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Hepatocutaneous syndrome in a dog with concurrent Ehrlichiosis: Case report

Síndrome Hepatocutáneo en un Perro con Ehrlichiosis Concurrente: Reporte de caso

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ABSTRACT

This report describes the diagnosis of hepatocutaneous syndrome in a dog concurrently affected by Ehrlichiosis. A 13-year-old Golden Retriever presented with lethargy, fever, lymphadenopathy, and dermatological lesions on the paws, perianal region, and testes, characterized by hyperkeratosis, erosion, ulceration, crusting, and exudation. Clinicopathological evaluation revealed regenerative anemia, lymphopenia, monocytopenia, basophilia, thrombocytopenia, and increased serum activities of alkaline phosphatase, alanine transaminase, and gamma-glutamyl transferase. After ruling out other vector-borne diseases (e.g., Leishmaniasis, Anaplasmosis, Babesiosis), Ehrlichiosis was diagnosed. Abdominal ultrasonography revealed a honeycomb-like hepatic echotexture, and differential diagnoses for hepatocutaneous syndrome included pemphigus foliaceus/vulgaris, systemic lupus erythematosus, drug eruptions, and zinc-responsive dermatosis. Ultimately, the clinical, laboratory, and ultrasonographic findings supported concurrent diagnoses of hepatocutaneous syndrome and Ehrlichiosis. The dog died, most likely due to severe hepatic dysfunction and associated coagulopathy; disseminated intravascular coagulation was suspected based on the clinical course, although it could not be confirmed due to the absence of coagulation testing, despite receiving combination therapy that included vitamin–amino acid infusion, ursodeoxycholic acid, antioxidant nutraceuticals (S-adenosylmethionine, Silybum marianum, phospholipids, zinc), omega-3 fatty acids, and benzoyl peroxide shampoo for hepatocutaneous syndrome, in addition to doxycycline and prednisolone for ehrlichiosis. This case report highlights the diagnostic complexity of hepatocutaneous syndrome, particularly when concurrent with infectious diseases such as Ehrlichiosis. It demonstrates how overlapping clinical signs can complicate diagnosis and delay appropriate treatment. To the authors' knowledge, this is the first documented case of hepatocutaneous syndrome in a dog concurrently diagnosed with Ehrlichiosis. By presenting this case, we aim to raise awareness among veterinary clinicians of the importance of a thorough diagnostic workup in dogs exhibiting compatible dermatologic and systemic signs, even in regions endemic for tick-borne diseases.

Key words: Diagnosis; dog; liver, dermatology

RESUMEN

Este informe describe el diagnóstico de síndrome hepatocutáneo en un perro con ehrlichiosis. Un golden retriever de 13 años presentó letargo, fiebre, linfadenopatía y lesiones dermatológicas en patas, región perianal y testículos, caracterizadas por hiperqueratosis, erosión, ulceración, formación de costras y exudación. La evaluación clinicopatológica reveló anemia regenerativa, linfopenia, monocitopenia, basofilia, trombocitopenia y aumento de las actividades séricas de fosfatasa alcalina, alanina transaminasa y gamma-glutamil transferasa. Tras descartar otras enfermedades transmitidas por vectores (p. ej., leishmaniasis, anaplasmosis, babesiosis), se diagnosticó ehrlichiosis. La ecografía abdominal reveló una ecotextura hepática en panal, y los diagnósticos diferenciales para el síndrome hepatocutáneo incluyeron pénfigo foliáceo/vulgar, lupus eritematoso sistémico, erupciones medicamentosas y dermatosis sensible al zinc. Finalmente, los hallazgos clínicos, de laboratorio y ecográficos respaldaron los diagnósticos concurrentes de síndrome hepatocutáneo y ehrlichiosis. El perro murió, probablemente debido a una disfunción hepática grave y coagulopatía asociada; se sospechó coagulación intravascular diseminada según el curso clínico, aunque no se pudo confirmar debido a la ausencia de pruebas de coagulación, a pesar de recibir una terapia combinada que incluía infusión de vitaminas y aminoácidos, ácido ursodesoxicólico, nutracéuticos antioxidantes (S-adenosilmetionina, Silybum marianum, fosfolípidos, zinc), ácidos grasos omega-3 y champú de peróxido de benzoilo para el síndrome hepatocutáneo, además de doxiciclina y prednisolona para la ehrlichiosis. Este informe de caso destaca la complejidad diagnóstica del síndrome hepatocutáneo, particularmente cuando es concurrente con enfermedades infecciosas como la ehrlichiosis. Este caso demuestra cómo la superposición de signos clínicos puede complicar el diagnóstico y retrasar el tratamiento adecuado. Según el conocimiento de los autores, este es el primer caso documentado de síndrome hepatocutáneo en un perro con diagnóstico simultáneo de ehrlichiosis. Con este caso, buscamos concienciar a los veterinarios sobre la importancia de un estudio diagnóstico exhaustivo en perros con signos dermatológicos y sistémicos compatibles, incluso en regiones endémicas de enfermedades transmitidas por garrapatas.

