CONFERENCE SUMMARY

The complex interaction of SARS-CoV-2 with various autoantibodies

Summary of the plenary session "COVID-19", which was presented at the 2021 virtual 12th International Congress on Autoimmunity

ust a few months after the new betacoronavirus SARS-CoV-2 was identified as the triggering agent of COVID-19 at the beginning of 2020, scientists around the world started publishing on possible links between the occurrence of different autoimmune disorders and SARS-CoV-2.[1] Other viruses that are associated with immune system hyperreactivity (e.g. Epstein-Barr virus or Cytomegalovirus) are already known to play an important role as triggers of autoimmune disorders. During a plenary session at the virtual 2021 International Congress on Autoimmunity, experts debated on the interaction between various autoantibodies and SARS-CoV-2 in COVID-19 patients, and on the possible link wityh disease severity. Another important topic discussed by the experts was the potential of SARS-CoV-2 to trigger the formation of autoantibodies in patients affected by COVID-19, and whether their presence is to be considered as a formal sign of an ongoing autoimmune disease.

Currently, 18 autoantibodies and 17 autoimmune diseases are are thought to be associated with SARS-CoV-2 (figure 1). Particular attention is being given to rheumatic autoimmune diseases, acute and reactive arthritis, psoriasis arthritis, systemic lupus erythematosus (SLE), autoimmune myositis and vasculitis.[2] According to many experts, the most frequent autoantibodies detected in the serum of COVID-19 patients are antinuclear antibodies (ANA), rheumatoid factor (RF), anti-CCP antibodies, antiphospholipid (aPL) and anti-thyroid peroxidase (TPO) antibodies.

The course and the severity of the COVID-19 infection are associated with the serum profiles of various autoantibodies

Several studies have shown the presence of rheumatism-associated antibodies in the serum of COVID-19 patients to be a risk factor leading to a more severe disease (longer hospitalization, admission in ICU, need for a mechanical ventilation). In severe cases of COVID-19, blood hypercoagulability often leads to thromboembolic incidents and accidents.[3] Serum concentration in anti-cardiolipin (aCL) antibodies is also directly associated with a risk of thrombosis.[4]

In a current study (n=104), aCL antibodies were found in 33.7% of COVID-19 patients and at least one aPL antibody was found in the serum of 47.1% of patients.[5] Another study which found at least one rheumatism-associated antibody in 69% of severely ill COVID-19 patients (n=29) showed similar results. Here, ANA, Anti-β-2-glycoprotein 1 (anti-β2GP1) and aCL were the most frequently detected autoantibodies (34.5 %, 34.5 % and 24.1 %, respectively).[6] Transient ischaemia of the upper and lower extremities as well as ischemic stroke also correlated with positive anti-βGP1 and aCL antibodies in severe courses of COVID-19.

Compared with a healthy control group, the lupus anticoagulant (LA) was found significantly more often in the serum of COVID-19 patients (n=35).[7] Disease severity is not just influenced by the presence, the presence of these autoantibodioes, but also by their concentration.

