

GPCR autoantibodies and post-vaccine syndromes

Background

A certain group of autoantibodies that are frequently found in post covid syndrome patients are autoantibodies against G-protein coupled receptors (GPCR-AABs), they are also called functional autoantibodies (fAABs). In the case of post covid, agonistic AABs are most common, but there are also antagonistic GPCR-AABs. Wallukat et al. examined sera from 31 patients with long covid symptoms, and functional autoantibodies were detected in all samples [1]. They also seem to play a role in the severity of a covid course [2]. Autoantibodies against ACE2, one of the entry ports into human cells for the SARS-Cov-2 virus, are also present in post covid sufferers in 80-90% of all cases [3]. According to our own experience in various support groups, these autoantibodies are also found in many post-vaccine syndrome sufferers (currently, according to our own estimate, a prevalence of 80-90%). A first official case report also suggests that these autoantibodies may also play a role in post-vaccine syndrome sufferers [4]. There are also initial case reports of post-vaccination dysautonomia that may have been triggered by these autoantibodies [5, 6].

Before the covid pandemic, these functional autoantibodies (fAABs) were predominantly known from the field of cardiovascular and neurodegenerative diseases, for example dementia, type 2 diabetes or cardiomyopathy but also rheumatic diseases [7, 8, 9]. In classical autoimmune diseases, the body's own immune system turns against the body's own structures through malformed antibodies, resulting in inflammation and organ damage. Functional autoantibodies, on the other hand, act as agonists at the receptor instead of natural ligands and, when bound, activate it in an uncontrolled and long-lasting manner. Thus, they exhibit a wide range of pharmacological properties [10, 11].

GPCRs are important mediators of signal transduction and as such are involved in numerous bodily functions, such as sensory stimulus processing, various metabolic functions, inflammatory processes, and cell growth and differentiation. Therefore, uncontrolled activation can thus lead to an improbably large number of different disorders. A well-known example is the β 1-adrenoceptor which plays a major role in regulating cardiac function. People with agonistic autoantibodies to the β 1-adrenoceptor may therefore experience a variety of cardiac symptoms, including dilated cardiomyopathy [12].

Other diseases associated with GPCR-AAB include myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), postural tachycardia syndrome (POTS), and chronic pain syndrome/fibromyalgia [9, 13, 14, 15]. These are all clinical pictures that also occur or develop frequently in post-covid patients and post-vaccine patients [5, 6]. Post-vaccine patients are currently anticipated to have a 10-20% rate of developing full-blown ME/CFS.

Post vaccine syndromes are likely to be severely under-reported because the vaccination campaign is recent, physicians are often reluctant to associate symptoms with vaccination, and clinicians lack diagnostic markers. However, reactions of this type are also known to occur after other vaccinations

and, due to the longer elapsed time period, are also found more frequently in the literature [16, 17, 18].

Recent research increasingly suggests that ME/CFS is a neuroimmunological disorder [18]. Even before the covid pandemic, there was research looking at the clustered occurrence of agonistic autoantibodies in ME/CFS patients. Here, a prevalence of 20-30% of all ME/CFS patients is assumed [19, 20, 21, 22, 23]. GPCR-AAB are also frequently found in the individual comorbidities of ME/CFS and many other diseases [9, 25, 26].

Treatment options

Unfortunately, immunosuppression is of little help with this type of autoantibody. At the beginning of the autoimmune reaction, while the autoantibodies are forming, cortisone seems to work well, but has little effect later on. Therefore, few therapeutic options remain besides generally immunomodulatory and anti-inflammatory measures. In the case of ME/CFS sufferers, there have been initial studies of partially successful removal of autoantibodies using immunoabsorption [27, 28]. There have also been successful attempts to cure other diseases associated with the autoantibodies by removal using immunoabsorption [29].

However immunoabsorption is very complex and expensive and in the process, besides the harmful agonistic autoantibodies, useful IgGs are also removed. Observations over a longer period of time and the fact that some patients are symptom-free long term indicate that autoantibodies do not reappear in successfully treated cases. [27, 28, 30].

