Reactivation of mild COVID-19 symptoms after vaccination during long COVID-19 and immediate control by nutrients and acetylleucine: Clinical case report

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A 74-year-old patient had moderate to severe COVID-19 symptoms at the end of August 2020. He measured his symptoms using a visual analogue scale (VAS) from 0 (no symptoms) to 10 (bothersome symptoms). The patient was suffering from severe cough (VAS 7-8/10), hyposmia (VAS 7/10), dysgeusia (VAS 6/10), fever (up to 39°3), loss of appetite (VAS up to 10/10), severe fatigue (VAS up to 9/10) and some gastrointestinal symptoms (VAS 3-4/10)⁻¹. The patient himself had proposed the hypothesis that Nuclear factor (erythroid-derived 2)-like 2 (Nrf2)-interacting nutrients may help to prevent severe COVID-19 symptoms ²⁻⁵. He therefore took broccoli seed capsules (150 mg) containing glucoraphanin 4.5 mg and myrosinase. The capsules were found to reduce many of the COVID-19 symptoms within 10-20 minutes and for a duration of 6-12 hours. He then used repeated dosing during the first COVID-19 phase and the cytokine storm. The patient had two positive RT-PCR tests to SARS-CoV-2, performed at a 2 week-interval, and IgG against SARS-CoV-2.

After the cytokine storm, the patient developed long COVID-19⁶⁻⁹ with (i) transient skin symptoms (pruritus and erythema of the lower legs, VAS 6-7/10) that resolved within 15 minutes under rupatadine 10 mg, an oral H1-antihistamine, ¹⁰ and (ii) persistent moderate-severe cough (VAS 6-7/10) that was completely controlled by broccoli seed capsules (150 mg, 4.5 mg glucoraphanin), curcuma (100 mg), black pepper (8 mg) and paracetamol 250 mg administered twice daily (capsules of Nrf2-TRP channel agonists). These nutrients were based on a N-of-1 challenge ¹¹ and showed a very rapid (1 minute) effect on COVID-19 respiratory symptoms which lasted for up to 12 hours. The mechanisms are likely to be associated with a cross-talk between antioxidants (Nrf2) and TRPA1/V1 (Transient Receptor Potential Ankyrin 1/vanillin 1) agonists ⁴. During the four months of long COVID-19, the patient suffered transiently from pruritus and erythema of the lower legs and, for around 4 weeks, from relatively severe atrial extra-systoles (VAS 7/10) December) that needed flecanide (150 mg daily) ¹². The patient was fit and was used to walking approximately 5 km a day on a treadmill.

First jab

On January 11th, still suffering from long COVID-19, and perfectly controlled by capsules of Nrf2-TRP channel agonists, the patient received the COVID-19 vaccine BNT162b2 (Pfizer-BioNTech). The first symptoms were experienced only on the following day.

Day 2: When the patient went to sleep, he suffered from severe pruritus of the legs, similarly to the beginning of the long COVID episode (VAS 9). This problem did not resolve under rupatadine and needed 20 mg of prednisolone. Milder symptoms reoccurred on days 5 and 6.

Days 3-5: Nasal congestion (VAS 6/10) was observed day and night. It was moderately improved for 2-4 hours by the Nrf2-TRP channel agonist capsules.

Day 7-12: Mild-moderate cough (VAS 4-5/10) occurred around 8 hours after the intake of the Nrf2-TRP channel agonist capsules. Cough was blocked within 2 minutes after the ingestion of one capsule.

The patient needed 3 capsules a day to imperfectly control cough (VAS 2/10). Still taking flecainide, the patient also had some extra-systoles (VAS 2/10), which could not be controlled by Nrf2/TRP agonists.

Fatigue was noted between days 3 to 11 and could be quantified given that the patient was used to walking around 5 km every day on a treadmill. From days 3 to 10, he was unable to walk for more than 3 km a day.

A nasal swab antibody test was negative.

Days 10-20: The patient had some mild ataxia symptoms (vertigo as well as instability when walking).

