Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

SARS-CoV-2 infection and parasitic diseases: A possible role for microbiome interaction?

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Dear Editor,

Lupia et al. [1] recently hypothesized a role of CD4+ cells lymphopenia, occurring in severe SARS-CoV-2 infection, as a facilitating factor for a latent *Giardia lamblia* infection reactivation.

Even if the links between parasitic and viral infection – namely SARS-CoV2 - is still unclear, a key role for microbiome interaction is increasingly recognized. In fact, COVID-19 may play a role in enhancing pre-existing parasitic diseases, but new experiences seem to hypothesized a protective role, mediated by the production of Interferon-gamma (IFN-γ) production.

We experienced a case of a previously health 30-years-old man, original from Senegal, found positive to SARS-CoV-2 and admitted with respiratory disease (mild bilateral infiltrates at chest X-ray; MuLBSTA-score 8, Murray 0.7), treated with steroids (dexamethasone 6 mg/die) and prophylactic low-weight-unfractioned-heparin. Later during the hospitalization, the patient presented a voluminous liver abscess diagnosed positive for *E.histolytica* and percutaneously drained, treated with metronidazole and paromomycin, with a slight improvement and subsequent discharge.

E.histolytica infection can be contracted via consumption of contaminated water or food containing mature cysts. In the small intestine, the parasite releases trophozoites that penetrate the mucosa of the colon causing flask-shaped ulcers (intestinal disease) [2].

Although the pathology is asymptomatic and self-limiting in about 90% of cases, it can happen that the commensal trophozoites interrupt the intestinal barrier and spread through the afferent blood flow of the portal vein reaching other organs such as liver, lungs, pericardium, brain. The inflammatory reaction in the liver necrotizes the hepatocytes, producing an abscess that can affect 3% -9% of infected people [3].

Among the factors that have been hypothesized to contribute to the alteration of the normal enteric microbiota, the immune regulation and, consequently, to increase the virulence of *E. histolytica*, there is the co-infection with pathogenic organisms, in particular enteropathogenic bacteria. It has been hypothesized that *E. histolytica* interactions with enteropathogenic *E. coli* (EPEC) modulated parasite virulence factors and host innate immune responses associated with disease pathogenesis [4]. Moreover, *E. histolytica* interaction with EPEC increases parasite virulence and cysteine protease activity, demonstrating that *E. histolytica*/EPEC interaction enhanced the production of key molecules associated with *E. histolytica* virulence.

Although no study has yet investigated the possible role of viruses in favoring *E.histolytica* infection, it is known that SARS-CoV2 infection modifies intestinal homeostasis, stimulating immune cells to produce more severe inflammation. In fact, the intestinal bacterial diversity of patients with COVID-19 is significantly reduced: the relative abundance of opportunistic pathogens such as *Streptococcus, Rothia, Veillonella, and Actinomyces*, but also coinfected fungi (*Aspergillus* and *Candida* spp.), are significantly higher, while the relative of beneficial symbionts is lower. The ecosystem of commensal microbiota can both regulate and be regulated by invading viruses, facilitating either stimulatory or suppressive effects. In this process, corticosteroids used in severe COVID-19 may also play a role in modifying gut flora and favoring parasitic infection.

Other studies have shown that IFN-γ binds on the surface of *E. histolytica* and reduces protein and DNA synthesis in cultured *E. histolytica* trophozoites. In a hamster model, IFN-γ coupling to *E. histolytica* IFN-γ receptor-like protein upregulated virulence factors that enhanced phagocytosis, cytopathic effects on colonic and liver cells, and liver abscess formation [5].

Similarly, considering the unpredictable nature of the transformation of asymptomatic and symptomatic intestinal amoebiasis into ALA, different unknown mechanisms may intertwine between the anti-amoebic and the anti-SARS-CoV-2 response. The immune hyper-responsiveness referred to as a cytokine storm, the subsequent inflammation and tissue damage; the compromised effectiveness of serum complement; the inhibition of IFN-γ secretion and the change in the gut microbiome may all be influenced by SARS-CoV2, and maybe concur to or speed up the development of the extra-intestinal form.

It is known that interferons are cytokines with antiviral effects, playing a critical role in viral multiplication drop off. The expression of IFN-γ receptors is limited to epithelial cell-enriched tissues (respiratory tract, skin, gastrointestinal) and has this specific tissue target. Recently, it has been reported that IFN-γ levels are negatively related to the increase in the amount of COVID-19 fibrosis at discharge [6].

It has even been demonstrated a decreased incidence and severity of

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COVID-19 in patients with parasitic infections (*Cryptosporidium, T. gondii, Blastocyst,* and *Giardia*) compared with those who had SARS-CoV-2 infection alone, supporting a protective role of parasitic infections against COVID-19 [7]. Furthermore, high levels of IFN-γ characterized mild cases, compared with low levels in severe cases of COVID-19 with parasitic infections.

All the factors listed above suggest evaluating the risk of reactivation of latent parasitic infections or the spread of invasive forms in COVID-19 patients. Further investigations are necessary to evaluate the potential protective role played by parasitic infection against the more serious forms of COVID-19.

Declaration of Competing Interest

None.

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