Palabras clave: Diagnóstico; perro; hígado, dermatología

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INTRODUCTION

Ehrlichiosis in dogs (*Canis lupus familiaris*) is an emerging, vector-borne, rickettsial zoonotic disease with a global distribution. *Three Ehrlichial* species, *Ehrlichia* (E) *canis, E. ewingii, and E. chaffeensis*, are commonly responsible for infections in dogs. Fever, anemia-associated pale mucous membranes, lymphadenomegaly, hemorrhagic tendencies, hepatomegaly, lethargy, lameness, vasculitis, and petechial or ecchymotic hemorrhages are typical clinical signs observed in spontaneously infected dogs. Major hematological abnormalities include a severe thrombocytopenia. Other hematological abnormalities include non-regenerative anemia, lymphopenia, neutrophilia or neutropenia, monocytosis, thrombocytopathy, hyperproteinemia, hypergammaglobulinemia, hypoalbuminemia, and hyperglobulinemia. Granular lymphocytosis, renal azotemia, slight increase of liver enzymes, and aplastic pancytopenia may be seen in the chronic type [1, 2].

Hepatocutaneous syndrome (HCS), also referred to as superficial necrolytic dermatitis (SND), is a rare and often fatal disorder with a multifactorial etiopathogenesis, characterized by concurrent skin and liver lesions. The dermatological manifestations commonly include hyperkeratosis, fissures, erosions, ulcerations, crusting, and exudation affecting the paws, face, perianal region, and pressure points [3]. Hepatic lesions are typically described as diffuse, severe, non-inflammatory, degenerative vacuolar hepatopathy [4].

Microcytosis and elevated serum alkaline phosphatase (ALP) activity are common clinicopathologic abnormalities [5]. A non-invasive method that incorporates standard blood testing, abdominal ultrasonography, and clinical evaluation can be used to diagnose HCS in dogs. A honeycomb pattern in the liver and the description of characteristic skin lesions are used to establish the diagnosis [6, 7]. Intravenous amino acid injection is the traditional method of treating HCS. Dogs with HCS are frequently managed with nutritional supplements and dietary changes in addition to these infusions [8].

To the authors' knowledge, HCS, typically associated with metabolic or hepatic disorders [7], has not been previously reported in conjunction with Ehrlichiosis. This case report documents a dog with concurrent HCS and Ehrlichiosis, emphasizing the diagnostic challenges posed by overlapping clinical signs and the importance of a comprehensive evaluation in such complex cases.

MATERIALS AND METHODS

Case description

A 13-year-old Golden Retriever was brought to a private veterinary clinic complaining of skin lesions on the paw, lethargy, and temperature (measured with a rectal thermometer (TFA Dostmann digital thermometer, Germany). Physical examination revealed anorexia, lymphadenopathy, inappetence, weight loss, lameness, hyperkeratosis, fissures, and painful, crusting, moist ulcerative lesions on the footpad, perianal region, and testes (FIGS. 1 and 2). Upon shaving the dog's legs, the extent and severity of the skin lesions on the feet, perianal region, testes, and tail were clearly observed (FIG. 2).

