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S Sinha
Teaching Veterinary Clinical
Complex, Dau Shri Vasudev
Chandrakar Chhattisgarh
Kamdhenu University, Anjora,
Durg, Chhattisgarh India

SK Maiti
Teaching Veterinary Clinical
Complex, Dau Shri Vasudev
Chandrakar Chhattisgarh
Kamdhenu University, Anjora,
Durg, Chhattisgarh India

HK Rathe
Teaching Veterinary Clinical
Complex, Dau Shri Vasudev
Chandrakar Chhattisgarh
Kamdhenu University, Anjora,
Durg, Chhattisgarh India

Corresponding Author:
S Sinha
Teaching Veterinary Clinical
Complex, Dau Shri Vasudev
Chandrakar Chhattisgarh
Kamdhenu University, Anjora,
Durg, Chhattisgarh India

Immune-mediated haemolytic anaemia in dogs associated with haemoparasitic infections: Pathogenesis, diagnosis, and treatment

S Sinha, SK Maiti and HK Rathe

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Abstract

Immune-Mediated Haemolytic Anaemia (IMHA) is a hematological disorder that impacts dogs, characterized by antibodies that directly attack and destroy red blood cells present in the bloodstream. This condition can be classified as primary (idiopathic) or secondary (resulting from neoplastic or infectious diseases). The defining feature of IMHA, a potentially life-threatening autoimmune disorder, is the immune system's assault on circulating red blood cells. Although this disease is observed naturally in both humans and dogs, it is notably more common in the canine population. The purpose of this review was to systematically evaluate the existing literature on the disease's clinical-pathological aspects, its treatment options, and to use these findings to develop recommendations that could be applied in the field of veterinary medicine.

Keywords: IMHA, dogs, hemolytic anemia, autoimmune disease, clinical pathology, treatment

1. Introduction

There are two main types of immune-mediated hemolytic anemia (IMHA): primary (which can be idiopathic or autoimmune) and secondary. Primary IMHA is the most common variant seen in dogs and is classified as a classic autoimmune disorder without a known specific cause. This condition often affects young adult to middle-aged animals. Moreover, IMHA can arise as a result of various inflammatory, cancerous, or infectious diseases. Certain medications have also been identified as potential triggers for IMHA. Secondary IMHA can impact animals of any age or breed, and those presenting atypical signs for the initial form of IMHA, such as older pets, should be particularly considered. Unlike dogs, cats generally exhibit secondary IMHA. Because secondary IMHA often responds poorly to treatment or recurs until the underlying cause is identified and removed, therapeutic distinction between primary and secondary IMHA is essential [1]. Therefore, this review focuses on the fundamental aetiology, symptoms, clinico-pathological findings, diagnosis, and therapy of IMHA linked to hemoparasitic infections in dogs.

2. Immune-mediated haemolytic anaemia etiopathology associated with canine haemoparasitic infections

Immune-mediated haemolytic anaemia (IMHA) is classified as a type II hypersensitivity reaction in which antibodies target antigens present on the surface of red blood cells (RBCs), leading to immune-mediated destruction of erythrocytes and the development of anaemia. The antibodies responsible for this reaction are usually immunoglobulin G (IgG) or immunoglobulin M (IgM). When antibody levels increase, activation of the complement cascade may occur, resulting in the formation of membrane attack complexes that damage the erythrocyte membrane and promote haemolysis [3].

Although haemolysis primarily affects circulating erythrocytes, antibodies may occasionally target erythroid precursor cells in the bone marrow, which can lead to non-regenerative anaemia [3]. In cases of primary or non-associative IMHA, the immune system produces autoantibodies directed against normal erythrocyte surface components. One of the commonly recognized targets is glycophorin, a glycoprotein present in the red blood cell membrane that contributes to membrane integrity and cellular stability.

The pathogenesis of secondary or associative IMHA is more complex and involves several possible mechanisms. These include modification of erythrocyte antigens, molecular mimicry between infectious agents and erythrocyte membranes, and the attachment of foreign antigens to RBC surfaces, which can stimulate T- and B-lymphocyte responses and lead to antibody production^[4]. A wide variety of infectious, parasitic, bacterial, viral, and neoplastic diseases have been associated with the development of secondary IMHA^[4].

