The Parasitosis-Cancer connection

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INTRODUCTION

Parasitosis is a disease that is thought to affect at least two billion people annually in just developing countries, and normally impacts 33% of the population. In animals, the numbers are estimated to be even higher,

particularly, non-marine species are all infected and have been multiple times in their lives.

It is evident in domestic animals, specifically in felines and canines, with special focus on felids, parasitosis can be transmitted via the orofecal route (from grooming), and can occur as early as birth, although diagnosis becomes harder as they age. This is obviously the case for protozoans, however, sometimes lab tests fail, for a variety of reasons, and it can then be hard to obtain the minimum count of helminths to establish that a parasitic infection is present, making it challenging for veterinarians. As discussed in a previous preprint, it is not unusual to find helminths and protozoans initiating cancer, however, co-infection involves the presence of bacteria and viruses too.

The role of viruses on immunity is particularly important when it comes to re-infections; in outdoor cats that are more at risk of being affected by retroviruses, such as by FCoV (Feline Coronavirus), FIV (Feline Immunodeficiency Virus), because feral animals tend to be unvaccinated, the possibility of recurrence of parasitosis is heightened. However, with the advent of the COVID-19 virus, it is possible to note that parasitic disease (caused by both helminths and protozoans), can occur repeatedly, due to a

weakening of the immune system, and that in fact viruses constitute the main trigger for infectious diseases to take place. Domesticating animals that share spaces with us, can improve both our and their life-expectancy and quality of life.

EVIDENCE IN CANCER

The previous preprint linked parasitic infections with cancer, as it involved a feline patient, whereby an investigation led to the discovery of the *Cystoisospora* species. Multi-organ "symptoms", a very common feature in parasites, initially manifested as a UTI with kidney disease, following the first few 7 months of the COVID-19 pandemic. The kidney stones improved by introducing a "salty buffer" in the diet, which role was that of adjusting the pH, but two years later, the lesions extended to the gastrointestinal (GI) tract and the pancreatic parenchyma, implying some form of "autoimmunity". This scenario is known by many veterinarians as *triaditis*, a form of multi-organ "failure", however, the kidneys are usually not considered a part of the process, usually it is just the colon, the stomach and the pancreas that are suffering. Further, blood tests revealed altered colorectal lining, denoting a form of late stage hypothesized autoimmune-

carcinogenic ongoing scenario, i.e. Inflammatory Bowels Disease IBD-lymphoma.

It is clear that the process of carcinogenesis in this case, could be assimilated to one of infection in which the agent doesn't struggle as much in moving across several compartments. Immunotherapy with the initial administration of a steroid improved nausea and vomiting, but the dysenteric symptoms persisted, up until a month later when the prednisolone (Prednicortone®) ceased to work at the second month of administration, provoking the resuming of the initial symptoms; vomiting, weight loss, lethargy, hind limb paresis, due to pain and cramps, as well as continued dehydration associated with the persistent diarrhea in the ailing cat. At that point a stool sample swap was analyzed, uncovering traces of "eggs", connecting the disease back to an infectious form (parasitosis), more specifically, to *Cystoisosporiasis*. By administering an anti-protozoan and anti-helminthic medication, quick improvement was seen, although the initial dosages were elevated. Following the above, the steroid began working immediately, providing relief; after a month the cat recovered his energy and appetite, and with the anti-helminth therapy, which was administered more frequently (four times / *toto*, instead of twice / *toto* as in the case of Mefloquine), faster

weight regain was noted (ca. 2 kg/*mensis*). Occasional *helicobacter* therapy also was carried out with Clarithromycin (with a single Omeprazole granule every 4.5 kg of the feline's body weight).

Recently, the dosage for the chemotherapy has been re-adjusted, for instance, a co-administration with 5-10 mg Mefloquine (MFQ), accompanied by 2-5 mg Clarithromycin, and one full 250 mg fenbendazole tablet, enhancing the full absorption of each drug, with particular focus on Mefloquine, was given provided. At higher doses, Mefloquine is less well-tolerated and could be expelled emetically, within 40 minutes post-administration, creating non-absorption and consequently, therapeutic failure. Several studies in the past few years, have proven that Platin-based compounds, and particularly Oxaliplatin® previously employed clinically for improving the life-expectancy of end stage colon cancer patients exert a mild antiparasitic (anti-protozoan activity).

This supports the clear link between cancer and infectious diseases, and particularly, cancer stem cell (CSCs) behaviors, such as undifferentiation, and how they are interconnected with parasitic evolution, as well as the mitotic rate for stem cells that is very close to that of the protozoan schizogony process, or parasitic reproduction.