Complete blood count (CBC; Sysmex pocH-100i autoanalyzer, Kobe, Japan) revealed a normal total leukocyte count (9.72 K/µL; reference interval [RI]: 5.05–16.76 K/µL), marked lymphopenia (0.05 K/µL; RI: 1.05–5.10), monocytopenia (0.02 K/µL; RI: 0.16–1.12), basophilia (0.25 K/µL; RI: 0.00–0.10), normocytic–normochromic anemia (RBC: 5.15 M/µL; RI: 5.65–8.87; hematocrit: 27.2 %; RI: 37.3–61.7; hemoglobin: 10.4 g/dL; RI: 13.1–20.5), and thrombocytopenia (platelet count: 66 K/µL; RI: 148–484; plateletcrit: 0.08 %; RI: 0.14–0.46). Red cell distribution width was mildly increased (RDW: 21.9 %; RI: 13.6–21.7). Blood serum biochemistry (Seamaty SMT-120 autoanalyzer, China) revealed a moderately increased ALT (225 U/L, RI: 10-125) and highly increased ALP (1.099 U/L; RI: 23–212 U/L) enzyme activities.

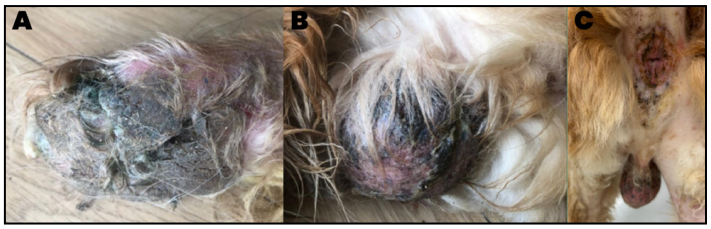

FIGURE 1. Cutaneous lesions associated with hepatocutaneous syndrome in a dog. (A) Severe hyperkeratosis, thick crusting, and fissures affecting the paw pads. (B) Erosions and ulcerative lesions on the scrotal skin. (C) Marked erythema, erosions, and ulceration in the perineal region.

Abdominal ultrasonography was performed by a board-certified veterinary radiologist using a 7.5 MHz convex probe (Mindray Z60, China). The examination revealed a heterogeneous echotexture of the hepatic parenchyma and characteristic HCS lesions, including a Swiss cheese–like or honeycomb pattern, parenchymal hypoechoic nodules, and an irregular liver border (FIG. 3) [4, 6, 7, 8].

Rapid diagnostic testing (IDEXX SNAP®) for blood parasites was considered due to the observation of clinical and hematological findings, including weight loss, depression, petechiae, pale mucous membranes, edema, lymphadenopathy, thrombocytopenia, anemia, and pancytopenia, which are typically observed in the chronic phase of Ehrlichiosis.

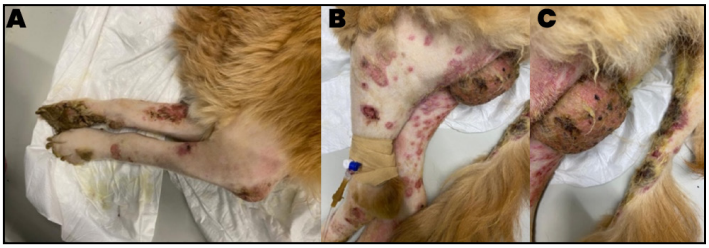

FIGURE 2. Cutaneous manifestations of hepatocutaneous syndrome in the dog, visible after shaving, showing petechiae (A, B, C), marked crusting (C), and erosions affecting the distal extremities (A, B).

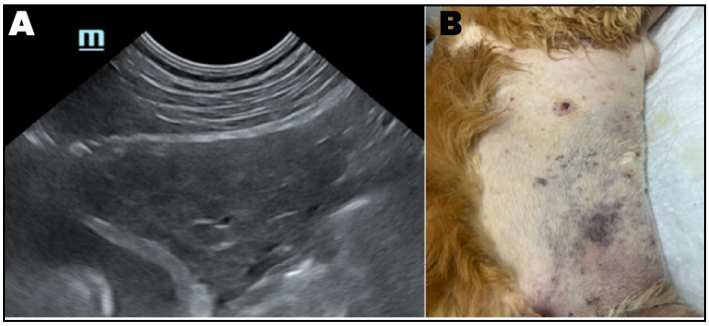

FIGURE 3. Transverse ultrasound image of the cranial abdomen showing a heterogeneous echotexture in the hepatic parenchyma with a Swiss cheese-like or honeycomb appearance (A), along with petechiae and ecchymoses in the skin of the abdomen, consistent with coagulopathy in the dog (B).

