No. (%) of dogs with positive results for pANCA	95% CI
Dogs in which IMHA was diagnosed or suspected clinically (n = 55)		
IMHA diagnosed (n = 16)	11 (69)	46-92
IMHA suspected; positive result for Coombs' test (n = 19)	6 (32)	11-63
IMHA suspected; negative result for Coombs' test (n = 20)	9 (45)	23-67
Dogs confirmed or suspected of having vector-borne infections (n = 140)		
Clinically suspected and seroreactive for ≥ 1 tick-borne diseases including <i>Rickettsia rickettsii</i> , <i>Bartonella henselae</i> , <i>Bartonella vinsonii</i> subsp. <i>berkhoffii</i> , <i>Ehrlichia canis</i> , and <i>Borrelia burgdorferi</i> infection (n = 97)	26 (44)	30-50
Clinically suspected and seroreactive for <i>Leishmania infantum</i> (n = 43)	28 (65)	51-79
Control dogs (n = 62)		
Dogs clinically suspected but seronegative for tick-borne pathogens (n = 20)	1 (5)	0-25
Dogs clinically suspected but seronegative for <i>L. infantum</i> (n = 22)	8 (36)	20-57
Healthy dogs (n = 20)	1 (5)	0-25

Leishmaniosi e Citopenie immunomediate

Leishmaniosi e IMHA (anemia emolitica immunomediata)

Review Cellular Immunology 292 (2014) 9-13

Leishmaniasis and autoimmune diseases in pediatric age

M. Nozzi*, M. Del Torto, F. Chiarelli, L. Breda

Pediatric Rheumatology Unit, Department of Pediatrics, "G. d'Annunzio" University, Chieti, Italy

Numerosi case report in letteratura di bambini con IMHA secondaria a *L. infantum* *

Descritta anche sindrome di Evans *

* Visceral leishmaniasis presented with Evans syndrome: a case report, B. Alioglu, Z. Arici, E. Ozyurek, N. Ozbek, Am. J. Hematol. 82 (2007) 1030-1031.

* Immune haemolytic anaemia due to visceral leishmaniasis in a young child, M. Boud, Eur. J. Pediatr. 162 (2003) 444.

*kala-azar associated with coombs-positive autoimmune hemolytic anemia in the patients coming from the endemic area of this disease and successful treatment of these patients with liposomal amphotericin B, E. Erduran, A. Bahadur, Y. Gedik, Pediatr. Hematol. Oncol. 22 (2005) 349-355.

*Immune mediated hemolysis in visceral leishmaniasis, V. Mahajan, R.K. Marwaha, J. Trop. Pediatr. 53 (2007) 284-286.



Leishmaniosi e Positività al test di Coombs → anemia emolitica immunomediata (IMHA) ?

Dati variabili in letteratura (21 - 84%*)

Mancanza di studi che correlino anemia & positività test di Coombs

→ Evidenza di IMHA ?



*A retrospective clinical study of canine leishmaniasis in 150 dogs naturally infected by Leishmania infantum, P. Caramella, G. Oliva, R. De Luna, L. Gradoni, R. Ambrosio, L. Cortese, A. Scalone, A. Parronchio - Veterinary Record (1997) 141, 539-543
*Canine Leishmaniasis. A review based on 95 cases in the Netherlands, R. J. Stappendael - THE VETERINARY QUARTERLY, VOL. 10, No. 1, JANUARY 1988

Received: 13 December 2018 | Accepted: 18 January 2019
DOI: 10.1111/jvim.15441

CONSENSUS STATEMENT Journal of Veterinary Internal Medicine 

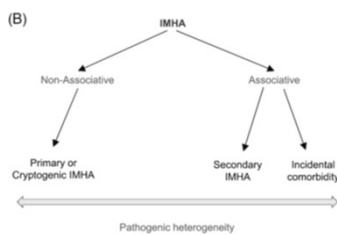
Consensus Statements of the American College of Veterinary Internal Medicine (ACVIM) provide the veterinary community with up-to-date information on the pathophysiology, diagnosis, and treatment of clinically important animal diseases. The ACVIM Board of Regents oversees selection of relevant topics, identification of panel members with the expertise to draft the statements, and other aspects of assuring the integrity of the process. The statements are derived from evidence-based medicine whenever possible and the panel offers interpretive comments when such evidence is inadequate or contradictory. A draft is prepared by the panel, followed by solicitation of input by the ACVIM membership which may be incorporated into the statement. It is then submitted to the Journal of Veterinary Internal Medicine, where it is edited prior to publication. The authors are solely responsible for the content of the statements.