In some cases, antibodies bind to foreign antigens that have attached to erythrocyte membranes or to self-antigens that have been altered or exposed by drugs or disease processes. This mechanism results in immune destruction of erythrocytes and is considered a form of secondary IMHA^[5]. Furthermore, systemic inflammatory responses characterized by elevated acute-phase proteins and increased leukocyte counts may contribute to the pathophysiology of the disease, particularly in severe cases involving multiple organs.

Loss of immunological tolerance is considered a key event in the development of IMHA. When B lymphocytes respond to erythrocyte antigens, the immune system begins producing antibodies directed against RBCs, resulting in haemolysis. Normally, erythrocyte antigens may remain hidden or cryptic; however, membrane damage or exposure to infectious agents may reveal these antigens and trigger immune activation^[6]. Secondary IMHA may therefore occur when antibodies react with newly formed antigens or with foreign substances such as drugs or infectious organisms attached to erythrocyte surfaces^[7].

Several diseases have been associated with the development of IMHA in dogs, including systemic lupus erythematosus, neoplasia, blood-borne parasites, and adverse drug reactions. However, many cases are still classified as idiopathic because a definitive cause cannot be identified^[8]. Parasite-induced antigenic stimulation may also promote hypergammaglobulinemia and immune complex formation, which can contribute to immune-mediated conditions such as polyarthritis, thrombocytopenia, glomerulonephritis, and IMHA^[9].

IMHA is considered one of the most commonly diagnosed immune-mediated diseases in dogs and is typically characterized by anaemia, reduced packed cell volume (PCV), reticulocytosis, and leukocytosis with a left shift^[2]. Mortality rates may reach approximately 50% within two weeks in severe cases, particularly when complications such as liver dysfunction, renal failure, inflammation, or coagulation abnormalities develop^[2].

Haematological and biochemical findings associated with IMHA often include spherocytosis, polychromasia, thrombocytopenia, and hyperbilirubinemia^[11]. Elevated concentrations of liver enzymes such as alkaline phosphatase (ALP) and alanine aminotransferase (ALT) have also been reported in affected dogs^[11]. Concurrent thrombocytopenia occurs in approximately 50-70% of dogs with IMHA, often resulting from immune-mediated platelet destruction, haemorrhage, or disseminated intravascular coagulation^[12].

Another major complication observed in dogs with IMHA is the development of thromboembolic disorders, which are believed to result from alterations in blood flow, endothelial damage, and increased coagulability^[13]. Dogs presenting with high white blood cell counts, neutrophilia with left

shifts, and toxic neutrophil changes may have significant tissue injury and a poorer prognosis^[14].

Haemoparasitic infections have been recognized as important contributors to secondary IMHA in dogs. Infection with *Ehrlichia canis*, for example, may stimulate antibody production against erythrocytes and result in immune-mediated haemolysis^[15]. Ehrlichiosis is considered a potentially serious disease affecting both domestic and wild dogs^[16]. Following an incubation period of approximately 8-20 days, the disease progresses through acute, subclinical, and chronic phases.

During the acute stage of infection, the pathogen multiplies within mononuclear phagocytic cells located in organs such as the liver, spleen, and lymph nodes. These infected cells transport the organism to other tissues, where it interacts with endothelial cells and induces vasculitis^[16]. Histopathological findings frequently include perivascular inflammatory infiltrates, plasma cell accumulation in parenchymal organs, and vascular lesions affecting organs such as the lungs, kidneys, spleen, meninges, and ocular tissues.

The organism enters the canine host through the bite of infected ticks and subsequently spreads through the bloodstream to various tissues^[18]. Within host cells, the pathogen survives, replicates, and disseminates throughout the body. Circulating infected cells can induce vasculitis and intravascular coagulation, which contribute to immune-mediated destruction of blood components. These processes may lead to reduced erythrocyte production, destruction of leukocytes and erythrocytes, and the development of leukopenia and anaemia.

