Feline Tritrichomoniasis

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Trichomonads are single-celled, flagellated protozoans that reproduce by binary fission and undergo direct transmission from host to host.[1] The distinctive feature of trichomonads is an undulating membrane that courses the entire length of the organism (Figure 1). There are both commensal and pathogenic species of trichomonads. Commensal species include *Pentatrichomonas hominis*, a trichomonad with five anterior flagella that inhabits the large intestine of a number of mammalian hosts, including cats, dogs, and humans. Trichomonads are occasionally observed in the feces of puppies with liquid diarrhea, although an unambiguous, causal relationship remains to be established. These organisms have been presumed to be *P. hominis*, based on their ease of eradication with metronidazole and the presence of other primary enteric pathogens in these animals. However, molecular characterization of these organisms has not been reported.

Tritrichomonas foetus is recognized as an important venereal pathogen of naturally bred cattle in which the organism is transmitted from the prepuce of the bull to the vagina and uterus of the cow. The primary clinical manifestation of infection in cattle is infertility, with occasional abortions during the first half of gestation.[2] The organism has also been described as an inhabitant of the porcine gastrointestinal and nasal mucosa, where its pathogenicity is uncertain.[3,4] *T. foetus* (cattle) and *Tritrichomonas suis* (pigs) are considered to be strains of the same species on the basis of morphology, ultrastructural analysis, random amplified polymorphic DNA analysis, enzyme homogeneity, and rRNA gene sequence identity.[5–11] Cross-transmission studies between cattle and swine with *T. foetus* or *T. suis* have revealed little host specificity.[3,12] Beginning in 1996, several reports have documented the presence of large numbers of trichomonads in fecal samples from young, densely housed cats with chronic large bowel diarrhea.[13–16] Based on detailed morphologic analysis and sequence identity of rRNA, the feline organisms have been identified as *T. foetus.*[17] Following experimental infection, *T. foetus* colonizes the feline ileum, cecum, and colon and results in diarrhea characteristic of the natural infection.[18]

SIGNALMENT, PREVALENCE, AND RISK FACTORS

Naturally occurring *T. foetus* infection is prevalent among young, densely housed cats.[13,16] Infections are seen in both nonpurebred (sheltered) and purebred (cattery) cats, and there is no sex predilection. The prevalence of *T. foetus* infection was 31% among 117 purebred cats from 89 cattery owners attending an international cat show.[16] Although there was no relationship between age and the presence of *T. foetus* infection among this group,[16] cats with associated diarrhea are typically young. In one study,[13] approximately 75% of cats were 1 year of age or younger at the time of diagnosis. Catteries in which *T. foetus* was identified had larger numbers of cats with diarrhea and more cats per square foot of cattery space, suggesting that crowding may be a significant risk factor for infection. Proximity of a cattery to agricultural species (pigs, cattle, horses), feeding of raw meat, type of water source, outdoor contact, and history of travel were not identified as significant risk factors for *T. foetus* infection. Coinfection by *T. foetus* and *Giardia* was common.[16] *T. foetus* was not demonstrated by either direct microscopic examination or protozoal culture of feces from 100 feral cats or 20 healthy indoor cats from geographic regions comparable to those of naturally infected cats.[7] Thus, *T. foetus* does not appear to be a component of the normal feline intestinal flora.

CLINICAL SIGNS

In domestic cats, *T. foetus* colonizes the colon, resulting in chronic large bowel diarrhea.[13,16–18] The diarrhea is characterized by a waxing and waning course and occasionally contains fresh blood and mucus. Diarrhea is semi-formed to cow-pie consistency and is malodorous (Figure 2). In very young cats and with poor housing conditions, the anus may appear edematous, erythematous, and painful; involuntary dribbling of feces or rectal prolapse may be seen. In general, cats otherwise maintain good health and body condition during infection. A consistent feature of *T. foetus* diarrhea is improved fecal consistency and disappearance of trichomonads during administration of antimicrobial drugs with a return of diarrhea containing trichomonads shortly after drugs are discontinued.[13] Misdiagnosis of *Giardia* is common in cats having *T. foetus* infection. Cats diagnosed with *Giardia* on the basis of direct fecal smear examination that fail to respond to appropriate antimicrobial therapy should be closely reevaluated for the possibility that the observed trophozoites were *T. foetus*.