ACVIM consensus statement on the diagnosis of immune-mediated hemolytic anemia in dogs and cats

Oliver A. Garden¹ | Linda Kidd² | Angela M. Mexas³ | Yu-Mei Chang⁴ |
Unity Jeffery⁵ | Shauna L. Blois⁶ | Jonathan E. Fogle⁷ | Amy L. MacNeill⁸ |
George Lubas⁹ | Adam Birkenheuer⁷ | Simona Buoncompagni¹⁰ |
Julien R. S. Dandrieux¹¹ | Antonio Di Loria¹² | Claire L. Fellman¹³ |
Barbara Glanemann⁴ | Robert Goggs¹⁴ | Jennifer L. Granick¹⁵ |
Dana N. LeVine¹⁶ | Claire R. Sharp¹⁷ | Saralyn Smith-Carr¹⁸ |
James W. Swann¹⁹ | Balazs Szladovits⁴



Diagnosi anemia emolitica immunomediata (IMHA) cane



Nuova classificazione

ACVIM consensus statement on the diagnosis of immune-mediated hemolytic anemia in dogs and cats



Diagnosi anemia emolitica immunomediata (IMHA) cane



Anemia

Sferocitosi

Autoagglutinazione («saline agglutination test» positivo)

Anticorpi anti-RBCs ?

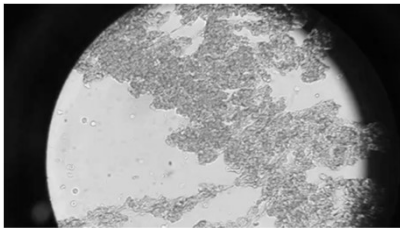
Iperbilirubinemia

Pigmenturia (emoglobinuria/bilirubinuria)

RBCs Ghosts (eritrociti fantasma)

+ identificazione di una potenziale causa

ACVIM consensus statement on the diagnosis of immune-mediated hemolytic anemia in dogs and cats



ACVIM consensus statement on the diagnosis of immune-mediated hemolytic anemia in dogs and cats

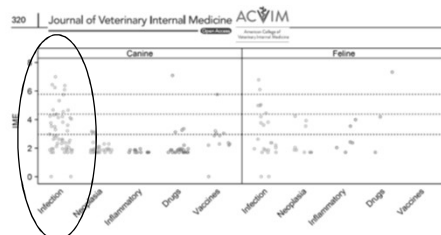
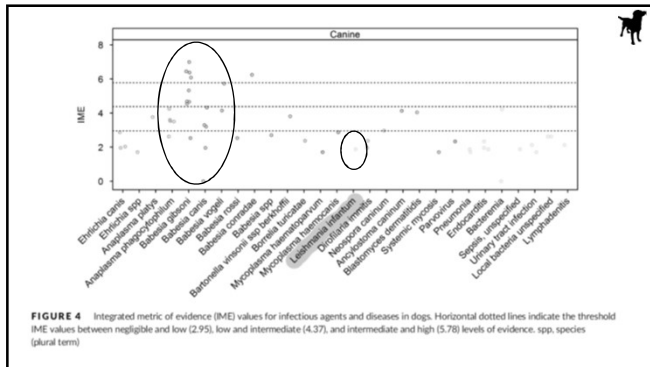


FIGURE 3 Integrated metric of evidence (IME) summary for all comorbidity categories. Horizontal dotted lines indicate the threshold IME values between negligible and low (2.95), low and intermediate (4.37), and intermediate and high (5.78) levels of evidence. Most IME values fell within the negligible and low zones of evidence, while a small number were 0, indicating evidence against that comorbidity inducing immune-mediated hemolytic anemia.



