

Pseudoexfoliation Syndrome Post COVID Vaccination

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ABSTRACT

In an attempt to rapidly control of the unprecedented effects of the COVID-19 pandemic, a series of vaccination programmes were rapidly rolled out across the world, with a paucity of studies on their side-effects or efficacy. Lack of testing may be the reason for why there have been an increasing number of reports of new-onset autoimmune phenomena following COVID-19 vaccination. These conditions include immune thrombotic thrombocytopenia, autoimmune liver diseases, Guillain-Barré syndrome, IgA nephropathy, rheumatoid arthritis and systemic lupus erythematosus). It has been postulated that production of autoantibodies may have been due the use of certain vaccine adjuvants such as PEG, used by Pfizer [1]. These side-effects are somewhat more serious than the systemic side effects seen following 2 injections of the Oxford-AstraZeneca (ChAdOx1 nCoV-19) COVID-19 vaccine (58.75%), or BNT162b2 (68.5%) [2]. We report evidence of an extensive and prolonged inflammatory response to a combination of 2 injections of ChAdOx1 nCoV-19, followed by 1 injection of BNT162b2, which subsequently lead to the development of irreversible eye damage typical of Pseudoexfoliation syndrome, in a 71 year old man, of excellent health with no predisposing sequelae apart from his age.

Keywords

Biochemistry, Pfizer vaccine, Pseudoexfoliation syndrome.

Introduction

The outbreak of the COVID-19 pandemic in late 2019 led to the rapid development of several vaccines designed to immunize against COVID-19 infection. Two of these vaccines were based on mRNA technology (Pfizer/BioNTech (BNT162b2, brand name Comirnaty) and of Moderna (mRNA-1273, brand name COVID-19 Vaccine Moderna). The principle behind the mRNA vaccine was rather simple in that the mRNA in the vaccine would be taken up by cells (of an unspecified type), whereupon the mRNA would be “read” and viral proteins expressed on the surface of the unspecified cell, and thereby stimulate the immune response. As part of the formulation, the mRNA was encapsulated within a lipid nanoparticle, which for some unknown reason (or none that we could find) was coated with poly-ethylene-glycol (PEG). What is curious about this choice is that PEG was originally designed as a mechanism to “avoid” the immune response, which is contrary to the normal purpose of a vaccine, to stimulate the immune response.

Part of the vaccine strategy was the absolute requirement of persons, particularly those over 50 to be injected with the vaccines, as they were excluded from places of entertainment, bar, clubs, and even shopping centres, and had to show proof of vaccination. The vaccine was “sold” to the public as being safe, yet soon it became apparent that many people experienced significant side-effects from the vaccine, such as a bad headache or bellyache that doesn’t go away for a long time, even with pain medication, blurred vision, difficulty with speech, drowsiness, seizures, shortness of breath, chest pain, and swelling in your leg. Over time, it became apparent that the vaccines could elicit symptoms similar to those of prolonged COVID infection (Long COVID), and a condition of “Long Vax” could result [2]. In which there was a higher incidence and severity of neuropathic symptoms and dystonia. In addition, both Long COVID and Long Vax can result in symptoms similar to chronic fatigue syndrome, and may also include clinical symptoms affecting the respiratory system, neurological/psychiatric, the musculoskeletal system, cardiovascular, autonomic, gastrointestinal system and the mucus membranes [3]. Hence in many cases the vaccine is FAR from safe.

We report the alterations in the metabolism of a 71 year old man who received both the Astra-Zeneca and Pfizer-BioNTech vaccines, resulting in significant metabolic deficiencies, which lead ultimately to the development of sight-threatening Pseudoexfoliation Syndrome (PEX).