In this presented case, vector-borne diseases (e.g. Leihmaniasis, Anaplasmosis and Babesiosis) other than Ehrlichiosis have been evaluated, and taken into account in the differential diagnosis [1, 2]. Blood for serological testing was collected from the dog into plastic tubes without anticoagulant, allowed to clot at room temperature for 2–3 hours (h), and then centrifuged (Nüve NF 400, İstanbul, Türkiye) at 800 × g for 3 minutes (min) to separate the serum.

The obtained serum was used for the indirect immunofluorescence assay (IFA). A formalin-inactivated suspension of E. canis-infected cells (2 cells/mL) was used for the titration of anti-E. canis antibodies using the IFA method. The E. canis antigen, supplied by Synbiotics Europe (Lyon, France), was applied to 12-well microscope slides, which were then fixed in cold acetone at –20 °C for four h (Thermo Scientific TSX freezer, California, USA).

Before being used, prepared slides were kept at -20 °C. The reference method was used to test serum samples that had been diluted 1:20. The existence of fluorescent intracytoplasmic morulae was seen as a sign of a successful outcome when slides were viewed under an ultraviolet microscope (x100 magnification, Olympus CX21 light microscope, Japan). As advised by the American College of Veterinary Internal Medicine, samples were examined using a diagnostic threshold titer of 1:80 [9].

Urinalysis (Eikon URIT-31 urine analyzer, Malaysia) was unremarkable, and serum thyroxine concentration was within reference range. The skin scrapings and dermatophyte culture were negative. Additionally, pemphigus foliaceus or vulgaris, systemic lupus erythematosus, drug eruptions, and zinc-responsive dermatosis were considered as differential diagnoses for HCS. A drug-induced cutaneous eruption was excluded, as the anamnesis did not reveal any history of drug intake that could trigger such a reaction.

If acantholytic cells are seen, direct cytology of the pustules can quickly diagnose pemphigus foliaceus. Although crusted lesions were seen in the dog in our case report, acantholytic cells were absent.

RESULTS AND DISCUSSION

Hepatocutaneous syndrome and concomitant Ehrlichiosis were strongly suggested by clinical, laboratory, and ultrasonographic results. However, because amino acid profiling and liver or skin histology were not carried out, definitive confirmation of HCS was not achievable. To the greatest extent feasible, differential diagnoses with comparable clinical presentations were taken into account and eliminated.

A protocol for combined treatment was started. Intravenous vitamin and amino acid supplements (Duphalyte®, Zoetis; 50 mL/5 kg BW, given slowly over 4–6 h daily) were given to the dog. Ursodeoxycholic acid (15 mg/kg BW, PO, q 12 h), antioxidant nutraceuticals including zinc, phospholipids, Silybum marianum, and S-adenosylmethionine (1 tablet/10 kg BW, PO; Hepatiale Forte®, VetExpert), and omega-3 fatty acids (25 mg/kg BW, PO, q 24 h) were further supportive therapy. Throughout the course of treatment, benzoyl peroxide shampoo was administered to the afflicted skin areas and a commercial hepatic-support diet was consumed. Treatment for ehrlichiosis included prednisolone (1 mg/kg BW, PO, q 24 h) and doxycycline (10 mg/kg BW, PO, q 12 h).

At first, the dog's overall health and skin lesions showed slight improvement. However, after day 15 of treatment, the skin acquired ecchymotic and petechial lesions, and the clinical status worsened (FIG. 3). Concurrent hematologic and biochemical results showed deteriorating hypoalbuminemia and significant elevations in ALP, ALT, and GGT activity, indicating growing hepatic dysfunction. The combined consequences of thrombocytopenia and compromised hepatic function were probably linked to the development of severe hemorrhagic lesions. The dog's condition worsened in spite of supportive therapy, and it eventually died.

