Hematologic Parasites

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Key points

- Cytologic observation of the etiologic agent in cases of hemoparasitism is possible with hemotropic mycoplasmosis, babesiosis, dirofilariasis, ehrlichiosis, cytauxazoonosis, leishmaniasis, and hepatozoonosis
- Immunofluorescent antibody tests, polymerase chain reaction based assays, and ELISA based antigen or antibody tests are available and often more useful in detecting and differentiating between similar groups of organisms.
- Treatment is usually rewarding in acute infections.

Hemotropic mycoplasmosis

This disease caused by a mycoplasmal organism that infects the erythrocytes of dogs and cats was previously called haemobartonellosis. The organism is genetically similar to *Mycoplasma* but distinctly different from *Bartonella*. Dogs rarely have hemotropic mycoplasmosis, and clinical signs of anemia usually only become apparent in splenectomized animals or those with splenic dysfunction.

Hemotropic mycoplasmosis in dogs is associated with *Mycoplasma haemocanis* and Candidatus Mycoplasma haemoparvum whereas hemotropic mycoplasmosis in cats is associated with *Mycoplasma haemofelis, Mycoplasma haeomominutum* or Candidatus Mycoplasma turicensis.

Pathophysiology

The parasite can be transmitted by ticks and fleas or by queens to their newborn kittens in the absence of blood-sucking arthropods. Splenectomy, immunosuppression caused by glucocorticoid therapy, or stress in cats with latent *M. felis* infection will predispose the development of clinical disease in the animal infected by the organism. An acute parasitemic phase in stressed animals usually occurs one week to months after infection. This phase involves cyclical parasitemia for weeks to months. An immune response elicited by the parasitized erythrocytes causes them to be rapidly sequestered in the spleen and other tissues where they become phagocytized. Parasites may be shed from the sequestered erythrocytes and thus re-enter the blood circulation.

Clinical presentation

Clinical signs include those generally observed with anemia. Weight loss may occur if the anemia develops slowly whereas acute, severe anemia produces sudden depression and icterus. Splenomegaly is often noted.

Diagnosis

Laboratory findings generally reflect a strong regenerative response in the CBC. The absence of marked anisocytosis or polychromasia in confirmed cases of feline hemotropic mycoplasmosis may suggest peracute infections with too little time to respond or concurrent infection with feline leukemia virus or feline immunodeficiency virus. Thin smears, made directly without anticoagulant, will assist in finding the epicellular organisms. Blood films should be well stained without precipitate to minimize any confusion in identifying the parasite. Cats often have coccoid or ring shapes whereas dogs mostly have linear chain forms. A positive Coombs' test may be associated with feline hemotropic mycoplasmosis. Recently feline PCR-based assays have been developed for identification of several strains of *these haemoplasmas* that are more sensitive than cytologic examination of blood smears.

Treatment

Blood transfusion is given if the anemia is severe. Prednisolone may be necessary initially to suppress the severe immune-mediated destruction of red cells. Doxycycline is preferred for dogs and cats given orally for three weeks. Tetracyclines can be given for three weeks, but this may cause fever and gastrointestinal disease in cats.Cats who recover may become latent carriers.

Babesiosis

This is a tick-borne protozoal disease affecting erythrocytes of dogs (Babesia canis, B. gibsoni). Babesia felis has not been reported in North American cats, but is reported in Africa and southern Asia.

Pathophysiology

Ixodid ticks are the major vectors of *Babesia* although there have been cases of infection through blood transfusion and transplacental transmission. Sporozoites are transmitted through the tick's saliva during a blood feed, but the parasite needs to feed for at least 2 days before transmission occurs. *Babesia* organisms become engulfed by erythrocytes, in which the parasites multiply to merozoites capable of infecting other erythrocytes. The incubation period is 10 to 12 days. Hosts are usually able to mount an effective immune response at this stage. If not, infected animals may develop a severe hemolytic anemia, hypotensive shock and multiple organ dysfunction syndromes. Although the parasites contribute to anemia an important factor is usually secondary immune mediated hemolytic anemia. Animals may relapse following therapy and affected dogs often remain as carriers.

Clinical presentation

Clinical signs of the acute disease include splenomegaly, icterus, anemia, thrombocytopenia, hemoglobinuria, bilirubinuria, and fever. It is common in kennel conditions and is especially associated with greyhounds.

Diagnosis

Examination of a blood smear reveals a clear, teardrop-shaped organism in erythrocytes, sometimes seen in pairs. An indirect fluorescent antibody (IFA) serum test is available which when titers are high indicates current infection. Concurrent infections *with Ehrlichia canis* may occur. A Coombs' test may be positive as in immune-mediated hemolytic disease. In severe cases, disseminated intravascular coagulopathy may be present and coagulation tests will be prolonged and fibrin degradation products increased.

