Review of: "[Case Report] Profound Symptom Alleviation in Long-Covid Patients After PAMP-Immunotherapy: Three Case Reports"

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Potential competing interests: No potential competing interests to declare.

The paper by is an interesting approach to the treatment of LC.

General comments: LC physiopathology is not yet explained. Hypometabolism in the brain is shown in 60% of cases on the TEP scanner (DOI below), and the location of these features may be compatible with patients' symptoms. Moreover, as reported in this paper, a preliminary paper recently published reports that the spike protein of SARS-CoV-2 is found in more than 60% of patients with LC, suggesting that either the infection is still ongoing or that integrated RNA is retrotranscribed in our human cells. For the first hypothesis, the human gut has been found to be a good candidate for SARS-CoV-2 persistence.

Bacterial pathogen-associated molecular patterns (PAMP) are exciting phenomena not clearly explained, however. It is reported that this team is a common user of this therapeutic approach in cancer. However, the application of this treatment to LC appears preliminary.

In their paper, few if any scientific substrata supporting the use of this approach are reported, except the fact that the therapy is inexpensive, safe, well tolerated, and simple to apply, but there is no scientific reference to support this assumption.

This raises a simple question of ethics and regulation of clinical studies. While this approach creates symptoms (a clinical disease) without clear benefit, should an IRB advice have been obtained?

Concerning the case reports, no conclusions can be drawn from such small cases (3 people).

I encourage the authors to complete their study by:

1) better establishing the scientific background allowing them to propose this approach to these patients

2) asking for an IRB advice, as my thinking is that it belongs to clinical studies

3) making a prospective controlled study against placebo as a pilot study first

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