Leishmaniosi e IMHA (anemia emolitica immunomediata)

ACVIM consensus statement on the diagnosis of immune-mediated hemolytic anemia in dogs and cats

Evidenza scientifica bassa / trascurabile !

→ Consigliato comunque testare i cani con IMHA in zone endemiche!

Daisy
Pit bull
FS
10 anni

Anemia
Sferocitosi
Iperbilirubinemia
Pigmenturia

IFI Leishmania + 1:1280
PCR midollo negativo

Campione di sangue EDTA		Consegnato il 29/03/2016	
ESAME	Valore Unità	Intervallo di riferimento	
Emoglobina	4.0 gr%	12 - 18	
Ematocrito	13.5 %	37.9 - 55.0	
Ematocriti	1820000 /mm ³	5500000 - 8500000	
Plasmeter	1030000 /mm ³	1400000 - 5000000	
Leucociti	7550 /mm ³	6000 - 17000	
MCV	74.2 fL	60.0 - 77.0	
MPC	22.1 fL	6.0 - 10.0	
MCRC	29.9 gr%	32.0 - 38.0	
MCR	22.2 gr%	19.5 - 24.5	
RDW	17.9 %	13.0 - 15.7	
Reticolociti	10.56 %	0 - 1.50	
Reticolociti	192400 /mm ³	0 - 60000	
Linfociti	12.2 %		
Miosociti	4.1 %		
Neutrofili	81.2 %		
Eosinofili	1.0 %		
Basofili	0.2 %	0 - 600	
Linfociti	920 /mm ³	1000 - 4000	
Miosociti	310 /mm ³	100 - 1400	
Neutrofili	6130 /mm ³	3000 - 12000	
Eosinofili	120 /mm ³	0 - 750	
Basofili	20 /mm ³	0 - 180	
PCV	14.0 %	37.0 - 55.0	
Observazioni	piastrine attivate...		
Sferociti	presenti	+---	
Autoociti	presenti	+---	
Policromasia	presente	+---	
Stima piastrinica	backscattered		
Macroplasmie	presenti	+---	
Aggregati piastrinici	assenti		

Daisy
Pit bull
FS
10 anni

Anemia
Sferocitosi
Iperbilirubinemia
Pigmenturia

IFI Leishmania + 1:1280
PCR midollo negativo

Daisy
Pit bull
FS
10 anni

Anemia
Sferocitosi
Iperbilirubinemia
Pigmenturia

IFI Leishmania + 1:1280
PCR midollo negativo

Leishmaniosi e IMT (trombocitopenia immunomediata)



Leishmaniosi e IMT (trombocitopenia immunomediata)

Veterinary Immunology and Immunopathology 100 (2006) 510–517

Presence of anti-platelet IgM and IgG antibodies in dogs naturally infected by *Leishmania infantum*

G. Terrazzano^a, L. Cortese^a, D. Piantadosi^a, S. Zappacosta^a,
A. Di Loria^a, D. Santoro^b, G. Ruggiero^a, P. Ciaramella^{a,b}

Veterinary Record (2009) 164, 170–172

Secondary immune-mediated thrombocytopenia in dogs naturally infected by *Leishmania infantum*

L. Cortese, M. Sica, D. Piantadosi, G. Ruggiero, M. E. Piro, G. Terrazzano,
V. Mestroni, P. Ciaramella

The Veterinary Journal 188 (2015) 518–521

Prevalence of anti-platelet antibodies in dogs naturally co-infected by *Leishmania infantum* and *Ehrlichia canis*

Laura Cortese^a, Giuseppe Terrazzano^{a,b}, Diego Piantadosi^a, Michela Sica^a, Michele Prisco^a,
Giuseppina Ruggiero^a, Paolo Ciaramella^a