Treatment

Treatment involves diminazene aceturate Berenil (Hoechst), imidocarb dipropionate 12% Imizol (Mallinckrodt Veterinary Inc.), or phenamidine isethionate.

Dirofilariasis

Dirofilariasis occurs worldwide and is caused by infection with nematode worms of the genus Dirofilaria. The disease is also known as "heartworm" because of the adult worms predilection for the pulmonary arteries and right ventricles.

Pathophysiology

Microfilariae are able to survive in hosts for up to 3 years. The parasite's life cycle continues when a mosquito ingests the microfilariae during a feeding. The infective larvae then migrate to the mosquito's stomach and mouthparts and are transmitted during future feedings. Infective larvae migrate to the pulmonary arteries where they develop into adults. Dirofilariasis may produce anemia following intravascular hemolysis as large numbers of adult heartworms (*Dirofilaria immitis*) obstruct blood flow, causing turbulence that mechanically disrupts erythrocytes. A postcaval syndrome results from obstruction of the caudal vena cava causes erythrocyte fragmentation (schizocytosis), hemoglobinemia, and hemoglobinuria, in addition to hepatic failure.

Clinical presentation

Some animals, particularly cats, may show "asthma-like" symptoms. Sedentary dogs are usually asymptomatic. In moderate disease the animal's condition is generally good but there may be occasional cough with exercise. In severe disease there is notable exercise intolerance with weight loss. Affected animals have an increased respiratory rate at rest and a persistent cough. Complications may include ascites and jugular venous distension.

Diagnosis

Definitive diagnosis involves detection of circulating microfilariae in the blood or serologic evidence of circulating antigens or antibodies. In-house tests such as IDEXX SNAP® and Heska Solo Step™ detect cuticular antigens of the adult female heartworm. A positive test result is considered diagnostic of heartworm disease. None of the available antigen tests for canine heartworm disease will detect infections with predominately male heartworms. Eosinophilia and basophilia are supportive laboratory findings as well as hyperglobulinemia related to the inflammatory response.

Treatment

The treatment of heartworm involves an adulticide, followed 3 weeks later by a microfilaricide and introduction of a monthly macrolide (for example, ivermectin). Tests should be conducted to ensure removal of the various parasite stages: an assay for microfilariae 2 weeks after the microfilaricide; an antigen assay 4 to 6 months after the adulticide, and heartworm status 6 to 12 months after treatment.

Ehrlichiosis/anaplasmosis

Cytauxzoonosis

This is a highly fatal protozoal disease caused by Cytauxzoon felis. It is tick-borne infection, most prevalent in the wooded areas of the southern United States. The bobcat and perhaps Florida panther are the natural reservoir hosts.

Pathophysiology

C. felis is transmitted by ticks of the genus Dermacentor. The organism is a piroplasm of the Theileriidae family. Schizonts and macroschizonts form in mononuclear phagocytes. Macrophages infected with merozoites line several veins throughout the body. When the merozoites are released into the blood circulation and the erythrocytes become infected. The rapid multiplication of the organism in the erythrocytes and tissue leads to organ dysfunction and eventually hypoperfusion, hypoxia and disseminated intravascular coagulation.

Clinical presentation

Initial clinical signs include anorexia, dehydration, and lethargy, with gradual development of fever. This progresses rapidly to icterus, moderate nonregenerative anemia, leukopenia, thrombocytopenia, and splenomegaly. Cats usually die within one week after clinical signs are recognized.

Diagnosis

Diagnosis is generally made post mortem by histologic identification of large schizonts in endothelial cells of the lungs, liver, bone marrow, or spleen. Terminally, blood films may contain small (1–2 μm in diameter) ring or "safety pin" structures within erythrocytes.

Treatment

Treatment is usually unsuccessful despite the use of antibiotics and supportive care. Untreated cases are nearly all fatal. Diminazene aceturate (2 mg/kg IM, repeated in 7 days) or imidocarb dipropionate (2 mg/kg IM repeated in 2 weeks) may sometimes be helpful in treating these cases along with heparin (100–150 U/kg SC every 8 hours) and intravenous fluids. Atropine (0.05 mg/kg) is recommended prior to treatment with imidocarb to reduce the immediate toxic effects of this drug. Blood transfusions are necessary for those cats with severe anemia.

Leishmaniasis

Leishmaniasis is an infrequent protozoal disease in dogs and rarely in cats caused by *Leishmania* spp. History usually indicates travel outside the United States to Mediterranean and Mid East countries, e.g., Greece, Spain, or Italy. The disease is also present in Central and South America and Asia. Endemic foci in Oklahoma and Texas have been reported, as well as a research colony in Ohio.

