



Dietary Natural Lutein and Its Impact on Hepatic Autoimmunity in Long COVID: A Clinical Case Study

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Case Report

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ABSTRACT

Introduction and Aims: Lutein is a nutrient that is found in many foods, particularly green vegetables. It has powerful antioxidant properties potentially to relieve oxidative-nitrosative stress in long COVID. Moreover, lutein is a promising natural agent to be used against liver damage. Our aim is to evaluate whether natural lutein supplementation by organic Extra Virgin Olive Oil (EVOO) can be therapeutic in alleviating liver damage associated with long COVID.

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Presentation of Case: We report a retrospective case study of a long COVID patient where autoimmune hepatitis markers were alleviated in a brief time, after consumption of organic EVOO stable in lutein. A 61-year-old Greek (unvaccinated) woman developed long COVID after SARS-CoV-2 infection. Long COVID symptoms included constipation, chronic fatigue, muscle pain, and blood markers that resembled autoimmune hepatitis (AIH). High anti-spike protein Immunoglobulin G (IgG) antibodies accompanied the symptoms. Magnetic resonance examination (MRI) was not conclusive for autoimmune hepatitis (AIH) diagnosis. The patient was advised to follow a healthy diet and repeat the examinations. As part of the healthy diet, the patient consumed 24 ml of lutein rich (6.5 mg/Kg) stable EVOO (SEVOO) per day. After two six months periods of testing, AIH markers were normal.

Discussion and Conclusion: Natural lutein consumption by means of SEVOO helped to alleviate liver damage as shown by the AIH markers and to ameliorate chronic fatigue and muscle pain in a long COVID patient.

Keywords: Long-COVID; liver damage; autoimmune hepatitis; natural lutein: extra virgin olive oil; mediterranean diet.

1. INTRODUCTION

Lutein is a powerful antioxidant that cannot be synthesized by the human organism but can only be acquired from diet. Lutein has a long history of human clinical trials showing its potential to combat eye disease, and it is regarded as a safe (Generally Recognized as Safe) nutrient to be consumed for a long-time period (Li et al., 2020). Exceptional are lutein's properties against liver damage. Lutein, by promoting lipophagy (a certain type of autophagy), regulates lipolysis and reduces inflammation and oxidative stress in the liver. For these reasons, lutein is considered to be a powerful nutrient to be used in the future against liver steatosis (Balboa et al., 2024).

A recent comprehensive review study has identified the potential beneficial role of dietary supplementation of lutein against oxidative and nitrosative stress in cases of long COVID (Kyriakopoulos et al., 2024). The pathogenic role of oxidative stress has long been found to be implicated in liver fibrosis, acute liver injuries, and infectious or metabolic related liver injuries (Allameh et al., 2023). A recent animal study has identified several key clinical reasons why dietary supplementation of lutein can reduce liver oxidative damage. These include the reduction of nuclear factor kappa-light-chain-enhancer of activated B cells (NF- κ B) inflammatory mediation, the restoration of lipid metabolism in the liver and the toll-like receptor 4 (TLR4) induced inflammatory response in the liver. Phenomenologically, lutein works on the restoration of liver-gut axis, by restoring the populations of essential microbial flora (probiotic bacteria) in the gut (Zhao et al., 2023).

Long COVID develops regularly after SARS-CoV-2 infection (COVID-19). COVID-19 causes type III hypersensitivity reaction and autoimmunity (Mutar Mahdi, 2020). There have been several recent case studies reporting on *de novo* AIH following COVID-19 infection (Durazo et al., 2022, Zhou et al., 2024, Yu et al., 2025, Wang et al., 2025). Autoimmune hepatitis (AIH) manifestation is considered a severe causality, and its pathogenesis is linked to molecular mimicry (Bril et al., 2021). Molecular mimicry due to SARS-CoV-2 spike protein antigens creates autoimmunity and induces anti-spike protein IgG neutralizing antibodies (Bondareva et al., 2023). The connection between gut microbiota and anti-spike IgGs is remarkable. We described recently that lutein, a powerful natural antioxidant, can relieve SARS-CoV-2 spike protein-induced pathology, including autoimmune reactions (Kyriakopoulos et al., 2024). We also describe that, preferably, lutein can be obtained by consuming EVOO when its natural content in lutein is highly preserved. It has been recently shown that natural lutein content in EVOO is highly preserved by applying a patented technique of molecular filtration to obtain EVOO that is stable over time (Lazarou et al., 2024). We report a case of a long COVID patient who consumed stable EVOO for six months (6.5mg/kg of natural lutein content), and this helped to alleviate blood markers indicative for liver damage and AIH and lowered the patient's high IgG anti-spike antibodies.