Studies have shown that *E. canis* organisms can be widely distributed throughout the organs of infected dogs, explaining the wide range of clinical manifestations associated with the disease^[19]. Severe pathological changes involving multiple organs may result from extensive vascular damage and inflammatory infiltration of tissues.

In addition to ehrlichiosis, canine babesiosis is another haemoparasitic infection closely associated with immune-mediated haemolysis. Babesiosis is caused by protozoan parasites belonging to the genus *Babesia*, which primarily inhabit red blood cells of the host^[21]. These organisms replicate within erythrocytes and can cause direct destruction of RBCs, leading to haemolytic anaemia.

Diagnosis of babesiosis is commonly confirmed through microscopic examination of blood smears, where the parasites can be directly observed within erythrocytes^[21]. Serological testing may also be used to detect exposure to the organism. Dogs infected with *Babesia* frequently exhibit thrombocytopenia and haemolytic anaemia, which result from both intravascular and extravascular haemolysis^[22].

Several mechanisms contribute to erythrocyte destruction during babesiosis, including reduced RBC lifespan, erythrophagocytosis, increased osmotic fragility, oxidative damage, and parasite-induced membrane alterations^[22]. Parasite antigens present on erythrocyte surfaces may trigger secondary immune-mediated haemolysis, further aggravating anaemia. Additional pathological processes such as vascular sludging, impaired haemoglobin function, and erythrocyte sequestration may also occur.

Clinical manifestations of canine babesiosis vary widely, ranging from mild infections to severe systemic disease. Reported complications include glomerulonephritis, acute or chronic nephropathy, coagulation abnormalities, jaundice,

immune-mediated haemolysis, metabolic disturbances, gastrointestinal signs, ocular lesions, respiratory complications, and systemic inflammatory responses [23].

Co-infection with multiple haemoparasites may significantly worsen disease severity. Dogs infected with *Babesia* species that also possess antibodies against *Ehrlichia* organisms have been reported to develop more severe anaemia and thrombocytopenia, demonstrating the complex interactions between haemoparasitic infections and immune-mediated disease processes [26].

3. Clinical symptoms of immune-mediated haemolytic anaemia associated with canine haemoparasitic infections

Dogs affected by immune-mediated haemolytic anaemia (IMHA) commonly present with a range of clinical signs associated with reduced oxygen-carrying capacity and systemic inflammatory responses. In one reported case, a dog diagnosed with primary IMHA showed weakness and anorexia lasting several days, accompanied by tachycardia, pale mucous membranes, and moderate hepatomegaly detected during abdominal palpation [27].

Other clinical manifestations frequently observed in dogs with IMHA include tachypnea, splenomegaly, hepatomegaly, pallor of mucous membranes, fever, pigmenturia, lymphadenopathy, and jaundice [28]. Jaundice is often easily recognized during clinical examination and generally becomes noticeable when serum bilirubin levels exceed 2-3 mg/dl, initially appearing on mucous membranes before affecting the skin.

Owners may also report nonspecific signs such as weakness, anorexia, vomiting, diarrhea, and pigmenturia, which are frequently associated with haemolytic anaemia in dogs and cats [29]. In approximately half of the affected animals, additional findings such as icterus, systolic heart murmurs, and enlargement of cranial abdominal organs may also be present. Elevated heart rate and increased respiratory rate have been observed in about 30% of dogs diagnosed with IMHA.

Haemoparasitic infections can further contribute to the clinical manifestations observed in affected animals. For example, parasitic infections may lead to loss of appetite, weight loss, and generalized weakness [32]. In cases of ehrlichiosis, epistaxis and corneal opacity have been reported as common clinical findings, which are often associated with thrombocytopenia resulting in persistent nasal bleeding.

Dogs infected with haemoparasites such as *Ehrlichia*, *Babesia*, or *Hepatozoon* species frequently develop anaemia and neutrophilic leukocytosis. These haematological changes may arise either from acute parasitic infections or from concurrent infestations involving multiple pathogens. In canine babesiosis, haemoglobinuria is commonly observed and may result in dark or coffee-colored urine, reflecting intravascular destruction of erythrocytes.

