Case Report

Small Intestinal Bacterial Overgrowth, Presumed Leaky Gut and Giardiasis Comorbidity in a Cat: Gut-Brain Axis Could Have Been Influenced by Triple Infection

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Abstract

In the present article we report a cat with small intestinal bacterial overgrowth with infectious co-morbidity. Recurrent hypersalivation, barborhytm, abdominal distension [both were detected by abdominal ultrasonography] and bad odor feces for several months duration. Referring veterinary surgeon on field conditions at private practice tried several antibacterial chioces with waxing and wanning clinical signs. On referral to the present authors university practice, all necessary and relevant laboratory work was deemed available including gut microbiota and PCR analytes. Small intestinal bacterial owergrowth (*E.coli* infection) was accompanied by viral (Herpesvirus) and parasitological (Giardiasis) co-morbidity and leaky gut (altered diamine oxidase and zonulin levels). To the present authors knowledge bacterial, viral and parasitological co-morbidity has never been reported in cats in our country associated with leaky gut and small intestinal bacterial owergrowth. The present case was well respond to 10 days rectal enema with Gut-cumin I, anti-leaky gut recipe, and other relevant nutraceuticals along with eubiotic antibacterial, rifaximine.

Keywords: Cat, leaky gut, SIBO

Case report with methodolody of diagnosis and relevant treatment outcome

A 1 year old cat referred to private practice several months ago with continuous hypersalivation. The owners tought that there was a gastric problem, in which referring veterinary surgeon used and attempted to treat with several gastrokinetic agents. Anti-acids and proton pump inhibitors were prescribed for several times along with several different antibiotics. Actually due to waxing and wanning clinical signs lastly the veterinary surgeon detected to take abdominal radiography in which bloat was evident along with obscured details within the abdomen. There was lost of sight with the abdominal details. Afterwards the cat was referred to our practice at University of Aydin Adnan Menderes, Faculty of Veterinary, Department of Internal Medicine. Feline Dermatology Group rendered all possible facilities at their owned equipments and performed all necessary laboratory work, as was shown below Table 1. PCR application was deemed available at our practice and leaky gut and intestinal injury biomarkers, namely zonulin and diamine oxidase, were analyzed by Sandwich ELISA at RDA Group facilities, in Istanbul

by experienced staff at ELISA. Comemrcially available feline test kits were deemed available. Patient bedside/ point of care rapid diagnostic test kits (Diagno Vet) were also purchased and used for quick analytes. The MiDOG® All-in-One Microbial Test (Irvine, CA, MiDOG® Test Center) was preferred for gut microbiota analysis. The latter test was a targeted, Next Generation DNA Sequencing Testing. Midog all in one microbial test could identify molecular signatures for specific microorganisms. Test material was sent to Germany and then transferred to Irvine, CA, USA.

Table 1. Well summarized all relevant diagnostic criteria adopted at this case report.

PCR analysis	
Gastroenterologic panel	Positive PCR respond
Feline coronavirus, *C. perfiringens, E. coli*, Feline rotavirus, *Salmonella spp., Campylobacter spp., Tritrichomonas feotus, T. gondii, Cystoisospora spp., Cryptsporidium spp.,* Feline parvovirus	*E. coli*
Feline Blood infection panel	Positive PCR respond
Feline calicivirus, Feline immunodeficiency virus, Feline herpesvirus, Feline leukemia virus, *T. gondii*, *Babesia sp., D, immitis, Microsporum felis, Chlamydophila felis*, Feline coronavirus,	Feline herpesvirus
Point of care /bedside test kit	
Diagno Vet three combo	
FPV+FCoV+Giardia	--+
Leaky gut Biomarker	
Zonulin Cat Zonulin CK-LAB Kits CK-bio24028 [detection range s 1.56ng/ml-50ng/ml	38 ng/ml
Intestinal mucosal injury biomarker	
Diamine oxidase [Diamine Oxidase, DAO ELISA Kit detection range 0.38-24ng/ml]	0.71 ng/ml
Small intestinal bacterial overgrowth biomarkers	
Vit B12/folate	Decreased/increased

Results

All relevant results were shared at table 1 above, commonly with the methodology. Figure 1. showed positive giardiasis reaction and result as was detected by point of care Diagno Vet test kits. On the other hand The MiDOG® All-in-One Microbial Test result showed potential clinically determined microbes, in which *E. coli* was also evident supporting the PCR results. Triple infection with *E. coli*, herpesvirus and giardiasis were all detected to table related with other relevant biomarker as shown in table 1 and figure 1,2. Taking into account leaky gut and intestinal injury biormarkers, all supported (table 1 and abdominal radiography of the present case, not necessary to be shown) small intestinal bacterial overgrowth and triple infection.