Day 21: The patient developed severe vertigo which prevented him from getting up. He then took acetylleucine (3g/day) and a vertigo medication, but was unable to ingest any other medication or nutrient. He was surprised to notice that his long-COVID-19 cough totally disappeared.

Days 22-24: The vertigo had considerably improved under acetylleucine (2 g/day), and, in order to control the cough, he was able to stop the broccoli capsules but not the curcuma nor the black pepper.

Second jab

On day 25, the patient received the second jab of the same vaccine and took prednisolone 20 mg daily for 2 days to prevent skin symptoms. He ingested acetylleucine (2 g) daily to control any vertigo and continued curcuma, black pepper and paracetamol for the next week.

On day 26, the patient had the same nasal obstruction for 5 days as well as an increased cough which required the addition of broccoli capsules BID.

The patient checked the efficacy of acetylleucine in an open cough challenge carried out as before. ¹ Acetylleucine blocked cough after 2 minutes.

On days 28-30, the patient experienced moderate extra-systoles (VAS 4/10) and fatigue.

Discussion

This clinical case suggests that vaccination may re-activate COVID-19 symptoms in a patient with long COVID-19. In this patient, the symptoms were similar to those experienced during the COVID-19 cytokine storm or long COVID-19. However, they did not occur in the same sequence and - except for skin pruritus - were milder. These symptoms were not associated with a new SARS-CoV-2 infection. Moreover, they responded similarly to Nrf2-TRPA1/V1 agonists, reinforcing the fact that COVID-19 symptoms re-occurred after vaccination. The doses of nutrients were those recommended.

Atrial extra-systoles are most likely to be associated with COVID-19: the patient had some very mild and infrequent extra-systoles before COVID-19 infection whereas, during long COVID-19, they were severe, persisted over days, and required flecainide. ¹² These cardiac features are not usually reported in COVID-19. Nrf2/TRP channel nutrients consistently reduced cough but not extra-systoles or loss of smell and taste.

The association of vertigo with COVID-19 is less clear. However, there are associations between COVID-19 and dizziness ¹³, vertigo and, more rarely, cerebellar ataxia. Thus, although not confirmed,

dizziness and vertigo may be associated with COVID-19. It should be noted that the patient had suffered two episodes of transient severe vertigo over the past 4 years.

Surprisingly, acetylleucine was very effective on cough and fatigue. The modified amino-acid acetylleucine has been used in some European countries for more than 50 years for the symptomatic treatment of vertigo. ¹⁴ It has been found to improve cerebellar ataxia ¹⁵ and is being tested in cerebellar ataxia ¹⁶ which is associated with Nrf2 defect ^{17 18}. Nrf2 may also be involved in some neurodegenerative diseases. ¹⁹ The basic leucine zipper (bZIP) transcription factor Nrf2 is the primary regulator of cellular oxidative stress. Transcription factors containing bZIP domains are found across eukaryotes, from budding yeast to humans. Under homeostatic conditions, Nrf2 is anchored to cysteine-rich Keap1 and sequestered in the cytoplasm. When challenged with oxidative stress, Keap1 functions as a redox-sensitive switch and releases Nrf2 that becomes active. Leucine also activates mTOR that plays a major role in autophagy. Acetylleucine was found to be effective in induced-cough challenges within 1-2 minutes. However, this observation requires confirmation.

This clinical case has major implications. First, Nrf2-TRPA1/V1 compounds appear to be effective in respiratory symptoms of COVID-19 and may also be of interest in neurologic symptoms. Second, side effects during vaccination mimic COVID-19 symptoms, may be reduced - and possibly even prevented - by such compounds. Third, acetylleucine is very safe and may be tested alone or in combination with potent TRP agonists. In hospitalized patients with respiratory problems, the impact of acetylleucine on certain objective measurements such as SaO₂ can be rapidly assessed. It is therefore important to test this combination of nutrients using appropriate trials before any recommendation is made.

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