Methods

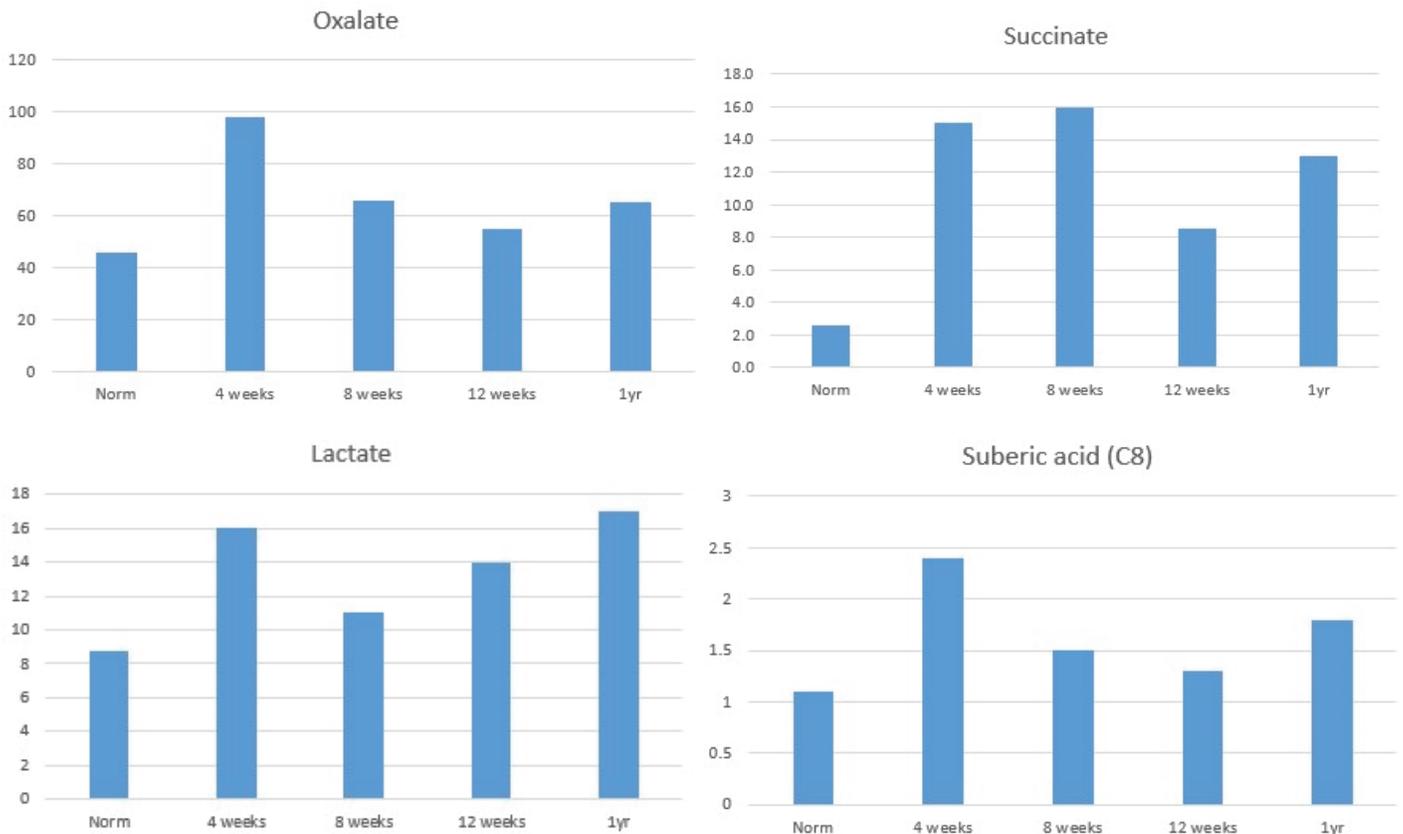
The Oxford-AstraZeneca (ChAdOx1 nCoV-19) COVID-19 vaccine was given as two doses administered 2 months apart, followed 3 months later by the Pfizer-BioNTech (BNT162b2) vaccine. Vaccinations on 10/06/21, 16/08/21, 14/01/22, OAT 14/07/22, 19/08/22, 7/02/23; PEX detection on 31/07/23. An Organic Acids Test (Oasis Laboratories) was used to monitor various biochemical parameters of the subject before vaccination and for 4 intervening times post the vaccination. Intraocular pressure was measured with a Goldmann Applanation tonometer, and Visual Field Testing performed. Diagnosis of Pseudoexfoliation syndrome occurred on 31/07/23 with approximately 20% field loss in Left eye, with intraocular pressure was R39, L46. Xalatan and Cosopt drops were prescribed and retesting was performed one month later (R15, L20), at which time alphagan was prescribed. Two months later, IOP had reduced to R12, L14, however visual field loss had reached 40% in the left eye.

