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Impact of Gaucher disease on COVID-19

Gaucher disease (GD), one of the two most common inherited lysosomal storage disorders, is considered rare, but in the Ashkenazi Jewish population its prevalence is approximately 1:850.[1] GD is an autosomal recessive disease caused by inherited mutations in the *GBA1* gene, leading to reduced activity of the lysosomal enzyme glucocerebrosidase and thereby to the accumulation of the glucocerebroside in macrophages in the spleen, liver, bone marrow and lungs. Recently, it has become apparent that chronic inflammation, immune dysregulation, and enhanced activation of the coagulation and fibrinolytic systems all play a part in the pathophysiology of the disease. Accordingly, many secretory products of activated macrophages, such as the pro-inflammatory cytokines interleukin (IL6, IL10) and tumour necrosis factor alpha (TNFα), have been reported in GD.[2] In addition, elevated levels of serum ferritin, D-dimers and soluble macrophage-derived CD163 are rather common in GD and are also markedly elevated in the cytokine storm seen in patients with COVID-19.[3]

The current coronavirus pandemic is characterised by high infection rates and higher mortality among the elderly and in patients with some underlying medical conditions, including those with a compromised immune system. This has naturally raised great concerns among many patients with GD, who in addition to the previously listed markers of disease, also have high levels of angiotensin-converting enzyme (ACE), although the correlation with the ACE-2 receptor is not clear.[4]

Interestingly, to the best of our knowledge, no serious cases of COVID-19 infections have been reported in GD. Among our cohort of approximately 550 adults from Israel and Australia with GD (median (range), 46 (18–94) years), we have only a single patient (age 24, in her eighth month of pregnancy) with confirmed COVID-19 infection, whose clinical course was mild and short, and was managed by quarantine for 14 days. It is important to emphasise that in both countries, only symptomatic cases were tested for possible COVID-19 infection, thus it is possible that other patients with GD were infected but they were not detected since they were asymptomatic.

As glycosphingolipids may impact the immune system in opposing directions,[5] we speculate that the accumulated glycosphingolipids in patients with GD promote mainly immune tolerance rather than inflammation when exposed to COVID-19, but a final conclusion should await a future report from an international consortium currently organised by the European Working Group of Gaucher disease.

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