# 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.

Background

- Long COVID is estimated to affect at least 10% of COVID-19 patients, leading to reduced quality of life and disability. Prevalence may be higher in hospitalized patients and the elderly.

- Symptoms are highly heterogeneous between patients and can be severe and disabling, including profound fatigue, brain fog, headaches, muscle and joint pain, exercise intolerance, dysautonomia, and mood disorders.

- The underlying mechanisms are unclear but may involve persistent viral reservoirs, autoimmunity triggered by the virus, and immune dysregulation.

- No proven effective treatments yet exist for long COVID. Current management focuses on symptom relief and rehabilitation.

- There is an urgent need for therapeutic approaches to alleviate this post-viral syndrome. Prior viral illnesses like Ebola have also been associated with post-infectious sequelae similar to long COVID.

- Historical fever therapy using bacterial extracts was reported to cure some cancers, attributed to stimulating the innate immune system against malignant cells. This inspired the development of PAMP immunotherapy to mimic these effects.

- PAMPs (pathogen-associated molecular patterns) activate innate immunity by binding Toll-like and other pattern recognition receptors on antigen presenting cells like dendritic cells.

- The hypothesis is that PAMP immunotherapy may broadly rebalance aberrant immune responses in long COVID patients by stimulating dendritic cell maturation and downstream immune activation.

Cases

- 3 patients with long COVID treated with PAMP immunotherapy - bacterial extracts that activate innate immune response.

- After 3-6 PAMP treatments over 4-6 weeks, all 3 patients reported marked improvement in symptoms.

- Benefits included increased energy, reduced pain, improved concentration and motor skills.

- Symptom questionnaires showed 20-46% improvement across various domains.

- Benefits persisted over months of follow-up.

Discussion

- This initial case series presents intriguing evidence that PAMP immunotherapy may provide rapid and substantial symptom relief in some long COVID patients. All 3 patients experienced marked improvements within 4-6 weeks. Otitis media is a frequent related symptoms. Cite doi:10.1007/s00405-021-06958-4

- The mechanisms are unclear but likely involve broad immunomodulation. Long COVID may be characterized by dysfunctional innate-adaptive crosstalk and impaired dendritic cell responses, which PAMPs may help restore. Vaccination also influence the phenotype and symptoms of covid-19 infection. cite doi:10.1007/s10072-021-05662-9.

- Fever induction may also play a role by enhancing dendritic cell activation and resetting aberrant immune responses. However, the role of fever and PAMPs specifically needs further study.

- The symptom improvements were more rapid than typically seen with PAMP cancer immunotherapy, suggesting distinct mechanisms in long COVID that warrant characterization through immunological analyses.

- Limitations include small sample size, lack of placebo control, and variability in symptoms and prior health status between patients.

- Additional research should include larger controlled trials with standardized outcomes and immunological studies of blood cytokine levels, cell subset phenotypes and activation states before and after therapy.

- Identification of any predictive biomarkers of response would be valuable for patient selection.

- Combinations with other agents like antivirals or immunomodulators may provide additional benefit and should be explored.

- In summary, these cases provide preliminary evidence that PAMP immunotherapy may effectively and rapidly alleviate long COVID symptoms, meriting further confirmation and mechanistic investigation.

Let me know if you would like me to expand on any other aspects of the discussion to provide more context and interpretation of the findings.