Figure 1. The present case and Diagno Vet combo diagnostic test kit showing giardiasis positivity. There was a weak positive repond, in which might be due to low giardia cyst numbers available at fecal sample.

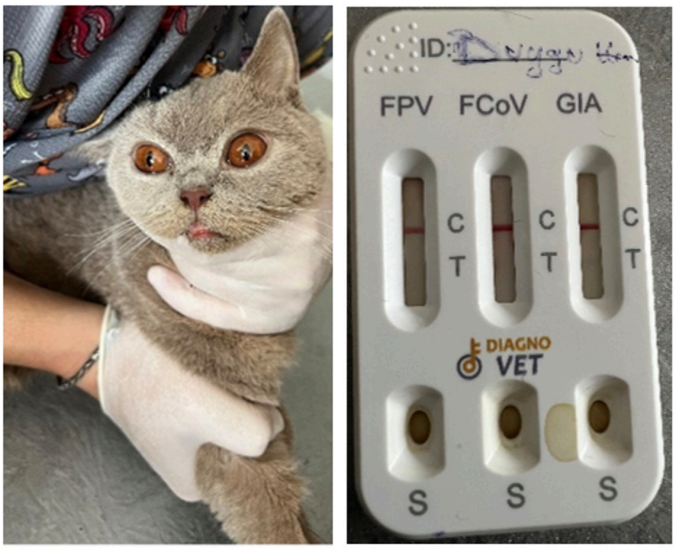
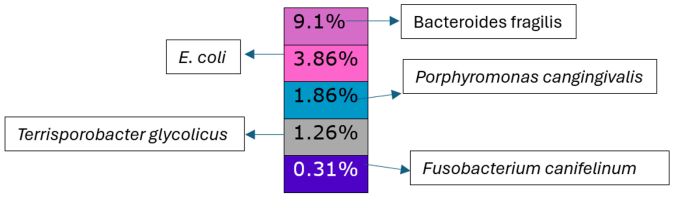


Figure 2. Composition of gut microbiota of a cat with leaky gut, sibo and triple infection Relative abundance of community at the species level.



Treatment outcome

The case was treated with rectal enema (on referral day and thereafterwards on day 10) and perorally on alternate days with Gut-cumin I, novel nutraceutical launched at March 2024. The latter liquid form nutraceutical contained trophic aminoacids and nutreacuticals (ginger, curcumin, licorice root, zinc and omega 3) and entirely formulated by the first author (K.U.) as an anti-leaky gut recipe. This formula was also directed to battle small intestinal bacterial overgrowth. Based on trophic aminoacids the dosage was 4 ml twice a day. In addition rifaximin was prescribed for 5 days p.o. at a dosage of 3 mg/kg fot its eubiotic efficacy.

Discussion

In a prior study detecting colony properties among 20 healthy cats and to those of 19 diseased cats with signs of chronic gastrointestinal signs within the duodenum, in which its undiluted fluid was analyzed for bacteriologic culture. In comparison to healthy cats, diseased cats exhibited significantly less counts of microaerophilic bacteria, indeed total, anaerobic, and aerobic bacterial colonies were not markedly altered. According to the latter authors healthy cats harboured elevated numbers of bacteria (obligate anaerobes) denoting that bacterial overgrowth in the small intestine is not frequently detected in cats with chronic nonobstructive gastrointestinal system disorders (Johnston et al., 2001). In contrast to this finding we can easily speculate that, in general practice with the academical staff involved at this case report saw more than 30 patients in a week, small intestinal bacterial growth is an epidemic that need to be addressed well. Several tests were deemed available in our practice directed to searching intestinal permeability/integrity, intestinal mucosal injury, leaky gut and small intestinal bacterial overgrowth giving us the oppurtunity to diagnose gastrointestinal issues in cats and dogs.

