

Towards a better diagnosis of long COVID

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Long-COVID patients have persistently elevated blood levels of a group of immune system proteins that could enable the development of diagnostic tests that can more accurately identify this disease.

About 10% of people infected with the coronavirus that causes COVID experience a number of health problems months and, in some cases, years after infection.

The manifestations of this long COVID can take several forms, including the appearance of cardiovascular problems (thromboses, stroke) and metabolic problems (type 2 diabetes), chronic fatigue syndrome (myalgic encephalomyelitis) or even postural orthostatic tachycardia (the heart gets carried away when going from sitting to standing).

Overall, around 200 different symptoms have been identified that can be attributed to long COVID, with extremely negative repercussions on the quality of life of those affected (1).

IMPROVED DIAGNOSIS

However, it is not easy to accurately diagnose long COVID, among other things because many of the symptoms associated with it are not specific to this disease.

This uncertainty means that patients may feel that their medical condition is not taken seriously enough, which could contribute to the high proportion (two-thirds) of people affected by long COVID who suffer from anxiety or depression.

A study recently submitted for pre-publication could greatly facilitate the management of patients with long COVID by greatly improving the accuracy of diagnosis of the disease (2).

In this study, researchers followed 166 patients, 79 of whom had been diagnosed with long COVID. By analyzing the blood plasma of study participants, researchers noted elevated levels of certain components in long-COVID patients, including four proteins that are part of the complement system (Ba, iC3b, C5a and TCC).

The degree of prediction of long COVID based on measured amounts of these proteins is impressive, reaching almost 80%.

This result therefore suggests that diagnostic tests capable of specifically detecting plasma levels of this group of proteins could make it possible to diagnose the disease with much more accuracy than at present.

Recently, a drop in levels of the neurotransmitter serotonin in patients affected by long COVID (which would contribute to the neurological effects of the disease) was shown (3), which allows us to consider the use of other biochemical markers to further improve greater diagnostic accuracy.



AN INFLAMMATORY DISEASE

Complement proteins are important elements of the immune system, particularly for their role in recruiting cells that attack and engulf bacteria and viruses at the site of infection (neutrophils and macrophages).

The deregulation of these proteins observed in long COVID strongly supports the hypothesis that it is chronic inflammation post-infection that plays a key role in the development of the multiple symptoms characteristic of this disease.

- (1) Davis HE et al. Long COVID : major findings, mechanisms and recommendations. *Nat. Rev. Microbiol.* 2023; 21:133-146.
- (2) Baillie K et al. Complement dysregulation is a predictive and therapeutically amenable feature of long COVID. *medRxiv* 2023.10.26.23297597; doi.org/10.1101/2023.10.26.23297597
- (3) Wong AC et al. Serotonin reduction in post-acute sequelae of viral infection. *Cell* 2023; 186:4851-4867.e20.