DIAGNOSIS

Feline *T. foetus* infection is diagnosed by direct fecal smear examination for trichomonads, cultivation of feces using a commercially available system (In Pouch™ TF, Biomed Diagnostics, White City OR; www.biomed1.com),[19] or extraction of DNA from feces and amplification of *T. foetus* rDNA by polymerase chain reaction (PCR) using species-specific primers.[20]

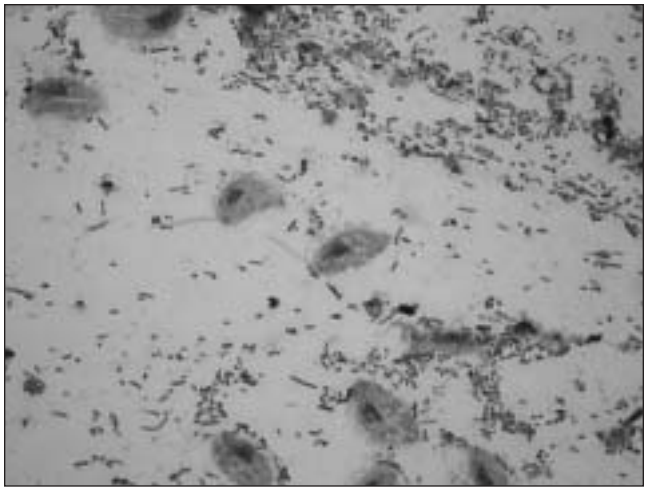

FIGURE 1. Tritrichomonas foetus *observed in a Wright's-stained rectal scraping from a cat with chronic large bowel diarrhea.*

Direct Fecal Smear Examination

Diagnosis is made by observation of trophozoites in feces diluted with saline solution and examined under a coverslip using a 20× or 40× objective. Lowering the microscope condenser to increase contrast may enhance visualization. Trichomonad trophozoites must be distinguished from those of *Giardia*. *Giardia* trophozoites have a concave ventral disk and motility reminiscent of a "falling leaf." In contrast, trichomonads are spindle-shaped, have an undulating membrane that courses the entire length of the body, and possess a jerky, forward motility. A video of the organisms can be viewed at www.cvm.ncsu.edu/mbs/gookin_jody.htm. *T. foetus* can be difficult to reliably distinguish from nonpathogenic intestinal trichomonads such as *P. hominis* on the basis of light microscopic appearance as the two organisms differ in appearance only by the number of anterior flagella.

Fecal samples should be freshly voided and diarrheic. Detection of trophozoites can be improved by collecting samples using a fecal loop[18] and by examining multiple fecal smears. Trichomonads will not survive refrigeration and are not observed after fecal flotation or sedimentation. Survival of trophozoites in feces can be extended from 0 to 4 days by removal of adherent litter and dilution of the sample with normal saline to avoid desiccation (3 ml 0.9% saline per 2 g of feces).[21] Concurrent antibiotic therapy will diminish the number of trophozoites present in feces, a fact that should be considered in cats with negative fecal smear results.[13] The sensitivity of direct fecal smear examination for diagnosis of trichomoniasis is low (2% in cats with experimentally induced infection and 14% in cats with spontaneous disease).[16,19]

Fecal Protozoal Culture

If repeated direct microscopic examination results are negative for trophozoites, feces may be cultured in-house using a commercially available system marketed for diagnosis of *T. foetus* infection in cattle (In Pouch™ TF).[19] For diagnosis of feline *T. foetus*, pouches should be inoculated with 0.05 g (about the size of a peppercorn) of freshly voided or loop-collected feces and incubated at room temperature (25˚C) in an upright position and preferably kept in the dark. Prior to microscopic examination, pouches are tapped against a benchtop to dislodge adherent organisms and then placed within a manufacturer-provided clamp that allows the pouch to be mounted onto the stage of a light microscope (Figure 3). Pouch contents should be examined every other day for motile trophozoites using a 20× or 40× objective and discarded if still negative after 12 days. Fecal culture using the In Pouch™ TF has a detection limit of 1000 or greater *T. foetus* organisms/0.05 g feces and is superior to direct fecal smear examination for diagnosis of *T. foetus* infection.[16,19] Neither *Giardia* nor *P. hominis* organisms can survive in In Pouch™ TF for longer than 24 hours, and thus positive cultures are strongly suggestive of *T. foetus* infection.[19] Strictly speaking, however, the types of trichomonads potentially hosted by cats and the specificity of In Pouch™ TF with regard to these other types of trichomonads is unknown. Positive In Pouch™ TF cultures do not preclude the possibility of coinfection with *P. hominis* or *Giardia*. Instructions on the use of the In Pouch™ TF system and where to purchase them can be found at www.cvm.ncsu.edu/mbs/gookin_jody.htm.