In some cases, concurrent infections with different haemoparasites may produce more severe clinical outcomes. For instance, a dog infected simultaneously with *Ehrlichia canis* and *Babesia gibsoni* showed signs including depression, lethargy, dehydration, weakness of the hind limbs, pale mucous membranes, and the presence of ticks on the body [33]. Clinical examination of the same animal

revealed hepatomegaly and enlargement of the popliteal lymph nodes.

Typical clinical signs associated with *E. canis* infection include fever, lethargy, anorexia, lymphadenopathy, splenomegaly, uveitis, haemorrhages, and pale mucous membranes [34]. In some cases, more severe complications such as ocular haemorrhage, ascites, skin lesions, paralysis, or blindness may also occur [35]. Haematological investigations in affected animals often demonstrate significant reductions in hemoglobin concentration, total erythrocyte count (TEC), packed cell volume (PCV), and platelet counts. Additionally, infected dogs frequently exhibit increased serum levels of bilirubin, ALT, ALP, blood urea nitrogen (BUN), and creatinine.

In most infections caused by *Babesia* species, the predominant clinical findings include fever, lethargy, and varying degrees of haemolytic anaemia [36]. These infections are often recorded more frequently during spring and summer seasons, likely due to increased tick activity during these periods.

Although some dogs develop severe disease, many animals experience acute infections that may progress into persistent infections with mild or minimal clinical signs. The severity of clinical manifestations can vary depending on factors such as the species of *Babesia* involved, the host immune response, and the presence of concurrent vector-borne infections.

Clinical signs reported in canine babesiosis include fever, pallor, jaundice, splenomegaly, weakness, collapse, pigmenturia, systemic inflammation, thrombocytopenia, and hypoxic tissue injury [23]. Gastrointestinal disturbances such as vomiting and diarrhea may also occur, although diarrhea is considered an uncommon manifestation in some cases [37].

The clinical presentation of ehrlichiosis can vary widely depending on the stage of infection, immune status of the host, and possible co-infection with other tick-borne pathogens. In addition to nonspecific symptoms such as fever and anorexia, dogs may develop splenomegaly, hepatomegaly, lymphadenopathy, exercise intolerance, and weight loss.

More severe manifestations may include vomiting, respiratory distress, edema of the tail or limbs, coughing associated with pneumonia, skin ulcers, petechiae, ecchymoses, prolonged bleeding during estrus, and gastrointestinal haemorrhage caused by thrombocytopenia or vascular damage. In chronic forms of ehrlichiosis, dogs may develop severe malnutrition, bleeding disorders, polyarthritis, endocarditis, and immune-mediated haemolytic anaemia [39].

During the subclinical stage of ehrlichiosis, infected dogs may appear clinically normal even though the pathogen persists within host cells. As the infection progresses into the chronic phase, animals may exhibit mucosal pallor, spontaneous bleeding, hepatomegaly, and splenomegaly [40]. Additional immunological complications such as Coombs-positive anaemia, hypergammaglobulinemia, pancytopenia, lymphadenopathy, and plasma cell infiltration of tissues have also been reported [41].

Veterinarians should suspect ehrlichiosis when dogs present with pale mucous membranes, thrombocytopenia, pancytopenia, epistaxis, ecchymotic haemorrhages, neurological abnormalities, or a history of tick exposure [42]. In one clinical report, a dog infected with *E. canis* showed fever, anorexia, weakness, haemoglobinuria, dehydration,

prolonged capillary refill time, pale mucous membranes, and splenomegaly, along with partial hepatomegaly detected during palpation^[43].

Infections caused by *Babesia* species have also been associated with autoimmune complications such as immune-mediated thrombocytopenia (ITP) and IMHA, which may occur independently or simultaneously^[44]. Physical examination findings in affected dogs may include abdominal distension, hepatosplenomegaly, petechial haemorrhages on the ventral abdomen, and tick infestations in areas such as the ears and interdigital spaces.