Results

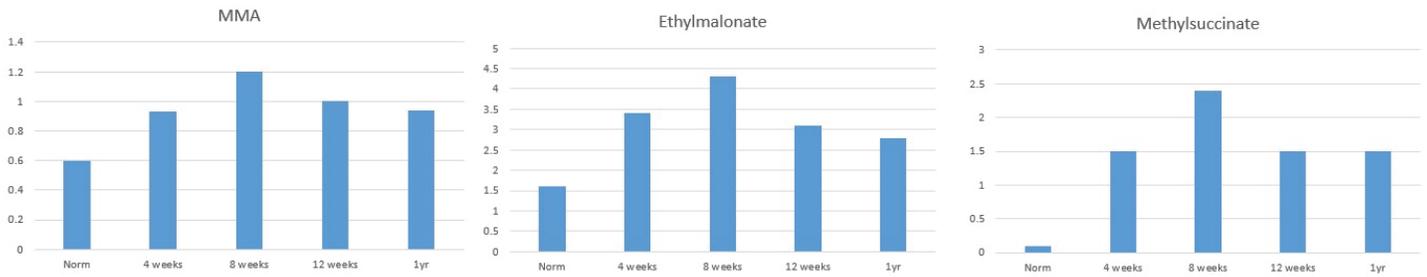
Alterations in metabolism were found using OAT data recovered before and during recovery from COVID-19 vaccination. The following deficiencies were found:

Visual Field Optical scanning revealed rapidly progressing loss of vision in the left eye of the subject. In the first scan, visual loss was around 20% with IOP 44L, 41R eye. Little loss of vision in the right eye. Four weeks later, following treatment with Xalatan and Cosopt, visual loss had increased to over 50% with IOP 24L, 19R eye.

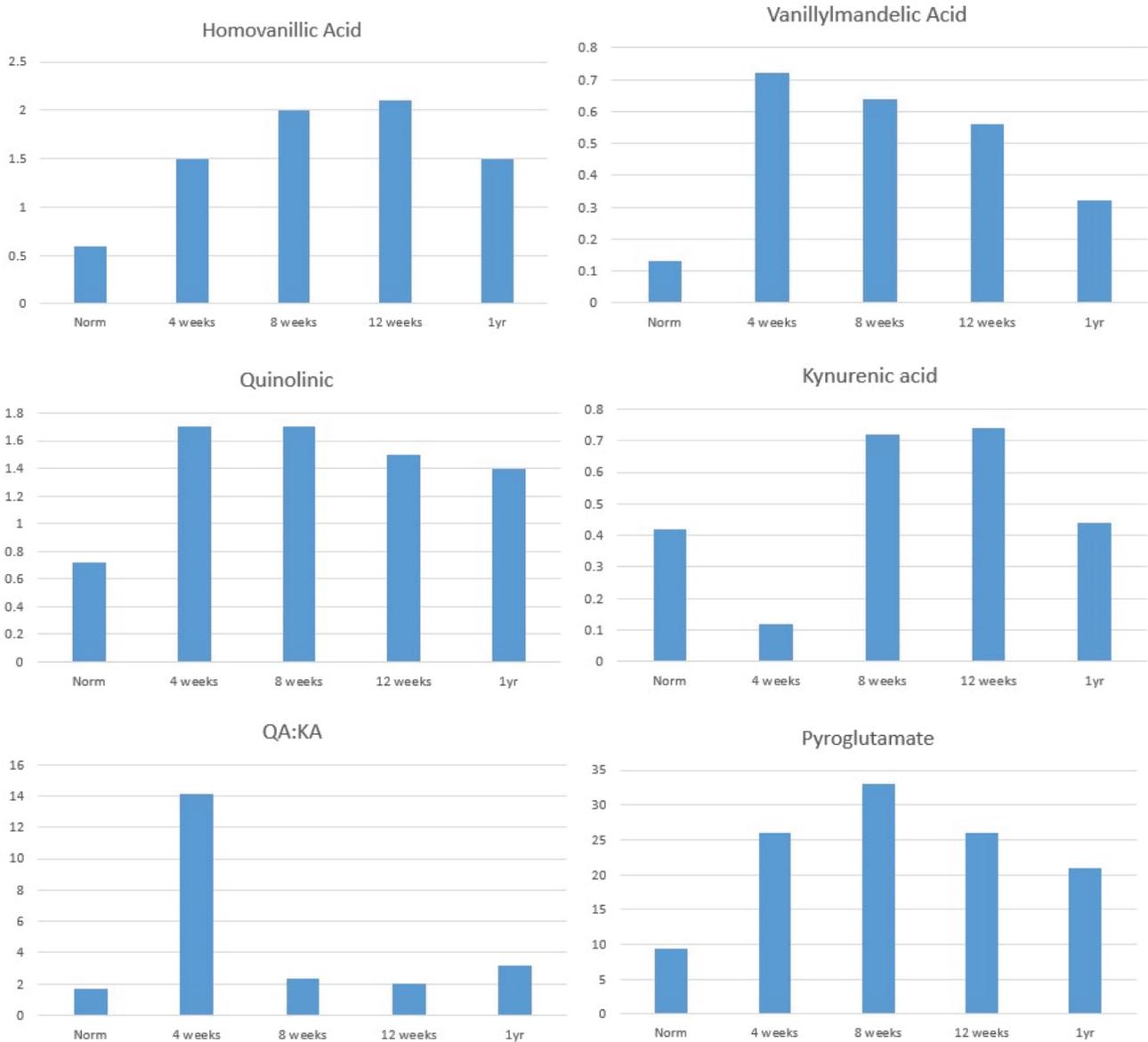
OAT analysis revealed a dramatic increase in markers associated with functional vitamin B2 deficiency, including oxalate, succinate, lactate, and suberate from 4 weeks post vaccination, extending until at least 12 months post vaccination. The deficiency was accompanied by increases in the methyl B12 deficiency markers, HVA, VMA, QA, KA and pyroglutamate and the Adenosyl B12 deficiency marker MMA. There was no resolution in the B12 deficiency markers 12 months after the COVID vaccination.