2. CASE DESCRIPTION

A 61-year-old Greek woman, after contracting COVID-19, developed long COVID symptoms of constipation, chronic fatigue, dizziness,

headaches/migraines, and intense neuromuscular pain. Initial haematological examination after COVID-19 showed increased eosinophil and neutrophil levels, increased mean platelet volume (MPV) and platelet-large cell ratio (PLCR) (see Table 1). Gamma Glutamyl Transferase (γ GT), was also elevated (Table 1). A year before COVID-19, the liver enzymes had been found to be at normal values. Further laboratory examinations after the elevated γ GT was detected, revealed intensely elevated levels of alkaline phosphatase (AP) and alanine and aspartate transaminases (SGPT/ALT and SGOT/AST), indicative of liver disease (Table 1). To exclude autoimmune-reactivity and AIH, as a consequence of long COVID, the patient was further examined for anti-nuclear-antibodies (ANA), anti-mitochondrial antibodies (AMA) and anti-smooth muscle antibodies (ASMA), and all were found positive, indicative for autoimmunity. Platelet-clotting defect examinations specific for AIH were not performed at that time. Anti-double stranded DNA (anti-dsDNA) antibodies were negative (0.1 AU/ml, normal <30 AU/ml), and other blood test values were normal (not shown in Table 1). However, the patient immediately underwent ultrasound and magnetic resonance imaging examinations, and both were negative for liver disease and therefore AIH. However, the blood markers indicated liver damage. Moreover, the patient tested negative for liver-associated infectious diseases (Hepatitis A, B and C viruses). Consulting hepatologists suggested that the patient follow a healthy diet and repeat examinations after six-month periods. However, the patient delayed the first six-month evaluation by one month for personal reasons. Moreover, four months after COVID-19, the patient underwent an anti-spike protein neutralizing IgG evaluation and was found to have an exceedingly high level, 14,967 AU/ml (normal <50).

The patient repeated examinations after two six-month periods (shown in Table 1) and was found to be negative for autoimmune hepatitis markers both times. The patient continued to consume a healthy diet the entire time. For the healthy diet, the patient incorporated the consumption of 24 ml of stable organic EVOO (SEVOO) that contained an amount of naturally derived (from olive fruits) lutein at a stable concentration of 6.5 mg/kg of EVOO per day (Lazarou et al., 2024). The patient was advised not to supplement her diet with any other seed oils. However, she did consume the natural oils and fats contained in full fat Greek Yogurt, in fresh wild fish, organic

meats, and cheese. For cooking, only EVOO was used. The patient, after the first month of SEVOO-lutein consumption, claimed that there was a remarkable relief in headaches, migraine and dizziness, and she felt stronger to perform daily house activities. Moreover, the patient noticed relief from fatigue and intense neuromuscular pain after two months of SEVOO-lutein consumption. Although constipation remained, there was a substantial improvement there as well, as the patient revealed. The two six-month laboratory examinations (first, seven months due to the patient's delay) as appointed from hepatology physicians for ANA, AMA, ASMA, eosinophil, neutrophil, platelet, and liver enzyme evaluations were remarkably improved, causing the patient to lose the diagnosis of autoimmunity, AIH and liver disease (Table 1). The IgG anti-spike protein antibody levels continued to drop also but remained at exceedingly higher-than-normal values. Finally, further examinations indicative of AIH, i.e., serum IgG, clotting defect (activated partial thromboplastin time (APTT, prothrombin time (PT) and clotting time (CT)) were found to be normal (not shown in Table 1).

3. DISCUSSION

A 61-year-old Greek Caucasian woman developed long COVID symptoms after SARS-CoV-2 infection (Davis et al., 2023). The patient suffered from autoimmune reactions after COVID-19. ANA, AMA, ASMA, and liver enzymes were indicative of autoimmunity, liver damage and probably AIH (Mieli-Vergani et al., 2018). However, MRI and ultrasound exams were inconclusive for AIH. Therefore, the patient was advised not to follow a prescription-based pharmaceutical therapy, but rather to follow a healthy diet and repeat examinations for AIH after two six-month periods. The sky-high elevated anti-SARS-CoV-2 spike protein antibodies were consistent with molecular-mimicry phenomena, creating autoimmunity after SARS-CoV-2 infection or mRNA (COVID-19) vaccination (Safary et al., 2023, Arévalo-Cortés et al., 2024). However, this patient has not been vaccinated for COVID-19. The patient tested negative for SARS-CoV-2 after 10 days of COVID-19 symptoms. The results after the two six-month periods revealed an exceptional alleviation of autoimmune reactivity, concurrent with significant lowering of anti-spike antibodies (although these remained at considerably very high levels).

