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PATHOPHYSIOLOGICAL MECHANISMS BEHIND POSSIBLE CATARACT PROGRESSION IN PATIENTS AFTER COVID-19

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Dear Editor,

Recently, we saw a 60-year-old male patient with bilateral cataract progression following a moderately severe SARS-CoV-2 infection. This led us to assess pathophysiological mechanisms possibly linking COVID-19 with the cataract progression.

Oxidative stress, defined as imbalance in the production of reactive oxygen species and antioxidant responses, was described in a variety of viral infections. Death of infected cells, activation of innate immune response and production of inflammatory cytokines, are all connected with oxidative stress. SARS-CoV-2 induces the expression of oxidative stress genes in immune and structural lung cells. Thus, COVID-19 patients have significantly reduced plasma levels of antioxidant enzymes (glutathione - GSH, glutathione peroxidase - GPx, catalase, superoxide dismutase - SOD), vitamins and trace elements and elevated levels of oxidative stress parameters, compared to healthy controls (Karkhanei et al. 2021).

Moreover, a preclinical study demonstrated that GSH depletion may have a role in COVID-19 pathophysiology, severity and mortality (Khanfar & Al Qaroot 2020). Antioxidant supplementation seems to be beneficial in terms of inflammatory cytokines level improvement and disease progression among non-critically ill COVID-19 patients. In contrast, significantly lower concentration of antioxidative agent total sulfhydryl (SH) groups and several enzymatic antioxidants, as well as higher concentration of malondialdehyde (MDA; a final product of lipid-peroxidation) have also been reported in the serum of patients with cataracts, when compared to healthy controls (Kaur et al. 2012).

Additionally, a positive correlation between the level of oxidative stress markers and total proteins in aqueous humor and severity of cataract have been observed, so it is likely that there is an association between the severity of COVID-19 infection and cataract progression. More than 50% of GSH, a principal lenticular antioxidant, can be found in its oxidized form during an oxidative attack. However, in cataractous lenses, concentration of reduced GSH is decreased, probably due to inactivation of glutathione reductase by disulfide bond formation and protein unfolding. Consequently, due to impaired antioxidant response and decreased efficiency of repair mechanisms in cataractous lenses, lenticular proteins, lipids and nucleic acids become more susceptible to oxidation, particularly during COVID-19 caused oxidative stress, when lens proteins may become considerably more modified, denaturated and aggregated (Berthoud et al. 2009).

High lipid peroxidation in combination with oxidation of membrane proteins causes breakdown of transmembrane ion gradients and loss of cellular viability. Thus, oxidative stress may trigger new somatic DNA mutations in lens epithelial cells thereby impairing their differentiation into fibre cells and disturbing lens homeostasis and transparency. Furthermore, as intercellular communication becomes altered due to lipid changes, activation of post-translational modification of connexins, their direct oxidation and somatic mutations, cause internal fibre cells to obtain neither essential nutrients nor antioxidants, making them incapable of removing toxic metabolites and maintaining resting potentials (Berthoud et al. 2009).

Last but not least, corticosteroids, which are prescribed in COVID-19 cases for respiratory insufficiency and during recovery, may also result in cataract development or progression, possibly due to osmotic imbalance, oxidative damage, disrupted lens growth factors and blockage of normal metabolism of connective tissue (Figure 1). Moreover, diarrhoea, dehydration, acidosis, malnutrition, high level of urea and related osmotic imbalance, which can all occur in COVID-19, have been associated with accumulation of cyanate and subsequent drop in the GSH level, thereby potentially also being cataractogenic.

Finally, it is unlikely that SARS-CoV-2 affects the eye lens directly, since there is neither substantial expression of ACE2 receptor nor type II transmembrane serine protease (TMPRSS2) gene present in human lens (Ma et al. 2020).

Besides providing potential pathophysiological explanations for cataract progression after SARS-CoV-2 infection, our aim is to point towards a potential new complication of COVID-19 and highlight the need to better evaluate patients with cataracts who are recovering from COVID-19 (Jakovljević et al. 2021).