In post covid and post vaccine affected patients, unfortunately, there is little experience to date. These range from complete cures to sustained improvements of varying degrees to improvement with relapse after a few weeks. There has not yet been reports of deterioration following immunoabsorption.

Another therapeutic approach, which is unfortunately not available at the moment, but which has been successfully used in four post covid patients so far, is the drug BC007 developed by the Eye Clinic of the University Hospital Erlangen and Berlin Cures [31]. This is a DNA aptamer that binds GPCR-AABs and thus renders them harmless. The drug, which was originally intended as a cardiac drug, functions like a selective immunoabsorption. So far, 4 post covid patients have been treated with it. All of them recovered completely from their symptoms within a very short time. From one patient we know that there was a relapse after a few months and the autoantibodies reappeared. Funds for the BC007 study for post covid patients have now been approved and funds for another study for BC007 for ME/CFS sufferers will most likely be approved in April. Therefore, at least one trial for this will start this summer.

Another treatment, but one that can only mitigate symptoms, is blocking the receptors with their corresponding antagonists. These block their associated receptors, protecting them from activation from autoantibodies. However, many sufferers have autoantibodies against different receptors, so treatment would require the use of several antagonists at once, which could potentially interact with each other. Combined, they may have a broad side effect profile.

Clinical usefulness of agonistic autoantibodies

Unfortunately, it is very difficult to develop a good test method for these autoantibodies. Since one would like to measure not only the binding to the receptor, but also whether the AAB do activate the corresponding receptors, i.e. have pathogenic potential. Unfortunately, there is still a lot of confusion and disagreement about this, and there is also disagreement between laboratories [32]. Different doctors and clinics also prefer different laboratories in each case. Likewise, the prevalence of autoantibodies in the normal population has conflicting data and few studies are available. Erde Labor state a prevalence of 3-5% in the normal population based on their investigations of blood samples from blood donors. Also according to Wallukat et. al, autoantibodies occur only in a small percentage in healthy controls [1].

Therefore, even with these autoantibody results, it is not easy to obtain medical treatment because the test results must always be considered together with the symptoms. This problem is not limited to agonistic antibodies. An elevated ANA titer can also occur in healthy individuals, for example. If a patient has a positive ANA titer as an incidental finding, he would not be treated without symptoms indicative of disease. On the other hand, seronegative autoimmune diseases also occur. So even with other autoantibodies, there are difficulties when symptoms and autoantibody levels don't match. However, if both symptoms and AABs corresponding to those symptoms are present, their pathogenicity should at least be considered.

Another problem with detection is that autoantibodies seem to fluctuate in post covid and post vaccine affected individuals, at least initially. In addition, only those autoantibodies that are not bound to the receptors at the time of blood draw can ever be detected in the blood. This also shows that the level of the values has only a very limited significance. Someone with low (or no!) values in the blood can have very strong symptoms if many autoantibodies are bound to the receptors (and vice versa). Also the eluate of an immunoadsorption can contain additional autoantibodies that were not found in the blood before. It might be helpful to test other values that give an indication of whether the autoantibodies are actually pathogenic (e.g. tryptophan metabolism, renin, angiotensin 2, aldosterone, blood glucose).

Another major problem is that the autoantibodies may be a by-product of other pathologies. Increased cytokine levels and/or chronic pathogenic infections, such as EBV and Borellia, may be the reason that the threshold to form autoantibodies is lowered. Therefore, therapy should not focus exclusively on autoantibodies. In general, it may be prudent to treat all pathogens in the body, to rebuild the gut microbiome and to stabilize the mast cells. All of the measures together should then reduce the risk of the autoantibodies reappearing after removal. Removing the autoantibodies together with other measures could give the whole system a chance settle into a non-pathogenic state.

Currently, four laboratories in Germany offer testing for autoantibodies:

CellTrend GmbH - celltrend.de
E.R.D.E. aak Diagnostik GmbH - aak-diagnostik.de
Berlin Cures GmbH - berlincures.de
IMD Berlin - ME/CFS Diagnostics Profile

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I am not a doctor, but affected myself and have created the text with the best of my knowledge and conscience after my own research. It does not represent a treatment recommendation!

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