Feline Leishmaniosis

Subjects: Veterinary Sciences

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Leishmaniosis is the third most important vector-borne disease in humans, preceded by malaria and lymphatic filariasis, and it is considered endemic in tropical and subtropical areas, where higher temperatures favor development of its vector, sandflies. This zoonotic disease is caused by infection of protozoa Leishmania spp. and the most serious mucocutaneous and visceral form is produced by Leishmania infantum, which predominates in the Mediterranean region. The usual hosts for this parasite are dogs and humans, but an increment in cases of L. infantum infection has been observed in cats in the last years. This increase could be due to the use of sandflies repellents in dogs, obligating the parasite to looking for other hosts. The role of cats in the epidemiology of this disease is unknown, although increase of prevalence of feline leishmaniosis has been observed in endemic areas in the last years. Diagnostic techniques and treatments in cats are not standardized, which makes it difficult to establish prevalence and epidemiology of feline leishmaniosis. Furthermore, the clinical signs and immune response against Leishmania in cats are different to those in dogs, with an observed increment of drug resistance. It is necessary to increase our knowledge about L. infantum infection in cats, including clinical signs, transmission, treatments, and the role of cats in the increasing of zoonoses. Finally, new alternative treatments are required for controlling the spread of this disease in all species of mammals.

Keywords: cats ; feline leishmaniosis ; Leishmania infantum ; zoonoses

1. Introduction

Leishmaniosis is a disease caused by the infection of protozoan parasite *Leishmania* spp. and transmitted by sandflies of the family Psychodidae (genus *Phlebotomus* in the Mediterranean region) [1][2][3][4]. The World Health Organization (WHO) estimates between 700,000 and 1,000,000 new cases in humans annually. This parasitosis is the third most important vector-born disease in humans, only preceded by malaria and lymphatic filariases, and it is considered endemic in tropical and subtropical areas, where the higher temperatures favor the development of sandflies [5]. Humans, together with domestic dogs (*Canis lupus familiaris*), are the main hosts, in which the diseases, caused by *Leishmania infantum*, represent an important problem for public health [6]. Infection in other animals, such as cats (*Felis catus*), wild canids, and horses, has been reported [7][8][9]. Although dogs used to be considered uniquely and mainly responsible for the spread of the disease to human, the increase in the number of cases diagnosed in domestic cats [10][11], and *L. infantum* parasites detected in cats sharing the same genetic characteristics with *L. infantum* strains isolated from humans and dogs [12][13][14], indicate that this species may play an important role currently in the epidemiology of infection in humans and dogs.

The first case of feline leishmaniosis (FL) was detected by Sergent et al. (1912) in Argelia [15]. FL cases have been described later in Europe, Latin America, and Asia, and their prevalence has increased considerably in recent years, with results of prevalence from 1.3% in Portugal or Qatar, to 22.5% and 25% in Brazil and Iran, respectively [10][16][17][18][19][20][21]. Although the highest prevalence of feline leishmaniosis has been found in countries where the disease is endemic, there are cases reported in other areas as well, such as the United States [22]. This FL rise could be connected with a host change due to the use of sandfly repellents in dogs, making them look for other hosts in which feed on [23][24]. In fact, the number of human leishmaniosis is also increasing, probably because the human companion animal bond is becoming higher with dogs and cats, rising the probability of infection [25]. Furthermore, some studies indicate that the use of secondary hosts by the parasite could be related to an increase in the virulence of *L. infantum* in humans. Concretely, human leishmaniosis outbreak in Spain with high virulence seems to be related to wild hares and wild rabbit's infection. Both species were found to be asymptomatic reservoirs for the parasite in an area with a low dog population density [26][27]. Early detection of infection in dogs and cats, together with its surveillance and treatments, are strategies to control and avoid human infection, following the "One Health" concept. In addition, and considering cats as emergent hosts with a possible role in the spread of the disease, a new evaluation for the epidemiology and control in this species is necessary [6][28]. However, detection in cats is often confused with other infections, as the clinical signs of leishmaniasis in cats are nonspecific. Furthermore, in some cases, disease appears without clinical signs, making its detection and control more difficult. Moreover, immunosuppression provoked by viruses such as those causing leukemia or feline immunodeficiency can increase parasite multiplication [7]. Due to the scarce information about the role of cats in the distribution of the disease or as reservoir, it is necessary to carry out studies focused on FL, as it could also constitute a point of infection for humans.