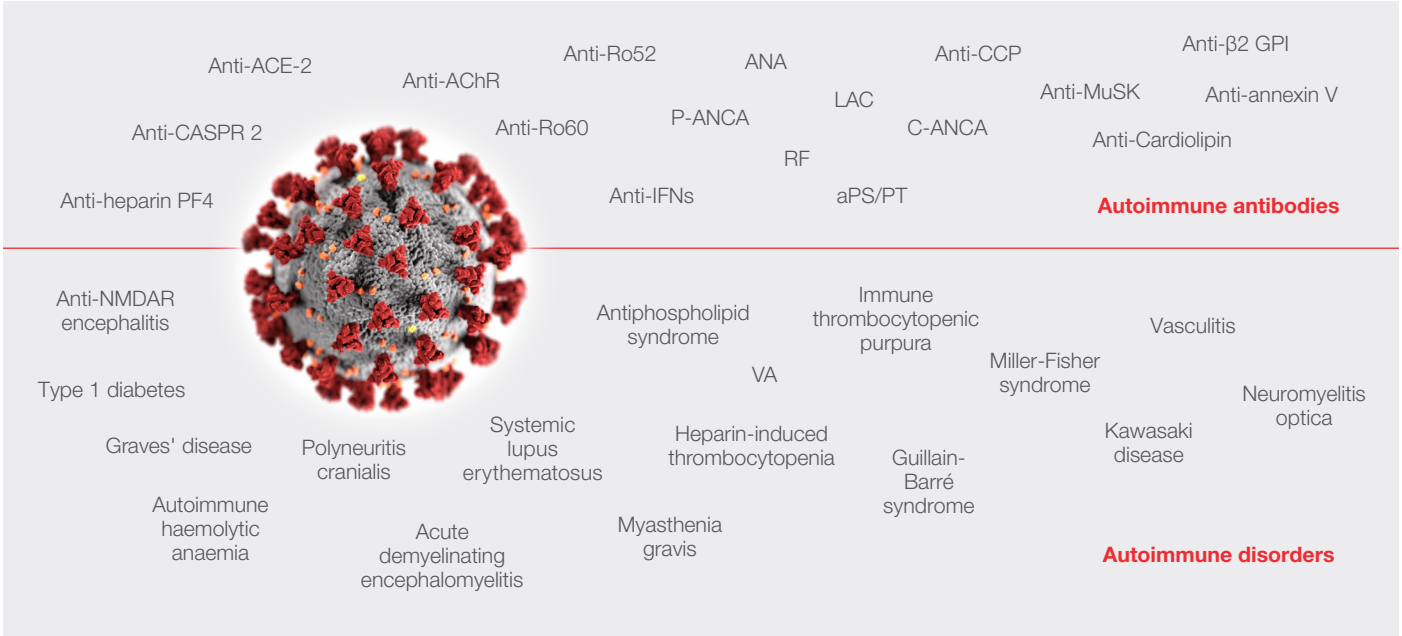

Figure 1: SARS-CoV-2 autoimmune virus

In 81.2% of severe cases, the aCL-IgG serum levels were above the positive cut-off, while just 18.8% of mild to moderate cases showed similar levels.[8] Researchers also found a positive correlation between autoantibody serum concen-trations in COVID-19 patients and inflam-mation parameters (C-reactive protein, CRP).[9]

The experts have pointed out, however, that in rheuma-tological practice, autoantibody levels in serum are often detected years before the onset of the autoimmune dis-ease, and current data do not allow any conclusion if the observed, often transient, changes in serum levels de-velop during or after a COVID-19 infection actually cause clinically relevant manifestations. For this reason, auto-antibodies levels in serum should be regularly checked to ensure that the point at which a transient autoimmune disease becomes acute is not missed.

Immunization against SARS-CoV-2: a trigger of autoimmune disease?

The experts reported of just a few cases of a potential link between immunization against SARS-CoV-2 and ma-terialization of an autoimmune disorder and/or transiently detectable autoimmune antibodies. The experts argued, however, that detectable levels in serum do not translate into a clinical autoimmune disorder and unanimously recommend immunization against SARS-CoV-2. They also agreed that mRNA vaccines are the safest option that can be offered to immunocompromised patients.

Immunomodulatory therapy for COVID-19

Neutralizing antibodies to type I interferons (IFNs) were found in the serum of 10% of critically ill COVID-19 patients (acute respiratory distress syndrome, hyper-inflammation). These antibodies were not detected in asymptomatic or mildly ill patients.10 The experts discussed the possibility that the autoantibodies to type I IFNs trigger a modulation in the immune system which is responsible for severe cases of COVID-19.

A similar approach is used in for the targeted immuno-modulatory therapy of rheumatoid arthritis. The interleukin (IL)-6 antagonists tocilizumab and sarilumab, as well as the IL-1 antagonist anakinra, used in this area of treat-ment, have the potential to counteract COVID-19 induced hyperinflammation. An international study (REMAP-CAP trial) showed that the death rate amongst patients with severe cases of COVID-19 was significantly lower in patients treated with a combination of IL-6 antagonists and steroids.[11]

Similarly, the IL-1 antagonist achieved an improvement of the clinical outcome in 72% of COVID-19 patients.[12] Despite the fact that the safety of these drugs has been proven in several studies[13], the European League Against Rheumatism (EULAR) currently does not recommend it for routine use.[14] The participants of the panel discussion nevertheless gave the use of the three IL antagonists a positive evaluation.

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Conclusion

Despite the latest findings, standard testing of all COVID-19 patients for potential autoimmune serum markers does not make sense. However, for patients with vascular manifestations who test positive for antiphospholipid antibodies, for instance, early, adequate treatment with anticoagulants may be indicated. Checking serum levels at intervals of 12 weeks or more is recommended in order to distinguish persisting post-infectious, COVID-19-induced autoimmune disorder from transient autoantibodies. The mere detection of autoan-tibodies after a COVID-19 infection does not necessitate rheumatological examinations, unless the patient is exhibiting clinical signs of autoimmune disease.

In the future, anamnesis will have to include asking about a past COVID-19 infection or immunization as a possible trigger of potential autoimmune disorder or the presence of antibodies.

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