Pathophysiology

Sandflies are the vectors of *Leishmania* species. Rodents and dogs are the primary reservoirs for people and cats are probably incidental hosts. The parasite produces visceral or cutaneous manifestations. Promastigotes are disseminated throughout the body likely within macrophages. Nonflagellate forms called amastigotes develop and multiply within macrophages, infecting new cells. Signs can develop from 3 months to 7 years after infection.

Clinical presentation

Clinical signs in dogs, which develop over months, include exercise intolerance, weight loss, lethargy, anorexia, diarrhea, lymphadenopathy, alopecia, ulcerative dermatitis, fever, lameness, and conjunctivitis. Cutaneous nodules are mostly seen in cats.

Diagnosis

Cytology or histopathology is often diagnostic. Characteristic organisms are present in macrophages of the bone marrow, lymph nodes, spleen, liver, kidney, and skin. Amastigotes are recognized by the presence of a small purple nucleus and a perpendicular rod-shaped kinetoplast in Romanowsky-stained smears. Serology and tissue culture are additional diagnostic aids. Demonstration of leishmanial DNA by polymerase chain reaction is a very specific and sensitive method of diagnosis recently developed. A mild to moderate normocytic, normochromic anemia may occur. Hyperglobulinemia with hypoalbuminemia occurs commonly but presents rarely as a monoclonal gammopathy and reflects the plasmacytosis found in tissues.

Management

The disease is zoonotic and infected dogs can serve as a reservoir to people. Euthanasia should be considered. Treatment involves antimony compounds, although these drugs may be difficult to obtain. These compounds have a low therapeutic-toxic index. A recent alternative to antimony is allopurinol (7 mg/kg orally TID) for one to eight months. Prognosis depends primarily on renal function at the beginning of treatment.

Hepatozoonosis

This tick-borne disease of dogs, domestic cats, and wild canids is found in Africa, South Europe, Italy, Middle East, Asia, and in the U.S. Gulf Coast states from Texas to Georgia. Infections in cats are found in India, Africa, Middle East, and California in the U.S.

Pathophysiology

The disease is caused by ingestion of ticks (e.g., *Rhipicephalus sanguineus)* that are infested with the protozoan, Hepatozoon *canis.* Another form, *H. americanum,* is prevalent in the United States as well. Ingested ticks release sporozoites which penetrate the intestinal wall and are carried by blood and lymph to the lungs, spleen, liver or muscle where cysts are formed. The schizont within the cyst develops into merozoites or meronts, which eventually become gametocytes or gamonts that infect leukocytes or endothelial cells. Following a blood meal containing infected leukocytes, the organism develops into sporozoites within the tick. Development of gametocytes in leukocytes takes 3–4 weeks from the time of tick exposure.

Clinical presentation

Clinical signs in non-North American countries commonly involve fever, lethargy, anorexia, petechiation, and epistaxis. North American signs involve muscle atrophy, hyperesthesia, stiff gait, ocular and nasal discharges, recurrent fever, weight loss, polydipsia, polyuria, and bloody diarrhea. Tick infestation may be evident.

Diagnosis

Laboratory findings include leukocytosis (often extreme neutrophilia), thrombocytosis, mild normocytic normochromic nonregenerative anemia, hyperglobulinemia, and biochemical changes reflective of organ disease. Depending on the geographic region, the gametocytes may be found within blood cells. In North America, ice-blue oblong structures are encountered rarely (0.1% of cells) within the cytoplasm of neutrophils and monocytes in the blood or bone marrow. Gametocytes in other countries are much more prevalent (60–90%). Radiographic evidence of periosteal proliferation may be found. Serology using an indirect fluorescent

antibody test is helpful where the disease prevalence is low. Tissue biopsy demonstrating schizonts within pyogranulomatous lesions of the lung, skeletal muscle, liver, spleen, and lymph nodes is diagnostic.

Treatment

Despite treatment to clear parasitemia, relapse is often expected within several months. Antiprotozoal agents have been used with limited success. Clindamycin (10 mg/kg orally TID) may be used in combination with trimethoprim-sulfonamide (15 mg/kg orally BID) and pyramethamine (0.25 mg/kg orally once daily) each for two weeks to obtain a good clinical response. Oral toltrazuril, a coccidiostat has been used in dogs at 5 mg/kg BID for five days. Nonsteroidal anti-inflammatory drugs are indicated to reduce pain. Imidocarb dipropionate or diminazene aceturate have been used for some cases.

Summary

Romanowsky-stained blood films are useful to detect the presence of several common hematologic parasites. The diagnosis of hemoparasites is improved with immunologic and molecular based assays. Anemia and thrombocytopenia are the most common laboratory abnormalities.