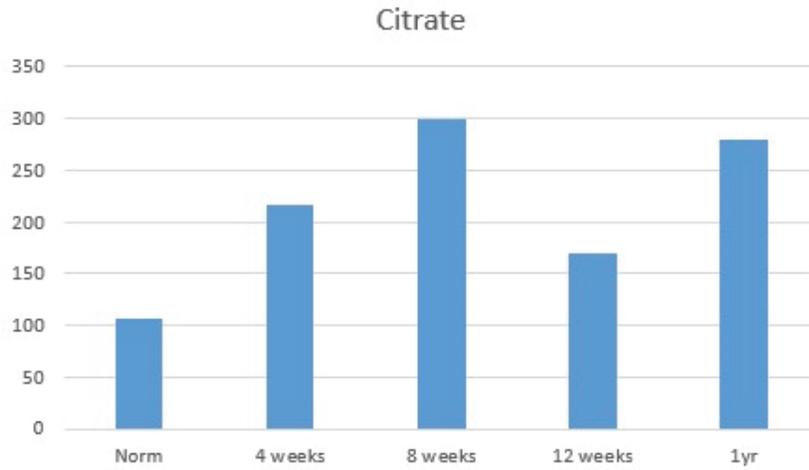
Indicative markers of functional vitamin B2 deficiency, including Oxalate, Succinate, and lactate and the fatty acid markers, suberic acid, and sebacic acid.



Indicative markers of Adenosyl vitamin B2 deficiency, including MMA (Methylmalonic acid), Ethyl malonic acid and methyl succinate.



Indicative markers of Methyl vitamin B2 deficiency, including Homovanillic acid, Vanillyl mandelic acid, Quinolinic Acid, Kynurenic Acid, and the QA:KA ratio (indicative of Iodide/Selenite deficiency) and Pyroglutamic acid. Elevated Pyroglutamic acid is indicative of lower glutathione synthesis, is a feature of functional B12 deficiency, and has been correlated with oxidative stress in a wide range of conditions, including PCOS [4], Septic shock [5], Sepsis [6]; acute kidney injury [7], and pulmonary viral infections [8].



Evidence of excessive use of iron could be seen by the uncoupling of the iron-protein enzyme aconitase, resulting in elevated citrate.