Based on clinical, biochemical, and abdominal ultrasonographic assessments, this case report details a dog with concurrent Ehrlichiosis and findings strongly suggestive of HCS. The instance demonstrates how overlapping clinical symptoms in dogs with dermatological and systemic diseases can be complicated.

Hepatocutaneous syndrome, the most frequent cause of SND in dogs, is caused by aminoaciduric canine hypoaminoacidemic hepatopathy syndrome (ACHE syndrome or ACHES) [10]. Canine HCS is a rare metabolic disease with a complex etiopathogenesis and a unique hepatopathy. This illness is frequently referred to by equivalent terminology, such as necrolytic migratory erythema, metabolic epidermal necrosis, and SND [3]. SND is rare, often lethal, and associated with both HCS and endocrine neoplasia [11].

Hepatocutaneous syndrome is characterized by SND lesions, a unique hepatopathy, hypoaminoacidemia, and aminoaciduria [12, 13]. A characteristic not seen in non-HCS chronic liver diseases, such as chronic hepatitis, vacuolar hepatopathy, or congenital vascular/biliary problems, is marked plasma hypoaminoacidemia in dogs with HCS. Specifically, concentrations of arginine,

citrulline, glutamine, glycine, and proline are frequently depleted to less than 30 % of the normal reference range. Plasma amino acid (PAA) profiling thus represents a simple, safe, and potentially valuable noninvasive biomarker for the diagnosis of HCS in dogs [14].

Crusting, ulcerative, and painful dermatosis are the hallmarks of cutaneous lesions in HCS instances, which usually affect the paws, pressure points, and mucocutaneous junctions. The typical histological characteristics of SND are present in these lesions [15]. Diffuse, severe, non-inflammatory degenerative vacuolar hepatopathy, which causes parenchymal collapse and the development of proliferative hepatocellular nodules, is the hallmark of hepatic lesions in HCS [4].

In a previous study, multifocal-to-coalescing foci of hepatocytes exhibiting severe ballooning degeneration, often accompanied by glycogen vacuolation and occasionally lipid vacuolation, were reported. These areas were intermixed with proliferative hepatocyte foci and regions of parenchymal collapse, producing a map-like appearance in hepatic sections. Ultrasonographically, 19 of 22 dogs (86 %) had a diffusely hyperechoic or complex heteroechoic hepatic parenchyma, and 14 dogs (64 %) displayed a Swiss cheese or honeycomb-like pattern typical of HCS [5].

In the present case, abdominal ultrasonography revealed a heterogeneous hepatic echotexture with a characteristic honeycomb-like pattern, consistent with findings previously reported in dogs with HCS. Although a definitive diagnosis of HCS could not be established due to the absence of histopathological confirmation and/or PAA analysis, the presence of this ultrasonographic pattern in combination with compatible dermatological lesions is considered highly suggestive of SND/HCS [3, 4].

Hepatocutaneous syndrome was first described by Veterinarians in 1986 as a dermatopathy associated with diabetes mellitus (DM) [8]. While HCS can occur alone as a dermatopathy [15], concomitant diseases such as DM [16], glucagon-producing pancreatic endocrine tumor, pancreatic endocrine tumour, hyperplasia of pancreatic neuroendocrine cells, extrapancreatic glucagonoma, insulin-producing pancreatic neuroendocrine carcinoma [17], hyperadrenocorticism, copper-associated hepatitis [18] associated with HCS have been reported.

It has been suggested that several affected metabolic pathways (e.g., hypoaminoacidemia, lipid metabolism, and biosynthesis) are associated with the pathophysiology of HCS [4].

The cutaneous lesions observed in this case are not pathognomonic and may also be encountered in several common canine dermatological diseases, including infectious pododermatitis, pemphigus foliaceus, leishmaniasis, canine distemper, and zinc-responsive dermatitis. These conditions were therefore included in the differential diagnosis. Although a definitive diagnosis of HCS could not be established, the exclusion of these alternative dermatologic disorders, together with the identification of a characteristic hepatic ultrasonographic pattern, strongly supported a clinical diagnosis of HCS. Overall, the clinical, biochemical, and ultrasonographic abnormalities observed in this case were consistent with those typically reported in dogs with HCS [3, 6, 7].