2. Epidemiology of Feline Leishmaniosis

Leishmaniosis is a zoonotic disease produced by parasites of genus *Leishmania*, mainly by the species *L. infantum* or *L. chagasi* in America [25]. Its principal host is domestic dogs (*Canis lupus familiaris*), but parasites have been isolated in rodents, lagomorphs, and wild canids, although the role of these species in the spread of the disease is not clear [8][26][29][30][31][32][33][34][35][36][37].

In cats, different species of *Leishmania* spp. have been identified, such as *L. infantum*, *L. mexicana*, *L. venezuelensis*, *L. braziliensis,* and *L. amazonensis* [25][38]. Recently, the first case of FL caused by *L. amazonensis* has been reported [39]. The transmission between host species is carried out through the bite of two genera of mosquitoes, *Phlebotomus* spp. and *Lutzomyia* spp. (*Psychodidae*) [19][25], but *L. infantum* has been isolated in fleas, ticks, and other arthropods, so they could also play an important role in the transmission even in cats [40][41]. Despite the fact that vertical and horizontal transmission are not well studied in felines [42], Vioti et al. (2021) have demonstrated by in vivo studies that infected cats are capable of transmitting *L. infantum* to sandflies [43]. Positive tests of *L. infantum* in cats have been reported in different countries in Europe and with different methods in the last twenty years (**Table 1**), showing the increasing relevance of cats in the transmission of the disease. Moreover, the existence of asymptomatic infection by *L. infantum* in apparently healthy stray cats has been demonstrated in Spain [44], which increases the importance of carrying out studies in cats as transmitters of the infection, mainly in endemic areas.

Table 1. Countries where high positive percentage of cases of *L. infantum* infection in cats have been reported and detection method (IFAT: immunofluorescence antibody test; DAT: direct agglutination test; PCR: polymerase chain reaction; ELISA: enzyme-linked immunosorbent assay). The material analyzed was serum samples for IFAT and ELISA tests, and whole blood for PCR test. * In this study, the authors analyze the antibodies to *Leishmania* spp.

Country	Method of Detection	Positive % Founded	References
Albania	**IFAT and PCR**	**0.7**	[45]
Cyprus	**ELISA and PCR**	**5.8**	[46]
Greece (Macedonia and Thessaly)	**IFAT, ELISA and PCR**	**46.0**	[47][48]
Italy (Sicily)	**ELISA and PCR**	**36.0**	[49]
Portugal (Lisbon)	**IFAT and PCR**	**20.4**	[24]
Portugal (Madeira Island)	**DAT**	**0.0**	[50]
Spain (South)	**IFAT and PCR**	**48.3**	[7]
Germany	**IFAT and PCR**	**4.0**	[51]
Qatar (Doha)	**PCR**	**1.3**	[21]
Brazil (Amazon region)	**IFAT**	**30.5**	[52]
Angola (Luanda) *	**DAT**	**3.9**	[53]
Iran (Kerman)	**PCR**	**13.9**	[54]
Israel	**ELISA**	**75.0**	[55]

Different prevalence of infection according to sex in non-neutering animals has never been observed, but factors such as age; neutering status; or co-infection with viruses as feline immunodeficiency virus (FIV) or feline leukemia virus (FeLV), mycoplasmas or other parasites, including *Toxoplasma gondii* (Protozoa), seem to be considered a determinant factor [53][56][57][58]. **Table 2** summarizes the different organisms, including bacteria, viruses, and other protozoan detected in co-infection with *L. infantum* in cats.

Table 2. Organisms (including bacteria, viruses, and protists) founded in co-infection with *L. infantum* in cats.

Organisms	Reference
Hepatozoon felis **and** ***Candidatus mycoplasma*** **haemominutum**	[59]
Toxoplasma gondii	[53][60]
Feline immunodeficiency virus (FIV) and feline leukemia virus (FeLV)	[56][61]
Mycoplasma **spp., FIV and FeLV**	[57]
Toxoplasma gondii **and FIV**	[58]
Rickettsia felis	[62]
Ehrlichia **spp. and** ***Bartonella*** **spp.**	[63]
Babesia **spp. (only in wild cats)**	[64]
Hepatozoon **spp. (only in wild cats)**	[64]

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