Table 1. Measured (raised) hematological indices and autoimmune hepatitis markers in the long COVID patient

Blood test values	1 month after COVID-19 Without SEVOO-lutein consumption	Eight months after COVID-19 following six months of SEVOO-lutein consumption	Fourteen months after COVID-19 following 12 months of SEVOO-lutein consumption
Eosinophils Normal values 1-6 %	9.0	6.0	6.1
Basophils Normal values 0.3-1.0 %	1.7	1.1	1.2
MPV Normal values 6-11 fL	11.8	11.1	11.2
PLCR Normal values 13-43 %	43.8	43.1	42.2
ANA Normal titre <1:640 dilution	>1:640	<1:640	<1:640
AMA Normal titre <1:80 dilution	>1:80	<1:80	<1:80
ASMA Normal titre <1:80 dilution	>1:80	< 1:80	< 1:80
γGT Normal values 5-36 IU/L	89	35	37
SGPT/ALT Normal values <33 IU/L	38	32	28
SGOT/AST Normal values <32 IU/L	34	31	25
AP Normal values 35-104 IU/L	135	102	96
SARS-CoV-2 spike protein IgG antibodies Normal values <50 AU/ml	14,976	6,891	4.831

There are cases (about 10%) where a natural course of autoimmune liver reaction is resolved spontaneously. However, these patients are more likely to be candidates for liver transplantation, and this was not the case for our patient (Dufour et al., 2002). Excessive liver damage was excluded for our patient by consulting hepatologists, due to the results of the ultrasound and liver MRI conducted at the time the autoimmune-inflammatory markers were

raised. The concurrent reduction of ANA, AMA and ASMA antibodies pinpoint to a reduction in inflammatory processes in our patient. Lutein is a well-known natural agent that lowers oxidative stress-mediated inflammatory reactions (Ahn & Kim, 2021).

This retrospective case study indicates that, in a healthy diet, the consumption of naturally derived (directly from the olive fruit) lutein contained in

EVOO nutrient, when its concentration remains stable over time, can be a promising nutritional supplement to lower long COVID symptoms and protect from autoimmune reactions, especially in the liver. Probably due to the increase in antioxidant defenses by lutein, the induction of autoimmunity through oxidative and nitrosative stress was alleviated. Lutein has the potential to alleviate liver steatosis by improving lipolysis and fatty acid metabolism (Balboa et al., 2024).

The regulation of autophagy is tightly associated with the progression or amelioration of liver disease (Kouroumalis et al., 2021). Liver steatosis is reversed by the induction of autophagy-induced lipophagy (Xiong et al., 2016). Remarkably, lutein, mainly through its potent activities in neutralisation of reactive oxygen radicles (ROS) and stimulation of multiple molecular pathways, activates autophagy (for review see (Pinelli et al., 2023).

The main pathological factor of SARS-CoV-2, its spike protein, readily mediates inflammation through the activation of TLR2 and TLR4 (Zhao et al., 2021). TLR2 and TLR4 signaling are a hallmark for autoimmune disease pathogenesis and in liver steatosis. Therefore, as has already been shown in our recent study, lutein can act as a potent inhibitor of TLR2 and TLR4 spike protein-mediated activation and attenuate inflammation caused by NF- κ B and activated protein 1 (AP-1) pathways (Zhao et al., 2021; Kyriakopoulos et al., 2024).

Moreover, EVOO consumption, due to its high antioxidant content, has been found to protect from mortality due to SARS-CoV-2 infection and other severe COVID-19 symptoms, and it can also be applied to combat long COVID symptoms, as seen in our patient (Dülger et al., 2023). Relevant pharmacokinetic studies have shown that, depending on food intake, the bioavailability of lutein in animals can reach levels of 5.2% (Sato et al., 2011). It may be the case in our patient that the intestinal absorption of lutein was markedly improved through the food she was consuming. The alleviation of constipation after SEVOO lutein consumption is an indicator of improved intestinal health after COVID-19 and long COVID. Naturally derived lutein in EVOO may have worked as a strong antioxidant and autophagy inducer to alleviate potential liver inflammation in this patient. However, further clinical studies involving more patients will help to clarify this indication.