Canine Ehrlichiosis is a tick-borne, endemic disease found worldwide, which can cause illness and, in severe cases, death in affected animals [19]. Ehrlichiosis in dogs is characterized by typical clinical manifestations, including fever, depression or lethargy, anorexia, lymphadenomegaly, splenomegaly, mucosal pallor, ocular abnormalities, and a tendency to bleed in naturally occurring cases.

Thrombocytopenia is the most frequent hematological abnormality regardless of the phase (acute, subclinical or chronic) of the disease [20]. Some infected dogs progress to a chronic phase, which can be mild or severe. This phase is characterized by recurrent clinical and hematological signs, including thrombocytopenia, anemia, and pancytopenia.

Affected dogs may exhibit weight loss, depression, petechiae, pale mucous membranes, edema, and lymphadenopathy, among other signs. In severe cases, the response to antibiotic therapy is poor, and dogs often die from massive hemorrhage, severe debilitation, or secondary infections [21]. Concurrent diseases and organ abnormalities, such as splenomegaly, renal disease, and hepatomegaly, hepatopathy, or hepatitis, have been reported in cases of [22].

The disease can be diagnosed based on clinical signs and confirmed by demonstrating the organisms as clusters or colonies. However, various serological tests, such as indirect immunofluorescence antibody and ELISA, have been recommended, as detecting the organisms in peripheral blood cells is often not possible [21]. In this report, Ehrlichiosis was diagnosed based on anti-*E. canis* IgG antibody titers, using a positivity threshold of 1:80, as recommended by the American College of Veterinary Internal Medicine and the presence of compatible clinical and laboratory findings.

Clinical findings commonly associated with *Ehrlichia* infection, including fever, anemia-associated pale mucous membranes, lymphadenomegaly, hemorrhagic tendencies, hepatomegaly, lethargy, vasculitis, and petechial or ecchymotic hemorrhages [20], were interpreted as factors that may have exacerbated the clinical manifestations of HCS in this case. Severe hepatic dysfunction, together with marked thrombocytopenia—one of the characteristic features of ehrlichiosis—and suspected coagulation abnormalities, likely contributed to the development of severe hemorrhagic complications [23]. DIC was considered a possible contributing factor based on the clinical course; however, this could not be confirmed due to the absence of coagulation testing. These combined factors were therefore considered to have contributed to the dog's death.

There are some limitations to this case report. Although the diagnosis of HCS can be made based on clinical and typical ultrasonographic findings, such as the Swiss cheese or honeycomb-like pattern [3, 7], liver biopsies and serum amino acid measurements [24] could help strengthen the diagnosis. However, liver biopsy was not performed due to the risk of complications associated with the dog's hematologic abnormalities, and amino acid analysis could not be conducted

due to economic constraints; therefore, HCS can only be considered highly suspicious in this case.

Dermatological manifestations, including hyperkeratosis, fissures, and painful, crusting, moist ulcerative lesions on the footpads, perianal region, and testicles, were consistent with SND [15]. Furthermore, ultrasonographic examination of the liver revealed a diffusely hyperechoic or complex heteroechoic parenchyma, displaying the characteristic "Swiss cheese" or honeycomb-like pattern typical of HCS [5]. Collective assessment of the clinical, laboratory, and imaging findings strongly supported a diagnosis of HCS in a dog with concurrent Ehrlichiosis.

CONCLUSIONS

This case report describes a dog in which HCS was highly suspected based on compatible skin lesions, clinical assessment, routine hematology and biochemistry, and abdominal ultrasonography, after ruling out other differential diagnoses such as pemphigus complex, lupus erythematosus, zinc-responsive dermatitis, and drug-induced cutaneous reactions. Liver histopathology and amino acid analysis were not performed; therefore, a definitive diagnosis could not be established.