4. Diagnosis of immune-mediated haemolytic anaemia associated with canine haemoparasitic infections

Accurate diagnosis of immune-mediated haemolytic anaemia (IMHA) requires careful differentiation between primary (autoimmune) and secondary forms of the disease, as underlying infections, neoplasia, or other systemic conditions may lead to similar clinical presentations^[45]. Both forms may cause destruction of erythrocytes through intravascular or extravascular mechanisms; therefore, identifying the underlying cause is essential for selecting appropriate treatment strategies.

A diagnosis of IMHA is generally based on demonstrating immune-mediated destruction of red blood cells together with evidence of haemolytic anaemia. Clinical indicators such as hyperbilirubinuria and icterus are often associated with regenerative haemolytic anaemia. In addition, diagnostic confirmation typically requires the presence of one or more of the following findings: spherocytosis, persistent erythrocyte agglutination, or a positive direct Coombs' test^[1].

The reactivity pattern observed in Coombs' testing may differ between dogs affected by primary IMHA and those with secondary forms linked to underlying diseases^[46]. However, there is currently no single gold standard diagnostic test for canine IMHA. Instead, diagnosis relies on a combination of clinical evaluation, laboratory findings, and exclusion of other potential causes of anaemia^[47].

Veterinarians must first determine whether the anaemia present is regenerative or pre-regenerative, followed by identification of evidence suggesting immune-mediated destruction of erythrocytes. This diagnostic approach also requires ruling out other causes of anaemia such as blood loss, nutritional deficiencies, or bone marrow disorders.

In certain geographic regions, IMHA may be associated with vector-borne infections, including species of *Anaplasma*, *Babesia*, *Bartonella*, *Mycoplasma*, and *Ehrlichia*. In approximately 70-75% of cases, however, diagnostic screening does not identify an underlying cause and the disease is therefore classified as idiopathic. Mortality rates for IMHA may reach up to 51%, and the prognosis is often considered guarded for both primary and secondary forms of the disease.

One of the characteristic laboratory findings supporting a diagnosis of IMHA is autoagglutination of erythrocytes, which may be detected during microscopic examination or saline agglutination testing^[48]. The presence of spherocytes, which are small and dense erythrocytes lacking central pallor, also strongly suggests immune-mediated destruction of red blood cells.

The diagnosis of IMHA is typically supported when low haematocrit levels occur in combination with one or more additional indicators, including autoagglutination,

spherocytosis, increased osmotic fragility of erythrocytes, or a positive Coombs' test result^[48]. Blood smear examination may also reveal abnormalities such as polychromasia, anisocytosis, and spherocytosis, which indicate regenerative anaemia and immune-mediated haemolysis^[27].

The Direct Antiglobulin Test (DAT), commonly known as the Coombs' test, is widely used in veterinary medicine for confirming immune-mediated haemolysis. This test detects the presence of antibodies or complement components attached to the surface of erythrocytes^[51]. Similar to its use in human medicine, DAT remains one of the most sensitive and specific methods for diagnosing IMHA in dogs when species-specific reagents are used^[52]. The test also appears to be relatively resistant to interference caused by sample storage, immunosuppressive therapy, or prior blood transfusions.

Clinical and laboratory investigations of dogs diagnosed with IMHA frequently reveal bilirubinuria, hyperglobulinemia, and macroautoagglutination^[53]. Additional abnormalities may include azotaemia in approximately 20-22% of cases and elevated urine protein-to-creatinine ratios in around 50-52% of affected dogs. In many cases, IMHA is associated with infectious diseases, particularly infections caused by *Ehrlichia* species.

In rare situations, IMHA may develop during pregnancy. A reported case described a pregnant dog showing progressive regenerative anaemia, spherocytosis, lethargy, and reduced appetite, accompanied by strong agglutination in saline agglutination tests and haemoglobinuria detected during urinalysis^[54].