Spontaneous remission of the autoimmune hepatitis markers cannot be excluded in this case, as this has been described in the literature (Dufour et al., 2002). Therefore, a continuous monitoring of liver enzyme levels is advisable.

4. CONCLUSION

The recovery of liver enzymes and autoimmune antibody levels to normal values after a twelve-month period of a healthy diet and consumption of naturally derived lutein in EVOO is remarkable. This long COVID case signifies a future potential role for reducing liver damage and other autoimmune reactions caused by the SARS-CoV-2 spike protein (long COVID) by natural lutein in EVOO when a healthy Mediterranean diet is followed. Larger scale clinical studies are advised to further assess and reinforce our clinical findings on whether lutein and/or other active constituents in EVOO help more generally in the alleviation of the autoimmune-liver injury markers.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of this manuscript.

CONSENT

All authors declare that 'written informed consent was obtained and signed from the patient for publication of this case report. A copy of the written consent form is available for review by the Editor-in-Chief of this journal. Principles of the Declaration of Helsinki were followed.

ETHICAL APPROVAL

The study was performed in accordance with the ethical standards laid down in the 1964 declaration of Helsinki.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

Ahn, Y. J., & Kim, H. (2021). Lutein as a modulator of oxidative stress-mediated inflammatory diseases. *Antioxidants (Basel)*, 10(9), 1448.

- <https://doi.org/10.3390/antiox10091448>
Allameh, A., Niayesh-Mehr, R., Aliarab, A., Sebastiani, G., & Pantopoulos, K. (2023). Oxidative stress in liver pathophysiology and disease. *Antioxidants (Basel)*, 12(9), 1653.
<https://doi.org/10.3390/antiox12091653>
- Arévalo-Cortés, A., Rodríguez-Pinto, D., & Aguilar-Ayala, L. (2024). Evidence for molecular mimicry between SARS-CoV-2 and human antigens: Implications for autoimmunity in COVID-19. *Autoimmune Diseases*, 2024, 8359683.
<https://doi.org/10.1155/2024/8359683>
- Balboa, E., Saud, F., Parra-Ruiz, C., de la Fuente, M., Landskron, G., & Zanlungo, S. (2024). Exploring the lutein therapeutic potential in steatotic liver disease: Mechanistic insights and future directions. *Frontiers in Pharmacology*, 15, 1406784.
<https://doi.org/10.3389/fphar.2024.1406784>
- Bondareva, M., Budzinski, L., Durek, P., Witkowski, M., Angermair, S., Ninnemann, J., et al. (2023). Cross-regulation of antibody responses against the SARS-CoV-2 Spike protein and commensal microbiota via molecular mimicry. *Cell Host & Microbe*, 31(11), 1866–1881.e10.
<https://doi.org/10.1016/j.chom.2023.10.007>
- Bril, F., Al Diffalha, S., Dean, M., & Fettig, D. M. (2021). Autoimmune hepatitis developing after coronavirus disease 2019 (COVID-19) vaccine: Causality or casualty? *Journal of Hepatology*, 75(1), 222–224.
<https://doi.org/10.1016/j.jhep.2021.04.003>
- Davis, H. E., McCorkell, L., Vogel, J. M., & Topol, E. J. (2023). Author Correction: Long COVID: Major findings, mechanisms and recommendations. *Nature Reviews Microbiology*, 21(6), 408.
<https://doi.org/10.1038/s41579-023-00896-0>
- Dufour, J. F., Zimmermann, M., & Reichen, J. (2002). Severe autoimmune hepatitis in patients with previous spontaneous recovery of a flare. *J Hepatol.*, 37(6), 748–752.
[https://doi.org/10.1016/s0168-8278\(02\)00329-x](https://doi.org/10.1016/s0168-8278(02)00329-x)
- Dülger, A., Aksoy, H. B., Aksoy, I., & Günaydın, S. (2023). Olive oil protection against Covid-19 infection. Aegean Miracle. *Clin Nutr ESPEN*, 54, 626.
<https://doi.org/10.1016/j.clnesp.2022.09.493>
- Durazo, F. A., Kristbaum, K., Miller, J., Saeian, K., Selim, M., & Hong, J. C. (2022). De novo autoimmune hepatitis after COVID-19 infection in an unvaccinated patient. *Case Reports Hepatol.*, 2022, 8409269.
<https://doi.org/10.1155/2022/8409269>
- Kouroumalis, E., Voumvouraki, A., Augoustaki, A., & Samonakis, D. N. (2021). Autophagy in liver diseases. *World J Hepatol.*, 13(1), 6–65. <https://doi.org/10.4254/wjh.v13.i1.6>
- Kyriakopoulos, A. M., Nigh, G., McCullough, P. A., & Seneff, S. (2024). Clinical rationale for dietary lutein supplementation in long COVID and mRNA vaccine injury syndromes. *F1000Res.*, 13, 191.
<https://doi.org/10.12688/f1000research.143517.3>
- Lazarou, K., Tsagkaris, A. S., Drakopoulou, S., Kyriakopoulos, A. M., Martakos, I., Pentogenis, M., et al. (2024). Long-term stability of extra virgin olive oil: Effects of filtration and refrigeration storage on the Kolovi variety. *J Sci Food Agric.*, 104(15), 9673–9683.
<https://doi.org/10.1002/jsfa.13792>
- Li, L. H., Lee, J. C., Leung, H. H., Lam, W. C., Fu, Z., & Lo, A. C. Y. (2020). Lutein supplementation for eye diseases. *Nutrients*, 12(6), 1721.
<https://doi.org/10.3390/nu12061721>
- Mieli-Vergani, G., Vergani, D., Czaja, A. J., Manns, M. P., Krawitt, E. L., Vierling, J. M., et al. (2018). Autoimmune hepatitis. *Nat Rev Dis Primers*, 4, 18017.
<https://doi.org/10.1038/nrdp.2018.17>
- Mutar Mahdi, B. (2020). COVID-19 type III hypersensitivity reaction. *Med Hypotheses*, 140, 109763.
<https://doi.org/10.1016/j.mehy.2020.109763>
- Pinelli, R., Ferrucci, M., Biagioni, F., Berti, C., Bumah, V. V., Busceti, C. L., et al. (2023). Autophagy activation promoted by pulses of light and phytochemicals counteracting oxidative stress during age-related macular degeneration. *Antioxidants (Basel)*, 12(6), 1183.
<https://doi.org/10.3390/antiox12061183>
- Safary, A., Akbarzadeh-Khiavi, M., Barar, J., & Omid, Y. (2023). SARS-CoV-2 vaccine-triggered autoimmunity: Molecular mimicry and/or bystander activation of the immune system. *Bioimpacts*, 13(4), 269–273.
<https://doi.org/10.34172/bi.2023.27494>
- Sato, Y., Kobayashi, M., Itagaki, S., Hirano, T., Noda, T., Mizuno, S., et al. (2011). Pharmacokinetic properties of lutein emulsion after oral administration to rats