To the authors' knowledge, this is the first report of a dog with highly suspicious HCS concurrently affected by Ehrlichiosis. With more noticeable skin lesions, hematologic abnormalities, and systemic symptoms than are usually seen in HCS alone, the case demonstrates how Ehrlichiosis may worsen the clinical severity of HCS. These results emphasize the necessity of a comprehensive, interdisciplinary diagnostic strategy for treating complicated or overlapping canine diseases.

Conflict of interests

The authors declare no conflicts of interest.

BIBLIOGRAPHIC REFERENCES

[1] Mylonakis ME, Theodorou KN. Canine Monocytic Ehrlichiosis: An Update On Diagnosis and Treatment. Acta Vet. [Internet]. 2017; 67(3):299-317. doi: https://doi.org/gdthgc

[2] Aziz MU, Hussain S, Song B, Ghauri HN, Zeb J, Sparagano OA. Ehrlichiosis in Dogs: A Comprehensive Review about the Pathogen and Its Vectors with Emphasis on South and East Asian Countries. Vet. Sci. [internet]. 2023; 10(1):21. doi: https://doi.org/qrzn

[3] Götze DM, Götze MM, Filho ICB, de Carvalho FCG. Superficial Necrolytic Dermatitis in a Dog. Acta Sci. Vet. [Internet]. 2022; 50(supl 1):822. doi: https://doi.org/qrzp

[4] Loftus JP, Rubio MED, Yant J, Bichoupan A, Zhang S, Miller AJ, Center SA, Ruiz MDR, Macho LP. Untargeted metabolomic profiles reveal widespread metabolic perturbations and identify candidate biomarkers in aminoaciduric canine hypoaminoacidemic hepatopathy syndrome. Am. J. Vet. Res. [Internet]. 2023; 84(12):ajvr.23.08.0186. doi: https://doi.org/qrzq

[5] Hall-Fonte DL, Center SA, McDonough SP, Peters-Kennedy J, Trotter TS, Lucy JM, Berger E, Byers C, Cummings CG, Burke E, Stegemen J, Pintar J, Kantrowitz L, Sharpe K, Weinkle T. Hepatocutaneous syndrome in Shih Tzus: 31 cases (1996-2014). J. Am. Vet. Med. Assoc. [Internet]. 2016; 248(7):802-813. doi: https://doi.org/f8f53b

[6] Hill PB, Auxilia ST, Munro E, Genovese L, Silkstone MA, Kirby B. Resolution of skin lesions and long-term survival in a dog with superficial necrolytic dermatitis and liver cirrhosis. J. Small Anim. Pract. [Internet]. 2000; 41(11):519-523. doi: https://doi.org/bzjfgx

[7] Jaffey JA, Backus RC, Sprinkle M, Ruggiero C, Ferguson SH, Shumway K. Successful Long-Term Management of Canine Superficial Necrolytic Dermatitis With Amino Acid Infusions and Nutritionally Balanced Home-Made Diet Modification. Front. Vet. Sci. [Internet]. 2020; 7:28. doi: https://doi.org/qrzv

[8] Byrne KP. Metabolic epidermal necrosis-hepatocutaneous syndrome. Vet. Clin. North Am. Small Anim. Pract. [Internet]. 1999; 29(6):1337–1355. doi: https://doi.org/qrzw

[9] Neer TM, Breitschwerdt EB, Greene RT, Lappin MR. Consensus statement on ehrlichial of small animals from the infectious disease study group of the American College of Veterinary Internal Medicine. J. Vet. Intern. Med. [Internet]. 2002; 16(3):309-315. doi: https://doi.org/c8bn3p

[10] Loftus JP. Aminoaciduric Canine Hypoaminoacidemic Hepatopathy Syndrome. Vet. Clin. North Am. Small Anim. Pract. [Internet]. 2025; 55(4):595-613. doi: https://doi.org/qrzx

[11] DeMarle KB, Webster CR, Penninck D, Ferrer L. Approach to the diagnosis of hepatocutaneous syndrome in dogs: a retrospective study and literature review. J. Am. Anim. Hosp. Assoc. [Internet]. 2021; 57(1):15-25. doi: https://doi.org/qrz2

[12] Outerbridge CA, Marks SL, Rogers QR. Plasma amino acid concentrations in 36 dogs with histologically confirmed superficial necrolytic dermatitis. Vet. Dermatol. [Internet]. 2002; 13(4):177-186. doi: https://doi.org/bm63pq