An interesting research analyzed alterations wlthin the duodenal microbiota of 12 healthy cats during a period, and detected the influence of dietary fructo-oligosaccharides. Mean aerobic, anaerobic, and total bacterial counts did not exhibited marked alterations. Among ½ of sampling *Enterococcus faecalis, Clostridium perfringens, Bacteroides, Pasteurella, and Streptococcus spp,* and others unidentified gram-negative (aerobic) rods were harboured. In that study duodenal microbiota was not influenced by dietary fructo-oligosaccharides (Sparkes et al., 1998). Another study aimed at investigation of the association among mucosal bacteria, gut inflammation and clinical disease activity through cats with inflammatory bowel disease. Duodenal biopsies were available (17 diseased, and 10 healthy cats). The count of mucosa-associated Enterobacteriaceae was elevated in diseased cats. Moreover *Enterobacteriaceae, E. coli,* and *Clostridium spp.* were exhibited correlation with mucosal atrophy and fusionindicating that mucosal bacteria were participated with in the etiopathogenesis of feline inflammatory bowel disease (Janeczko et al., 2008). We, herein at this case report identify, debug gut microbiota and detected relative abundaces of 5 different pathogens at species level. *Bacteroides fragilis* and *E.coli* was deemed exhibited the vast majority with their relative abundaces as 9.1 and 3.86%, relatively. *Escherichia coli* harboured various growth rates and motility rather at ileum vs colon, in association with variences among short chain fatty acids ratio between these two intestinal anatomical locations (Zhang et al., 2020). The actual physiological concentrations of secondary bile acids within the intestine is significant for swaying probable enteropathogens [i.e., *E coli, C. perfringens* and *C. difficile* (Berry et al., 2019; Weingarden et al., 2014)]. Nearly 30% of cats with chronic enteropathy CE exhibited diminished relative abundance for *C. hiranonis* and thus diminished secondary BA (Marsilio et al., 2019). In the present case report elevated *E.coli* abundance could be attributable to probably diminished bile acids, in which we were unable to demonstrate this. Our subsequent large surceyed study would thus be aimed at detecting differences of

core microbiome and probable metabolic signatures at different intestinal sites.

The vast majority of butyrate-producing bacteria among colon are *Lachnospiraceae* and *Ruminococcaceae* (phylum Firmicutes) families among people, in which the latter abundances are diminsihed during dysbiotic intestinal environment (i.e. ulcerative colitis and Crohn Disease) (Halfvarson et al., 2017; Nagao-Kitamoto & Kamada, 2017). Similarly among cats with chronic enteropathy butyrate-producing bacteria was depleted (Marislio et al., 2019). In the present case there was also depletion of *Lachnospiraceae* and *Ruminococcaceae* families.

Given small intestinal bacterial overgrowth, denotes existence of high loaded colonic bacteria within in the small intestine, elevated numbers of microorganisms consequently caused several gastrointestinal issues (Rao & Bhagatwala, 2019). Regarding the proximal anatomical location of small intestine, in which strictly composed of relatively less bacteria in association with harbouring of stomach acid and existence of natural peristaltic movements. In humans Lactobacilli, facultative anaerobes, Enterococci along with gram-positive anaerobes are predominant through the small intestine. On the other hand *Bifidobacteria, Lactobacillus, Bacteroides* and *Clostridium* are the vast majority with relative abundaces through colon (Khoshini et al., 2008). Even if preventive measurements (peristalsis, stomach acid, acidic environment) against exceeding bacterial growth fail, fall down, small intestinal bacterial overgrowth (sibo) could exist (Sorathia et al., 2024). In the present case report anti-acid treatment was used previously by referrring veterinarians.