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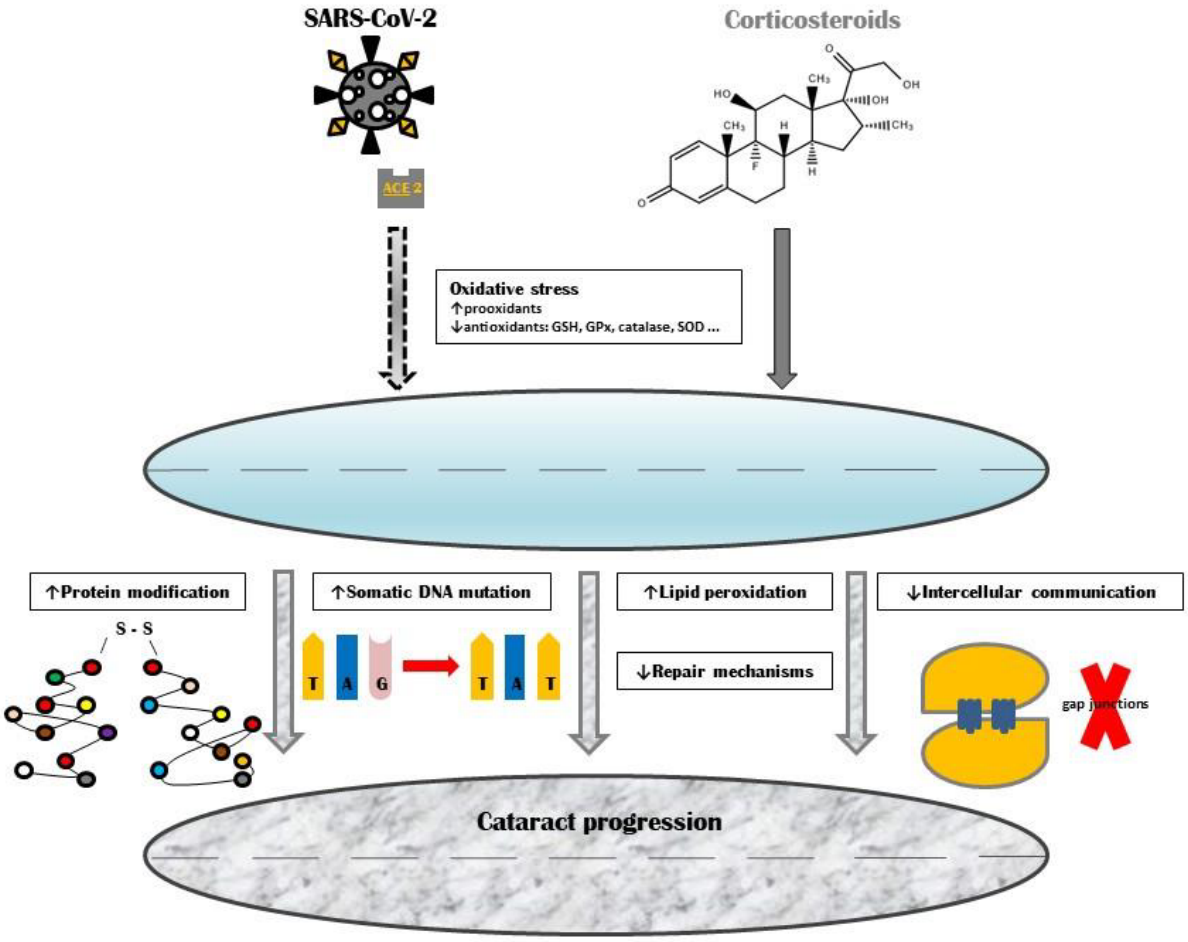

Figure legend: DNA – deoxyribonucleic acid; GPx – glutathione peroxidase; GSH – glutathione; SOD – superoxide dismutase

Figure 1. Pathophysiological explanations for cataract deterioration after SARS-CoV-2 infection

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