Fecal samples can also be cultured in antibiotic-fortified, modified Diamond's medium.[16,18] Such cultivation requires shipment of feces to a research laboratory, preparation and

FIGURE 2. *A cat naturally infected with* T. foetus. *Bowel movements are characteristically semi-formed to cow-pie consistency. Involuntary dribbling of feces may also be seen.*

FIGURE 3. *The In Pouch™ TF system can be used in clinic for the culture diagnosis of* T. foetus *using cat feces. The culture contents can be viewed directly by mounting the pouch onto the stage of a light microscope.*

maintenance of sterile medium, and 37˚C incubation. There is minimal evidence to suggest that modified Diamond's medium culture provides any greater diagnostic sensitivity than in-house fecal culture using In Pouch™ TF.[16]

Polymerase Chain Reaction

A sensitive and specific single-tube nested PCR based on amplification of a conserved portion of the *T. foetus* internal transcribed spacer region (ITS1 and ITS2) and 5.8S rRNA gene from feline feces has been described.[20] The PCR test is superior to fecal culture for diagnosis of naturally infected cats[16] and is commercially available. Information on how to submit fecal samples to North Carolina State University for PCR testing can be found at www.cvm.ncsu.edu/mbs/gookin_jody.htm.

Clinicopathologic Findings

Hematologic and serum biochemical analysis results from cats with *T. foetus* infection are invariably normal. Coexisting enteric infection by recognized feline pathogens (e.g. *Giardia*, *Cryptosporidium*, or internal parasites) is not a consistent feature. Infected cats usually test negative for FeLV antigen and FIV antibody.[13] Histopathologic changes in colonic mucosal biopsies from infected cats have been consistent with mild to severe lymphoplasmacytic colitis, with trichomonads observed in the superficial mucus and colonic crypts.[21]

Pathophysiology

It is likely that multiple organism, host, and environmental factors are involved in the pathogenesis of diarrhea in cats with *T. foetus* infection. Pathogenic factors associated with trichomonads include interaction with endogenous bacterial flora, adherence to host epithelium, and elaboration of cytotoxins and enzymes.[1] Infection of specific-pathogen-free cats with axenically cultured *T. foetus* results in chronic colonization of the terminal ileum, cecum, and colon and large bowel diarrhea akin to that observed in naturally infected cats.[18] In naturally infected cats, *T. foetus* antigen can be demonstrated within the superficial mucus and in contact with the surface epithelium of the cecum and colon. There is also evidence of antigen uptake by surface epithelial cells.[18] Whether long-term infection of cats with *T. foetus* is a predisposing factor for development of inflammatory bowel disease is unknown. The predominance of young cats from dense housing conditions may reflect an increased opportunity for exposure or enhanced susceptibility to infection because of environmental stress or immunologic immaturity.

TREATMENT

An effective antimicrobial treatment for feline *T. foetus* infection has not been identified. Cats infected with *T. foetus* have failed treatment with recommended (and in many cases higher) dosages of numerous antimicrobial drugs, including metronidazole, fenbendazole, albendazole, sulfadimethoxine, trimethoprim–sulfadiazine, furazolidone, tylosin, enrofloxacin, amoxicillin, clindamycin, paromomycin, and erythromycin.[13] Furthermore, *in vitro* studies of feline *T. foetus* in culture have revealed multiple drug resistance (e.g., to paromomycin, furazolidone, metronidazole, anisomycin, azithromycin, ciprofloxacin, chloroquine, doxycycline, tinidazole, and clotrimazole).[22] Although nitazoxanide inhibited growth of *T. foetus* in culture, rapid resistance to the drug was acquired *in vivo*.[18] In contrast to prior reports, paromomycin is not an effective treatment for *T. foetus* infection and has precipitated acute renal failure in infected cats.[23] Despite their failure to eradicate the infection, some cats have improved fecal consistency while receiving antimicrobial drugs.[13] This may be related to a dependence of trichomonads on endogenous bacterial flora and host secretions for acquisition of essential nutrients. Prolonged use of antibacterial drugs has not been uniformly useful for long-term control of diarrhea and may delay the onset of clinical remission.[21]

PROGNOSIS

In a long-term study of 26 cats with diarrhea and *T. foetus* infection, 88% (23 of 26) of cats had resolution of their clinical signs within 2 years of onset of *T. foetus*–related diarrhea (median, 9 months).[21] On the basis of fecal PCR, more than half of these cats remained infected with *T. foetus* despite resolution of their clinical signs a median of 39 months prior to testing.[21] These findings suggest that infections without clinical signs can be prolonged. Cats treated with paromomycin or undergoing a change in diet had significantly longer time to eventual resolution of *T foetus*–associated diarrhea.[21] There was also a positive correlation between the number of cats in each household and the duration of the interval to resolution of *T foetus*–associated diarrhea.[21] This could be attributed to increased stress or reinfection of cats under dense housing conditions.

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