Someone, may be readers or other relevant academical/clinical environments might speculate the relationship of sibo and *E. coli* or herpesvirus/ giardiasis, which were all detected at the present case. The vast majority of bacteria detected with sibo were *Escherichia coli, Aeromonas,* and *Klebsiella species* (Bouhnik et al., 1999). Anaerobic bacteria caused direct epithelial injury and exhibited enterotoxins. Indeed aerobic microorganisms solely fabricated enterotoxins, consequently asscoiated witin intestinal inflammation (Kirsch, 1990). Gastric herpes simplex virus type 1 infection has been linked with chronic gastrointestinal issues in a recent article (Duffy et al., 2022). This is not a random finding as feline herpesvirus has been also associated with gastric injury (Breuer & Hermanns, 2003; McGregor et al., 2016). Altough we could not speculate this cat in the present article showed triple infection due to herpevirus, this finding should be further warranted to investigate, probably after understanding virome. On the other hand giardiasis should be taken into consideration seriously. At calf model leaky gut and giardiasis link has been very well explained previously (Alic Ural, 2022). Moreover in a well written review the authors explained the mechanisms beyond giardiasis and its relationship with leaky gut. The group of authors aimed at explaining enrollment of the protease activated receptor 2 (PAR2) in giardiasis-facilitated intestinal defects (Vanessa et al., 2023). Previously Dubourg et al. (2018) interestingly reported a valuable research. Through exbition of proteins looking and acting similarly to selected human cells, Giardia parasites can covertly divide opening via intestinal cells of the host and let them open. This could have helped probably baring the host gastrointestinal system to a bacterial feeding hysteria (Dubourg et al., 2018). Best comment on this article has been written by Brandon Specktor on 2018 with spectacularly indicating that giardiais uses host own gut bacteria against.

Briefly we need to discuss small and large intestinal bacterial load separetely. Osbaldiston and Stowe (1971) were initally recognized gastrointestinal microbiota among 12 cats. In that research, coliforms, *Streptococcus, Enterococcus*, and *Lactobacillus* were detected as relatively abundant. Regarding other investigations on feline gastrointestinal tract *Bacteroides* and *Clostridium spp*. among duodenum (Johnston et al., 2001; Papasouliotis et al., 1998), *Clostridiales* and *Lactobacillales* (~ 90%) on jejunum along with *Clostridiales* and relatively few

Actinobacteria (~ 5%) on colon (Ritchie et al., 2008). On the other taking into account large intestine, something new must be shared.

Regarding different investigations among feline gut microbiota *Actinobacteria, Bacteroidetes, Firmicutes, Fusobacteria*, and *Proteobacteria* (Ganz et al., 2022; Ritchie et al., 2008, 2010; Tun et al., 2012) were 5 phyla determined. On the other hand solely 3 of the latter phyla, without *Fusobacteria* and *Proteobacteria* (Desai et al., 2009; Handl et al., 2011). In the present case, we herein reported, all 5 phyla were evident. *Lactobacillales* were the vast majority probiotic bacteria of the cat, dog and human gut microbiome (Fusi et al., 2019; Rastogi & Singh, 2022; Strompfová et al., 2017). In a large perspective research detecting core microbiota among 161 North American domestic cats, genera were exhibited over 55% of the healthy ones enfolled by *Prevotella, Bacteroides, Collinsella, Catenibacterium, Blautia, Faecalibacterium* and *Megasphaera* as the vast majority (Ganz et al., 2022). As was also aforementioned above in the present article treatment efficacy along with anti-infective propects of Gut-cumin I used at the present case consequently resulted with clinical cure. As an anti-oxidant rich polypehol source, Gut cumin I composed of also ginger and curcumin might have helped priority treatment of sibo. Curcumin's anti-bacterial (Tyagi et al., 2015) or anti-herpesvirus activities (Kutluay et al., 2008) along with ginger's anti-bacterial (Gupta et al., 2005; Wang et al., 2020; Zainal et al., 2022) and virucidal (Camero et al., 2019; Koch et al., 2008) efficacy could have influenced the positive treatment repond at the present case, via Gut-cumin I liquide support used as an enema and oral routes. Moreover curcumin also holds passport for anti-giardial acvitity (Gutiérrez-Gutiérrez et al, 2017; Pérez-Arriaga et al., 2006; Ural et al., 2022), in which triple infection and sibo repond to Gut-cumin I treatment at the present case.

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