Secondary infection by anaerobic bacteria possibly ensues a battle for oxygen in SARS-Cov2 infected patients: anaerobe-targeting antibiotics (like doxycycline/Metronidazole) to supplement Azithromycin in the treatment regimen of COVID19?

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Letter

The Covid19 pandemic [1], triggered by novel strain of a coronavirus SARS-Cov2 [2] first detected in Wuhan City, China, has spread globally like a wildfire [3], resulting in significant loss of life [4] and endangering health care providers and community health care workers [5]. Understanding and interpreting the underlying metagenome of this disease will help provide direction for the right treatment regimen.

RNA-sequencing as a more sensitive and comprehensive diagnostic test:

RNA-sequencing is a more sensitive and comprehensive test (albeit more time-consuming and expensive), providing information on a larger range of organisms (metagenomic profile) present in the patient sample in comparison to reverse transcription PCR or antibody-testing. For example in one study, Covid19 patients were tested for four bacterial species, including Mycoplasma, with negative results. However, the sequencing data clearly reveals the presence of Mycoplasma [6]. Another study of 2 patients in Wuhan [7] used the Metaphlan2 program to conclude that Capnocytophaga and Veillonella are the only bacterial species present in one patient, and found none in another, when this clearly was not the case [8].

Other RNA-sequencing data submitted in NCBI has identified several potentially pathogenic bacteria in multiple patient samples from across the globe [6, 9–12]. The obligate anaerobe Prevotella had significant abundance in one patient, over-expressing immune-suppression proteins [13]. While all studies reveal Prevotella in varying abundance, other bacteria (Lautropia, Cutibacterium, Haemophilus, Pseudomonas, Sphingomonas etc.) are also found in significant quantity to attract attention to secondary infections [6, 12]. RNA-seq also reveals extremely low viral loads in many patients, explaining the high false negatives (8 times negative before a positive) [14] and failure to detect virus using RT-PCR in severely sick patients, who were CT+ve [15].

Anaerobic bacteria hypothesis:

Recent studies from Italy have suggested that Covid-19 does not lead to a “typical” acute respiratory distress syndrome (ARDS) [16]. Furthermore, elevated D-dimer levels suggest hemoglobin degradation leading to coagulation [17, 18].

A simple hypothesis that emerges from RNA-seq data is over-representation of anaerobic bacteria in Covid19 patients, not found in BALF samples from normal patients (unpublished data), in a battle for oxygen. These bacteria express hemoglobin degrading proteins [19], heme-binding proteins sequestering heme after hemoglobin degradation [20], ‘plundering’ iron, and thereby sequestering oxygen [21]. Hypoxia could also result from formate, the by-product of anaerobic respiration, which inhibits mitochondrial cytochrome oxidase, causing hypoxia at the cellular level [22].

Our proposal for anaerobe-specific antibiotics as a therapy:

We propose the use of anaerobe-specific antibiotics, like doxycycline/Metronidazole, in the treatment regimen to supplement Azithromycin being used currently [23] since some anaerobic bacteria have resistance for Azithromycin [24] (along with anti-coagulants [25]).

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