[13] Brenseke BM, Belz KM, Saunders GK. Pathology in practice. J. Am. Vet. Med. Assoc. [Internet]. 2011; 238(4):445-447. doi: https://doi.org/d7k2p3

[14] Leela-arporn R, DeMarle KB, Heinze CR, Webster CRL. Plasma amino acid profiles of dogs with the hepatocutaneous syndrome and dogs with other chronic liver diseases. J. Vet. Intern. Med. [Internet]. 2025; 39(1):e17285. doi: https://doi.org/qrz6

[15] Almendros A, Sandy JR, Kirberger RM. Hepatocutaneous syndrome in a Maltese, diagnosis, treatment and the value of CT in the diagnosis. Vet. Rec. Case Rep. [Internet]. 2019; 7(4):e000918. doi: https://doi.org/g4nrf2

[16] Yoshida M, Barata K, Ando-Lu J, Takahashi M, Maekawa A. A case report of superficial necrolytic dermatitis in a beagle dog with diabetes mellitus. Toxicol. Pathol. [Internet]. 1996; 24(4):498-501. doi: https://doi.org/cx293j

[17] Isidoro-Ayza M, Lloret A, Bardagi M, Ferrer L, Martínez J. Superficial Necrolytic Dermatitis in a Dog With an Insulin-Producing Pancreatic Islet Cell Carcinoma. Vet. Pathol. [Internet]. 2014; 51(4):805-808. doi: https://doi.org/qrz7

[18] Talbot C, Kearns S, Mouser PJ. Treatment of superficial necrolytic dermatitis with copper chelation in a dog with copper-associated hepatitis. J. Am. Anim. Hosp. Assoc. [Internet]. 2023; 59(1):1–6. doi: https://doi.org/qrz8

[19] Bilgin BH, Kirli PG, Murat H, Turin K. A retrospective epidemiological study: the prevalence of Ehrlichia canis and Babesia volgeli in dogs in the Algean region of Turkey. Acta Vet. [Internet]. 2019; 69(2):164-176. https://doi.org/qrz9

[20] Qurollo BA, Buch J, Chandrashekar R, Beall MJ, Breitschwerdt EB, Yancey CB, Caudill AH, Comyn A. Clinicopathological findings in 41 dogs (2008-2018) naturally infected with *Ehrlichia ewingii*. J. Vet. Intern. Med. [Internet]. 2019; 33(2):618–629. doi: https://doi.org/qr2b

[21] Angkanaporn K, Sanguanwai J, Baiyokvichit TO, Vorrachotvarittorn P, Wongsompong M, Sukhumavasi W. Retrospective analysis of canine monocytic ehrlichiosis in Thailand with emphasis on hematological and ultrasonographic changes. Vet. World. [Internet]. 2022; 15(1):1-9. doi: https://doi.org/pxbg

[22] Mylonakis ME, Kritsepi-Konstantinou M, Dumler JS, Diniz PPVP, Day MJ, Siarkou VI, Breitschwerdt EB, Psychas V, Petanides T, Koutinas AF. Severe Hepatitis Associated with Acute Ehrlichia canis Infection in a Dog. J. Vet. Intern. Med. [Internet]. 2010; 24(3):633–638. doi: https://doi.org/d3xdr3

[23] Kaewmongkol G, Lukkana N, Yangtara S, Kaewmongkol S, Thengchaisri N, Sirinarumitr T, Jittapalapong S, Fenwick SG. Association of Ehrlichia canis, Hemotropic Mycoplasma spp. and Anaplasma platys and severe anemia in dogs in Thailand. Vet. Microbiol. [Internet]. 2017; 201:195-200. doi: https://doi.org/f9z89j

[24] Loftus JP, Miller AJ, Center SA, Peters-Kennedy J, Astor M. Treatment and outcomes of dogs with hepatocutaneous syndrome or hepatocutaneous-associated hepatopathy. J. Vet. Intern. Med. [Internet]. 2022; 36(1):106-115. doi: https://doi.org/qr2c