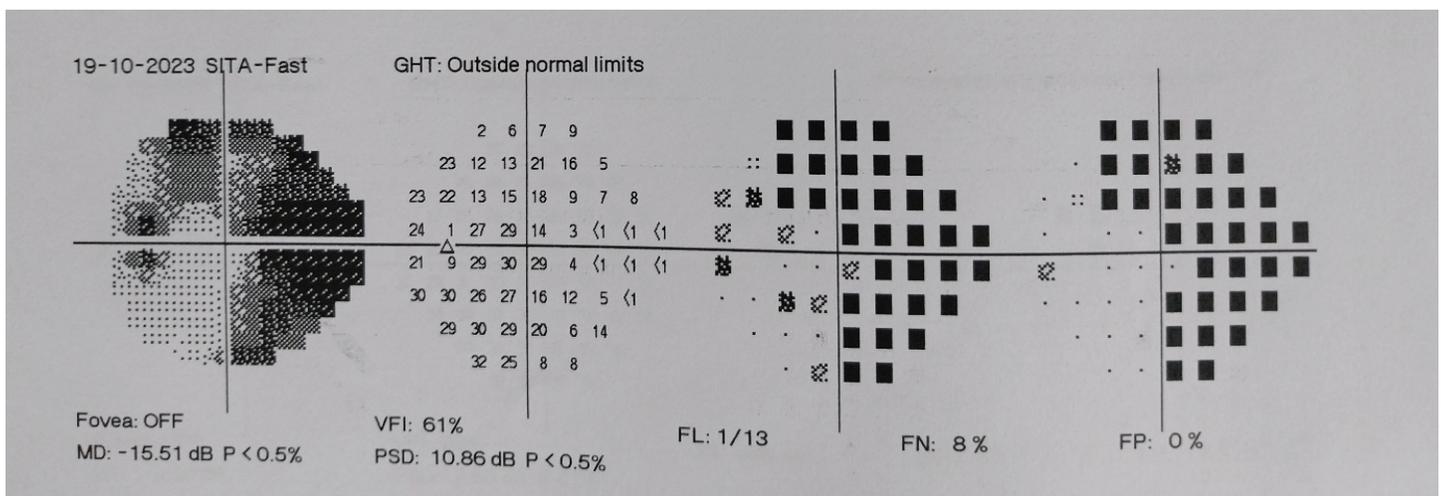
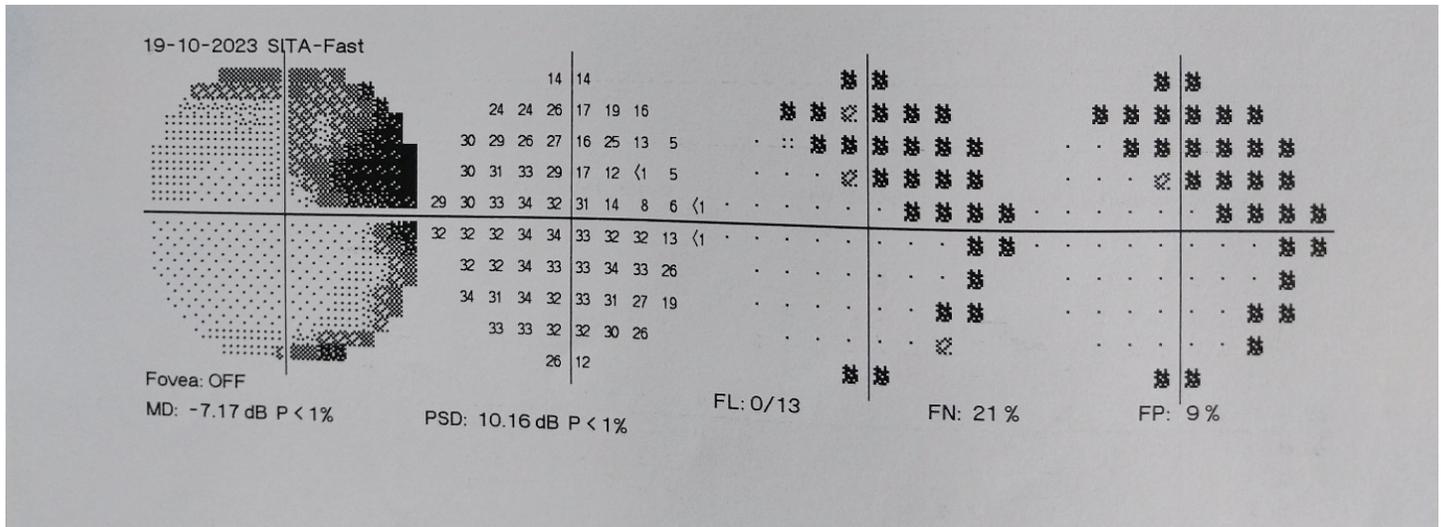


Figure 2: Visual Field Optical scanning of the left eye of the subject. Upper panel scanning on the first visit to an ophthalmologist, lower panel, scanning one month later. Black dots represent areas of the eye non-responsive to light.

