



Mini-Review

CANINE GRANULOCYTIC ANAPLASMOSIS

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ABSTRACT

A review on the literature on canine granulocytic anaplasmosis is performed. The newest contributions to the aetiology, epidemiology, clinical manifestation, diagnosis, therapy and prevention of the disease are emphasized. A lot of data are cited, mainly focused on public health and the first canine clinical case of the disease in Bulgaria.

Key words: *Anaplasma phagocytophilum*, epidemiology, clinical manifestation, therapy, public health, Bulgaria.

INTRODUCTION

Granulocytic anaplasmosis is a tick-borne disease caused by *Anaplasma phagocytophilum* – a rickettsial pathogen, causing granulocytic blood infections in humans and animals (1, 2, 3, 4, 5).

The clinical appearance of *A. phagocytophilum* infection in dogs is defined in different ways: granulocytic ehrlichiosis (6, 7) – most commonly; anaplasmosis (8); granulocytic anaplasmosis (9).

Aetiology

Anaplasma phagocytophilum is a Gram-negative, obligate intracellular pleiomorphic agent. Up to 2001, *A. phagocytophilum* belonged to the genus *Ehrlichia phagocytophila*. This genus included *E. phagocytophila* (causative agent of the tick-borne fever in cattle, goats and sheep), *Ehrlichia equi* (causing granulocytic ehrlichiosis in horses) and an unnamed agent of human granulocytic ehrlichiosis (HGE) (4). On the basis of sequential analysis of 16S rRNA and groES1 operons, these three aetiological agents were united in one species and renamed to *A. phagocytophilum* (3,10). Target cells for *A. phagocytophilum* are neutrophil leukocytes and sometimes eosinophils (11). The earliest time when anaplasmae could be seen is 4 to 18 days after the infection as elementary bodies of 0-6 µm

or morules of 4-6 µm size in the cytoplasm of blood neutrophils. Microscopically, morules could be registered for a short period of time – usually for 4-8 days (4,12).

Epidemiology

Granulocytic anaplasmosis in dogs is sporadically detected in different European countries: Sweden (12, 13); Norway (14); Switzerland (15); Italy (16, 17); Austria (18, 19); Great Britain (6, 20); Slovenia (21); Germany (8, 22, 23); and Czech Republic (24).

In the USA, the disease (neutrophilic ehrlichiosis) was detected for the first time in 1971 in a German shepherd dog from Arkansas (25). In 1998 it was also studied in 6 dogs from North Carolina and Virginia (26). The latest data showed a remarkable wide prevalence – it was found in all states except for Mississippi and Nebraska (27, 28). *A. phagocytophilum* was evidenced for the first time in Australia in 2001, whereas the first incidence in Canada was in 2005 (29).

Granulocytic anaplasmosis is a vector-borne disease. The commonest vector of *A. phagocytophilum* in Europe is the tick *Ixodes ricinus*. In 1995 it was identified as a disease vector for the first time in Sweden (30), and then in Switzerland (31). The vectors in America are the ticks *I. scapularis* and *I. pasificus* (2,32). *A. phagocytophilum* is characterized with a trans-stage transmission.

An infection with *A. phagocytophilum* could occur through blood transfusion (25). There is no sex-related predisposition in dogs

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with regard to granulocytic anaplasmosis (33, 34, 35).

Pets are not a real source of infection for humans, but are sentinel animals (36). Such are also cats, among which the disease is also encountered. The seroprevalence in cats is different – from 4.3% to 38% (32, 37).

Clinical signs

The symptoms of granulocytic ehrlichiosis are not specific – fever (up to 41°C), anorexia, lethargy, depression, vomiting, diarrhoea, polyarthritis, splenomegaly, lymphadenopathy, anaemia (12, 13, 26, 34, 38, 39).

There are cases of co-infections with *B. burgdorferi*, *Babesia* spp. and the tick-borne encephalitis virus (17, 40, 41).

In experimental infection, the clinical manifestation is not significant (42).

The described haematological deviations in this disease are: leukopenia, rarely leukocytosis, normocytic normochromic anaemia and mild thrombocytopenia, eosinopenia (4, 19, 26). In the beginning of granulocytic ehrlichiosis, thrombocytopenia could be stronger (43).

Diagnosis

The detection of *A. phagocytophilum* morules in granulocytes is a sufficient prerequisite to identify the disease. Lester et al. (2005), Kirtz et al. (2000, 2005) and Pusterla et al. (1997) evidenced between 5% and 37% infected granulocytes in dogs with clinical signs of *A. phagocytophilum* infection.

For a more reliable diagnosis however, the performance of additional analyses is advised (19, 42, 44), such as: indirect immunofluorescence, PCR and isolation. Until now, all isolated strains have been cultivated on the human cell line HL-60 (45). Since 2006, the ELISA SNAP 4Dx test kit appeared on the market (IDEXX Laboratories, Westbrook, Maine, USA), that has a high sensitivity (99.4%) and specificity (100%). It detects IgM and IgG antibodies against *A. phagocytophilum*.

Therapy

The most efficient anti-ehrlichial/anaplasmatic preparation is doxycycline at a daily dose of 10 mg/kg for 3-4 weeks (27). The clinical effect is manifested within a week after the application. The premature discontinuation of the therapy however could however result in *A. phagocytophilum* carriership.

Public health

The first cases of human granulocytic ehrlichiosis (known today as anaplasmosis) were reported in 1994 in the USA (46). The clinical manifestation of the infection is accompanied with fever and non-specific symptoms. According to the severity of the clinical signs, the diseases could be from asymptomatic to life-threatening with lethal issue.

In Europe cases of granulocytic ehrlichiosis were reported in Holland (47), Spain (48), Norway (36), Sweden (49), Poland (50), Italy (51) and France (52).

Bulgarian Case Study

The results of a recent study by Hristova and Dumler (53) in people bitten by ticks in Bulgaria showed that antibodies to the agent of HGE were present in 20% of patients with fever, 8% - with lymphadenitis and 4% of clinically healthy people. Seropositive for HGE were 9.7% of patients with Eritema migrans and 2.9% of blood donors. These data indicated that probably, HGE is widely distributed in Bulgaria (11). Hristova and Bakardzhiev (2001) (54) described the first clinical case of granulocytic ehrlichiosis in a 47-year old patient from Burgas complaining of cold sensation, fever, strong headache and moderate muscle and joint pains.

In 2008, Tsachev et al. detected for the first time in Bulgaria granulocytic anaplasmosis in a 8 year-old male American Cocker spaniel. The dog was in a good overall condition – preserved vitality and appetite and normal body temperature. The ophthalmic examination showed enhanced purulent catarrhal discharge from both eyes and in-growth of blood vessels on the cornea. The diagnosis was confirmed with a serological ELISA test and detection of *Anaplasma phagocytophilum* morules in 12% of neutrophils. The 28-day therapy with doxycycline was effective (55).

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