Diagnosis of haemoparasitic infections associated with IMHA often involves identification of specific pathogens. In canine babesiosis, two main species responsible for infection are *Babesia canis* and *Babesia gibsoni*^[55]. Clinical suspicion usually arises when dogs present with fever, anaemia, and thrombocytopenia, and confirmation may be achieved through microscopic examination of blood smears^[56].

Microscopic examination remains one of the fastest and most practical diagnostic techniques for detecting *Babesia* organisms within erythrocytes^[57]. Although this method is widely used due to its simplicity and accessibility, parasitemia levels may be very low in some cases, making detection difficult. In a study involving dogs infected with *B. gibsoni*, severe haemolytic anaemia and thrombocytopenia were common findings despite low levels of parasites observed on blood smears^[58].

Clinical investigations of babesiosis cases often reveal significant reductions in red blood cell counts, haematocrit values, and haemoglobin levels, accompanied by signs such as weakness, anorexia, and high fever^[59]. These findings, together with blood smear examination, can support confirmation of the disease.

In addition to babesiosis, ehrlichiosis is another important vector-borne disease associated with IMHA. Diagnostic testing for *Ehrlichia canis* infection may include rapid immunodiagnostic tests, serological assays, PCR analysis, and blood smear examination^[62]. In one study, blood samples from dogs suspected of ehrlichiosis were analysed using the Immunocomb® rapid diagnostic kit, which detected antibodies against *E. canis*^[60].

Haematological changes in dogs with ehrlichiosis commonly include decreased haemoglobin concentration, reduced RBC counts, thrombocytopenia, and decreased

packed cell volume. Changes in leukocyte profiles may also occur, including increased neutrophil counts and decreased eosinophil, basophil, and lymphocyte levels [60]. Biochemical analysis may show elevated concentrations of serum glutamic pyruvic transaminase (SGPT), serum glutamic oxaloacetic transaminase (SGOT), and creatinine, along with reduced total protein levels.

Additional diagnostic indicators have also been investigated for predicting disease prognosis. For example, the plasma mean platelet component (MPC) concentration measured at the time of initial examination may help predict survival outcomes in dogs with IMHA [61].

Several diagnostic techniques may be used to confirm infection with *E. canis*, including blood smear examination, polymerase chain reaction (PCR), and commercial diagnostic kits such as Snap 4Dx [62]. Studies have reported that *E. canis* infection is significantly more common in dogs with severe anaemia (PCV <15%) compared with those exhibiting moderate or mild anaemia [63].

Serological testing methods have also been evaluated for detecting antibodies against *E. canis*. In one comparison study, approximately 59.5% of samples tested positive using indirect immunofluorescence assays, whereas 64.9% were positive using rapid antibody detection tests [64]. The sensitivity and specificity of rapid ELISA-based diagnostic kits for detecting antibodies against *E. canis* have been reported to reach 96.2% and 100%, respectively, demonstrating high diagnostic reliability [65].

5. Treatment of immune-mediated haemolytic anaemia in dogs associated with haemoparasitic infections

Management of immune-mediated haemolytic anaemia (IMHA) primarily focuses on suppressing the immune response responsible for erythrocyte destruction while simultaneously addressing any underlying diseases. Immunosuppressive therapy remains the cornerstone of treatment in both veterinary and human medicine. Several therapeutic strategies currently under investigation include adoptive transfer of regulatory T cells, administration of low-dose recombinant interleukin-2 to stimulate regulatory T-cell activity, antigen-specific tolerance induction through peptide administration, and monoclonal antibody therapies designed to reduce B-cell mediated autoantibody production [69].

Glucocorticoids are considered the first-line treatment for IMHA due to their ability to suppress immune-mediated destruction of red blood cells. However, some dogs do not respond adequately to glucocorticoid therapy alone and may require additional immunosuppressive agents [70]. In certain cases, severe anaemia may develop during the early stages of treatment, which can lead to mortality despite therapeutic intervention. Furthermore, even when clinical improvement occurs, relapse remains a significant concern.