Discussion

Evidence suggests that the pressure change seen in the eye is due to some sort of progressive response, and there is mounting evidence to suggest that there is a strong role of the immune response in the development of glaucoma [9] with several workers suggesting some sort of autoimmune response as being causative for the condition [10-13]. Prolonged immune responses, such as those seen with COVID infections or COVID vaccination, have been shown to result in significant oxidative stress, with reduction in levels of active vitamin B12, and an accompanying increase in levels of homocysteine. In many cases the response to vaccination is similar to that seen in Long COVID, and has been termed Long Vax. In this regard, elevated homocysteine levels are a feature of PEX (Koc and Kaya, 2020; Rebecca et al., 2019, and so would be associated with functional B12 deficiency (as per data) [14,15]. There are many reports of COVID-19 vaccine associated ocular adverse effects [16-25] as well as various ocular manifestations of COVID-19 [16]. Apart from the above there are an increasing number of rarer conditions occurring, such as VHL syndrome, and some common complications such as cerebrovascular disorders, including transient ischemic stroke, venous sinus thrombosis, intracerebral hemorrhage, and demyelinating disorders including MS, neuromyelitis optica, and transverse myelitis [26], and various other neurological conditions [27]. In addition, there has been an increase in multi-system Inflammatory Syndrome [28], and many neurological complications after the first dose of vaccine and subsequent COVID [29]. These complications have been documented since 2021, with increasing reports of problems from 2022 onwards, and yet governments have not moderated their calls for vaccination, and as such should be liable for the damage from the vaccines.

The prolonged response as described above, as well as all of the Long Vax-type reports could potentially be caused by the abnormal biodistribution due to PEGylation of the mRNA-lipid nanoparticles. PEG-nanoparticles have been shown to shield the nanoparticles from opsonization and phagocytosis, thereby prolonging circulation time, and completely changing the biodistribution from that observed with non-PEGylated nanoparticles, as such are ideal for protein delivery. In contrast, however, they are NOT what is required to stimulate a prolonged immune response, which is targeting to the local lymph node and liver, which is what is required from vaccination. In contrast PEG-nanoparticles are much more likely to promote numerous systemic complications, such as those described above.

The control of the inflammatory process is intimately dependent upon Selenium and its role in the activation of glutathione peroxidase. Part of the inflammatory cascade involves the activation of oxygen by NADPH Oxidase to generate the reactive oxygen species O_2^{**} . This in turn is further activated to generate hydrogen peroxide (H_2O_2). Under normal circumstances the H_2O_2 is then converted to hydroxide and then water by the Selenoprotein Glutathione-Peroxidase (GSHPx(Se)). In Selenium deficiency this reaction is reduced and so dangerous H_2O_2 can accumulate inside the cell and cause massive intracellular damage. Control

of oxidative stress involves the anti-oxidant molecule GSH, and the reduction of oxidized glutathione (GSSG) requires the FAD-dependent enzyme glutathione reductase (GSH reductase). In Selenium deficiency activation of vitamin B2 is incomplete and hence levels of FMN and FAD are lower inside the cell. This has the dual effect of reducing the activity of GSH-reductase, but also, because of the requirement for FMN and FAD in the cycling of methyl B12, lack of FMN and FAD also leads to lower methylation and reduced production of GSH, through lower activity of the sulphation cycle in Methyl B12 deficiency. The result would be a greatly increased reaction of H_2O_2 and potentially cause death due to an over-active inflammatory response. Oxidative stress is further increased because methyl B12 is required for the production of the cellular anti-oxidant, melatonin. The prolonged immune response generated by the combined Astra Zeneca viral vaccine, which is further exacerbated by the PEG-mRNA vaccine, appears to have resulted in a prolonged Inflammatory response, and would be expected to result in reduced levels of Selenium in the aqueous humour, thereby exacerbating the inflammatory response in the eye, with resultant increased damage to the optic nerve. In this regard, reduced Selenium levels are common in the aqueous humour in PEX [30].

Examination of the OAT data with time supports the above hypothesis. Hence, at 4 weeks post COVID vaccination there is an increase in the functional B2 deficiency markers, succinate, lactate, oxalate, suberate and the FMN deficiency marker the QA:KA ratio. With further time, evidence of the secondary effect of functional B2 deficiency can be seen in the increase in the functional B12 deficiency markers, QA, KA, HVA, VMA, Pyroglutamate, MMA, ethylmalonate, and methylsuccinate. Potentially the resultant lack of methylation would have deleterious effects on the methylation of lysine and of various proteins, leading to structural alterations, which in turn could lead to autoimmunity reactions, and formation of protein aggregates, typical of PEX. Of particular concern is the elevation of the inflammatory markers QA and KA, both of which have been associated with neurotoxicity [31-38], which remained elevated one year after the vaccination.