Recent works on prostate cancer denote that Toxoplasmosis (etiologic agent *T. gondii*) and *S. haematobium*[1], are some common protozoan infestations in patients during their initial stages of Benign Prostatic Hyperplasia (BPH), but also elevated quantities of certain toxic strains of *Lactobacilli*, whose role at the site remains controversial, have been found[2-3]. For example, it is our belief that *Lactobacilli* are transported and dropped at diverse sites by other infectious agents, likely by parasites themselves, to further alter the homeostasis of the organic host they are invading. This hypothesis is backed by the common knowledge that shows how *fungi* and *algae* can trap and harm parasites. Bacteria could colonize parasites too, and in the case of *protozoans*, create hybrids, this could be the evolutionary step that some kingdom *Protista* (or good *protozoa*) took when were isolated and targeted by bacterial colonies, whilst the "socialist" ones survived. Siding with the "good guys" made them pretty much invincible, whilst siding with the bad ones induced devolution. Tamoxifen®[4], also has been recently associated with anti-parasitic activity, and parasitic *schistosomiasis* has been reported in the breast as well[5], concocting supplementary proof to the initial theory published on *Engrxiv*[6].

Likewise, the presence of “deformed” WBC (white blood cells) in the previously evolving lymphoma, reminds us of the well-known disease sickle-cell anemia caused by *P. Falciparum*, which can only lead us to believe that a connection exists between malformations in both lymphomas and leukemias with parasitosis (sickle-cell delineates “deformed shapes” in pathology).

Ultimately, one year and a half on steroid therapy, we noted that the feline patient, who did not experience any other episodes since his remission, aside from the occasional hairball discomfort, did go through another occurrence of nausea and dysentery two weeks after contracting the COVID-19 from the owner. The combination treatment of the 5 mg anti-protozoan MFQ, 2 mg Clarithromycin and 250 mg Fenbendazole, administered *per os*, led to a 3.5-12 h disappearance of dysentery (recurrent loose and watery stool passing occurred *qid* due to infection), loss of appetite (uncommon during steroid therapy) and lethargy also ceased to show as symptoms.

Although further studies in the human need to be considered, and duly cited, it is very likely that the efficacy of the chemotherapeutics of choice hereby discussed and their structure alone potentially exerting multiple actions, seem far-fetched, because therapeutic effectiveness seems to direct us

towards the co-existence of parasitosis and cancer, since parasitic-like behavior is seen in CSCs. As mefloquine and fenbendazole are two potent anti-parasitic agents, it isn't just that they work because they target the rapid mitotic rates in late-stage liquid cancers, but it is because of the parasites being the source of the cancers themselves and because they play an active role in it, by enrolling local cells, like they do bacterial cells when they transport them from one compartment to another. In fact, by carrying bacteria and perhaps even *fungi*, they are capable of inducing hybridization, and engaging them into schizogony; they can remove all those host-differentiated "cell species" they don't need, whilst taking advantage of their newly-recruited "cell servants", whether animal, or bacterial, and strip them of any specific function.

The "PDF" moiety as confirmation of Parasitic-Bacterial Hybridization

The PDF moiety was primarily mentioned on *Engrxiv,* highlighting how Mefloquine acts like a mimicker of this structure, displacing and tricking parasitic structures destabilizing them via adhesion disruption mechanism[5]. Recently, we have found that the PDF *moiety* may play an important role in the hybridization process of encystment in both *protozoa* and *protists* under stressful conditions, such as of extreme dehydration as well as in a dire

situation of engulfment by numerous bacterial colonies. Because of this, it is highly probable that hybridization occurs between these species, and that the PDF *moiety* may play a dominant role in hybridizing structures through an adhesion “tightening” mechanism, which is why the structure of mefloquine, functions as an effective drug in depressing protozoan infections. On the other hand, reproductive manipulation is not novel and not unheard of across helminths and pluricellular organisms further adding back-up proof to prevailing hybridizing processes.

Conclusion

This preprint article depicts the clinical case of a cat, regarding the leadership role of parasitic infections in co-infection, across the animal population with a propensity to adopting parasitosis; e.g. when immune-suppressed, i.e. when they are subjected to retroviral agents specifically. The same perspective is certainly beneficial for humans, in terms of cancer future therapy, but it also aims at explaining how the domestication of animals can benefit us mutually, and how mutual therapeutic engagement can lead us to further helpful discoveries.

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