Recent studies have demonstrated that combining glucocorticoids with mycophenolate mofetil (MMF) may provide effective short-term control of the disease while potentially reducing adverse effects associated with prolonged corticosteroid use [71]. Mycophenolate mofetil is a prodrug that is converted into mycophenolic acid (MPA) after intestinal hydrolysis. This active compound suppresses immune responses by inhibiting the enzyme inosine monophosphate dehydrogenase (IMPDH), which is necessary for the synthesis of guanosine nucleotides in lymphocytes. By inhibiting this pathway, MMF reduces

proliferation of both T and B lymphocytes and decreases the production of antibodies responsible for erythrocyte destruction.

In addition to suppressing lymphocyte proliferation, MMF may also reduce recruitment of inflammatory cells such as monocytes and inhibit the activity of dendritic cells involved in immune activation [72, 73]. These immunomodulatory effects contribute to its usefulness in treating immune-mediated and inflammatory disorders.

Clinical investigations have shown that prednisolone therapy alone or in combination with MMF can be effective in the management of IMHA in dogs. One study reported that prednisolone administered at a dosage of 1.4 mg/kg/day combined with MMF at 10 mg/kg/day produced beneficial therapeutic outcomes in affected animals [74]. Improvements in haematological parameters have also been observed when MMF is incorporated into treatment protocols [75].

In some treatment approaches, prednisolone may initially be administered at an immunosuppressive dose of approximately 3.6 mg/kg during the first few days of therapy, followed by the addition of other immunosuppressive drugs such as cyclosporine when necessary. Although severe haemolysis may occur during the course of disease, several studies have reported favourable clinical responses in dogs treated with combinations of prednisolone and MMF [76].

Additional clinical research has indicated that combining MMF with glucocorticoids appears to be well tolerated and may positively influence the progression of acute IMHA in dogs [77]. In a small case series involving dogs diagnosed with idiopathic IMHA, several animals survived for at least two weeks following diagnosis when treated with MMF-based therapy [78]. These findings suggest that MMF may be a valuable adjunctive treatment; however, gastrointestinal toxicity has been reported as a potential limitation when higher doses are used.

Comparative studies evaluating different immunosuppressive protocols have also demonstrated that MMF combined with corticosteroids may produce outcomes comparable to those achieved with cyclosporine-based therapy in dogs with immune-mediated disorders. Furthermore, the incidence of adverse effects and treatment costs were reported to be lower in animals treated with MMF-containing regimens [79].

When IMHA occurs secondary to haemoparasitic infections, treatment must also address the underlying parasitic disease. In cases of canine babesiosis, relapse of infection has been reported despite the use of commonly prescribed anti-protozoal drugs, particularly in infections caused by *Babesia gibsoni*. This persistence highlights the difficulty of achieving complete elimination of certain haemoparasites. For infections caused by *Ehrlichia canis*, doxycycline therapy has been shown to be highly effective. Following treatment with doxycycline, the organism's DNA may no longer be detectable in the blood or tissues of infected dogs. In addition, antibody titres against *E. canis* tend to decrease and platelet counts typically return to normal ranges [81]. Successful treatment of the underlying infection may therefore contribute significantly to the recovery of dogs affected by secondary IMHA.

6. Conclusion

Immune-mediated haemolytic anaemia represents a serious and potentially life-threatening disorder in dogs, particularly

when associated with haemoparasitic infections. The disease involves complex immunological mechanisms that result in destruction of erythrocytes and may lead to severe anaemia and systemic complications. Early recognition of clinical signs, accurate diagnosis, and appropriate treatment are essential for improving patient outcomes.

Although considerable progress has been made in understanding the pathogenesis, diagnosis, and treatment of IMHA, many aspects of the disease remain poorly understood. Current therapeutic approaches rely largely on immunosuppressive drugs and treatment of underlying infections, but treatment responses and long-term prognosis can vary widely among affected animals.

Because much of the existing evidence is derived from limited clinical studies, there is a continuing need for well-designed research investigating both conventional and emerging treatment strategies for IMHA associated with haemoparasitic infections in dogs. Improved understanding of disease mechanisms and therapeutic interventions may contribute to better clinical management and improved survival rates in affected animals.

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