Conclusions

The compulsory vaccination of the subject with the COVID vaccine, has resulted in a deleterious reduction in functional vitamin B2 and vitamin B12 levels, leading to an increase in oxidative stress markers, elevation in blood pressure, and ultimately has contributed to the induction of elevated intraocular pressure, Pseudoexfoliation syndrome and potential loss of sight in an otherwise extremely healthy individual. Apart from the devastating loss of sight, this has been accompanied by repeated bouts of depression in an individual who was previously known to be a highly optimistic person with an "Up-beat" personality. The lack of understanding of the biochemistry of this response and the lack of responsibility shown by the medical profession and the local health department and the Therapeutic Good Association has been outstanding. A vaccine that ultimately threatens the sight of the vaccinated, should never have been released onto the market, nor made mandatory for the general public.

References

1. Chen Y, Xu Z, Wang P, et al. New-onset autoimmune phenomena post-COVID-19 vaccination. *Immunology*. 2022; 165: 386-401.
2. Menni C, Klaser K, May A, et al. Vaccine side-effects and SARS-CoV-2 infection after vaccination in users of the COVID Symptom Study app in the UK a prospective observational study. *The Lancet. Infect Dis*. 2021; 21: 939-949.
3. Couzin-Frankel J, Vogel G. Vaccines may cause rare Long Covid-like symptoms. *Science New York NY*. 2022; 375: 364-366.
4. Koutsiaris AG, Riri K, Boutlas S, et al. COVID-19 hemodynamic and thrombotic effect on the eye microcirculation after hospitalization A quantitative case-control study. *Clinical hemorheology and microcirculation*. 2022; 82: 379-390.
5. Turathum B, Gao EM, Yang F, et al. Role of pyroglutamic acid in cumulus cells of women with polycystic ovary syndrome. *J Assist Reprod Genet*. 2022; 39: 2737-2746.
6. Gamarra Y, Santiago FC, Molina-López J, et al. Pyroglutamic acidosis by glutathione regeneration blockage in critical patients with septic shock. *Critical care London England*. 2019; 23: 162.
7. Gueta I, Perach Ovidia Y, Markovits N, et al. Is Pyroglutamic Acid a Prognostic Factor Among Patients with Suspected Infection. A Prospective Cohort Study. *Scientific reports*. 2020; 10: 10128.
8. Davidson JA, Robison J, Khailova L, et al. Metabolomic profiling demonstrates evidence for kidney and urine metabolic dysregulation in a piglet model of cardiac surgery-induced acute kidney injury. *Am J Physiol Renal Physiol*. 2022; 323: F20-F32.
9. Oiry J, Puy JY, Mialocq P, et al. Synthesis and in vitro anti-HIV activity in human monocyte-derived macrophages of 2-oxothiazolidine-4(R)-carboxylic acid derivatives. *J Med Chem*. 1999; 42: 4733-4740.
10. Kamat SS, Gregory MS, Pasquale LR. The Role of the Immune System in Glaucoma Bridging the Divide Between Immune Mechanisms in Experimental Glaucoma and the Human Disease. *Semin Ophthalmol*. 2016; 31: 147-154.
11. Rieck J. The pathogenesis of glaucoma in the interplay with the immune system. *Invest Ophthalmol Vis Sci*. 2013; 54: 2393-2409.
12. Grus FH, Joachim SC, Wuenschig D, et al. Autoimmunity and glaucoma. *Journal of glaucoma*. 2008; 17: 79-84.
13. Bakalash S, Kipnis J, Yoles E, et al. Resistance of retinal ganglion cells to an increase in intraocular pressure is immune-dependent. *Invest Ophthalmol Vis Sci*. 2022; 43: 2648-2653.
14. Tezel G, Wax MB. The immune system and glaucoma. *Curr Opin Ophthalmol*. 2004; 15: 80-84.