- and effect of food intake on plasma concentration of lutein. *Biopharm Drug Dispos.*, 32(3), 151–158.
<https://doi.org/10.1002/bdd.746>
- Wang, Y., Chen, X., Aragao, A. P., & Ding, X. (2025). COVID-19-associated autoimmune hepatitis: A case report and literature review. *J Clin Transl Pathol*. Epub ahead of print.
<https://doi.org/10.14218/JCTP.2025.00010>
- Xiong, J., Wang, K., He, J., Zhang, G., Zhang, D., & Chen, F. (2016). TFE3 alleviates hepatic steatosis through autophagy-induced lipophagy and PGC1 α -mediated fatty acid β -oxidation. *Int J Mol Sci.*, 17(3), 387.
<https://doi.org/10.3390/ijms17030387>
- Yu, C., Wang, W., Zhang, Q., & Jin, Z. (2025). Autoimmune hepatitis under the COVID-19 veil: An analysis of the nature of potential associations. *Front Immunol.*, 16, 1510770.
<https://doi.org/10.3389/fimmu.2025.1510770>
- Zhao, S., Zhang, Y., Ding, H., Hu, S., Wu, X., Ma, A., et al. (2023). Lutein prevents liver injury and intestinal barrier dysfunction in rats subjected to chronic alcohol intake. *Nutrients*, 15(5), 1229.
<https://doi.org/10.3390/nu15051229>
- Zhao, Y., Kuang, M., Li, J., Zhu, L., Jia, Z., Guo, X., et al. (2021). SARS-CoV-2 spike protein interacts with and activates TLR41. *Cell Res.*, 31(7), 818–820.
<https://doi.org/10.1038/s41422-021-00495-9>
- Zhou, Y. J., Jin, Q. F., Wang, C., Zhang, X. J., Liu, H., & Bao, J. (2024). Onset of acute severe autoimmune hepatitis after severe acute respiratory syndrome coronavirus 2 infection: A case report. *J Int Med Res.*, 52(3), 3000605241233450.
<https://doi.org/10.1177/03000605241233450>

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