63,3% (21/33) avevano anticorpi anti-piastrine

- 9/33 trombocitopenici
- 15/21 CanL sintomatica
- 21/21 PBIGM+
- 9/21 PBIGM& PBIGG +

72,7% (32/44) avevano anticorpi anti-piastrine

- 20/44 trombocitopenici
- 20/32 PBIGM&PBIGG +
- 12/32 PBIGM +

Positivi a anticorpi anti-piastrine:

- 80% (8/10) co-infetti *L.infantum* e *E. canis*
- 50% (5/10) *L.infantum*
- 60% (6/10) *E. canis*

Leishmaniosi e IMT (trombocitopenia immunomediata)



- Trombocitopenia non così frequente
 - Elevate positività anticorpi anti-PLT anche in pazienti non trombocitopenici
- correlazione tra trombocitopenia & anticorpi anti-PLT ?
- altri meccanismi patogenetici?
- Soggetti con co-infezioni maggiore frequenza di anticorpi anti-PLT, ma non più trombocitopenici
- Alterata funzionalità piastrinica?

<p>JAVMA, Vol 235, No. 8, October 15, 2009</p> <p>Underlying diseases and clinicopathologic variables of thrombocytopenic dogs with and without platelet-bound antibodies detected by use of a flow cytometric assay: 83 cases (2004-2006)</p> <p>Regina Hühner-Buck, DVM, Elvira-Jean-Beth Schuchter, DVM, DABVP, Brinkhoff Mischke, DVM, DABVP</p> <p>From the Small Animal Clinic (DVM, Elvira-Jean-Beth Schuchter and Brinkhoff Mischke) and the Institute for Diagnostic Laboratory Medicine (DVM, Regina Hühner-Buck), University of Veterinary Medicine, Vienna, Austria; and the Department of Clinical Pathology, University of Veterinary Medicine, Vienna, Austria.</p> <p>Submitted for publication June 10, 2008; accepted for publication September 10, 2008.</p>			
Disease category	Disease	Positive PBA test	Negative PBA test
Infectious (n = 26)	Anaplasmosis	1	3
	Babesiosis	5	0
	Borrelia	0	1
	Ehrlichiosis	2	4
	Leishmaniasis	1	0
	Leptospirosis	2	2
	Sepsis	2	3
Inflammatory* (n = 15)	Cholecystitis	0	1
	Chronic hepatitis	1	2
	Inflammatory bowel disease	0	1
	Myelitis	0	1
	Pancreatitis	0	1
	Pancreatitis-associated hepatitis	1	0
	Pneumonia	0	1
	SIRS	2	2
	Systemic vasculitis	0	2
	Unspecified	1	0
Neoplasia associated (n = 10)	Histiocytic sarcoma	1	0
	Malignant histiocytosis	0	2
	Malignant lymphoma	2	2
	Metastatic carcinoma	0	2
	Metastatic sarcoma	0	1
Autoimmune (n = 18)	Immune-mediated hemolytic anemia	0	3
	gIMT	12†	1
	SLE	1	1
	Unspecified	1	0
Miscellaneous (n = 7)	Chronic renal insufficiency	2	0
	Drug-associated	0	2
	Endocrine	0	2
	Idiopathic aplastic anemia	1	0
	Unspecified	1	0
Undetermined (n = 7)	Not known	1	6

Leishmaniosi e Citopenie



Meccanismi immunomediati sono possibili

+ frequenti → meccanismi diversi dalla distruzione immunomediata :

- | | |
|------------------------------------------|--------------------------------------|
| coinvolgimento diretto del midollo osseo | ➢ piastrinopenia, anemia, leucopenia |
| flogosi | ➢ anemia (leucocitosi) |
| alterazioni emostatiche | ➢ piastrinopenia, anemia |
| perdita | ➢ anemia |
| CKD | ➢ anemia |

Leishmaniosi e malattie immuno-mediate correlate: terapia

Cortisone sì o no?

Cortisone ~ sì o no ?

Dosaggio ?

Altre terapie immunosoppressive ?