15. Koc H, Kaya F. Relationship between homocysteine levels anterior chamber depth and pseudoexfoliation glaucoma in patients with pseudoexfoliation. *Int Ophthalmol*. 2020; 40: 1731-1737.
16. Rebecca M, Gayathri R, Bhuvanandar R, et al. Elastin modulation and modification by homocysteine a key factor in the pathogenesis of Pseudoexfoliation syndrome. *Br J Ophthalmol*. 2019; 103: 985-992.
17. Ichhpujani P, Parmar UPS, Duggal S, et al. COVID-19 Vaccine-Associated Ocular Adverse Effects An Overview. *Vaccines*. 2022; 10: 1879.
18. Habet-Wilner Z, Neri P, Okada AA, et al. COVID Vaccine-Associated Uveitis. *Ocul Immunol Inflamm*. 2023; 31: 1198-1205.
19. Pang K, Pan L, Guo H, et al. Case Report Associated Ocular Adverse Reactions With Inactivated COVID-19 Vaccine in China. *Front Med*. 2022; 8: 823346.
20. Singh RB, Parmar UPS, Kahale F, et al. Vaccine-Associated Uveitis after COVID-19 Vaccination Vaccine Adverse Event Reporting System Database Analysis. *Ophthalmology*. 2023; 130: 179-186.
21. Mahendradas P, Mishra SB, Sangoram R, et al. Ocular manifestations following COVID-19 vaccination. *J Ophthalmic Inflamm Infect*. 2023; 13: 44.
22. Chaudry E, Singh G, Khan H, et al. Post-COVID-19 vaccine uveitis A case series. *J Fr Ophtalmol*. 2023; 46: 720-725.
23. Pillar S, Weinberg T, Amer R. Posterior ocular manifestations following BNT162b2 mRNA COVID-19 vaccine: a case series. *Int Ophthalmol*. 2023; 43: 1677-1686.
24. Wang MTM, Niederer RL, McGhee CNJ, et al. COVID-19 Vaccination and the Eye. *Am J Ophthalmol*. 2022; 240: 79-98.
25. Kamoi K, Ohno-Matsui K. Long Vax in the Eye: Long Post-COVID Vaccination Syndrome Presenting with Frosted Branch Angiitis. *Diseases Basel, Switzerland*. 2024; 12: 36.
26. Guo M, Liu X, Chen X, et al. Insights into new-onset autoimmune diseases after COVID-19 vaccination. *Autoimmunity reviews*. 2023; 22: 103340.
27. Hosseini R, Askari N. A review of neurological side effects of COVID-19 vaccination. *European journal of medical research*. 2023; 28: 102.
28. Chatterjee A, Chakravarty A. Neurological Complications Following COVID-19 Vaccination. *Curr Neurol Neurosci Rep*. 2023; 23: 114.
29. Elsaid M, Nune A, Hesham D, et al. Multisystem Inflammatory Syndrome (MIS) following SARS-CoV-2 vaccinations; a systematic review. *Trop Dis Travel Med Vaccines*. 2013; 9: 19.
30. Patone M, Handunnetthi L, Saatci D, et al. Neurological complications after first dose of COVID-19 vaccines and SARS-CoV-2 infection. *Nat Med*. 2021; 27: 2144-2153.
31. Yilmaz A, Ayaz L, Tamer L. Selenium and pseudoexfoliation syndrome. *Am J Ophthalmol*. 2011; 151: 272-6.e1.
32. Guillemin GJ. Quinolinic acid the inescapable neurotoxin. *The FEBS journal*. 2012; 279: 1356-1365.
33. Yan J, Kothur K, Mohammad S, et al. CSF neopterin quinolinic acid and kynurenine/tryptophan ratio are biomarkers of active neuroinflammation. *EBioMedicine*. 2023; 91: 104589.

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34. Heyes MP. Quinolinic acid and inflammation. *Annals of the New York Academy of Sciences*. 1993; 679: 211-216.
 35. Guillemin GJ. Quinolinic acid: neurotoxicity. *The FEBS journal*. 2012; 279: 1355.
 36. Hestad K, Alexander J, Rootwelt H, et al. The Role of Tryptophan Dysmetabolism and Quinolinic Acid in Depressive and Neurodegenerative Diseases. *Biomolecules*. 2022; 12: 998.
 37. Lugo-Huitrón R, Ugalde Muñiz P, Pineda B, et al. Quinolinic acid an endogenous neurotoxin with multiple targets. *Oxidative medicine and cellular longevity*. 2013; 2013: 104024.
 38. Lee JM, Tan V, Lovejoy D, et al. Involvement of quinolinic acid in the neuropathogenesis of amyotrophic lateral sclerosis. *Neuropharmacology*. 2017; 112: 346-364.