Study helps explain how COVID-19 heightens risk of heart attack and stroke

September 28 2023

Credit: CC0 Public Domain

In some patients, infection with the pandemic virus SARS-CoV-2 can trigger a dangerous immune response in hardened fatty deposits (plaques) lining the heart's largest blood vessels, a new study shows.

The findings are based on the body's immune system, which evolved to destroy invading microbes but also drives disease when triggered in the wrong context. Doing so brings on a set of responses termed inflammation, including swelling, which results as immune cells and signaling proteins home in on infection sites.

Misplaced inflammation can lead to both immediate and longer-lasting heart issues, such as the breaking up of artery-clogging plaques, and may contribute to the group of symptoms referred to as "long COVID," the authors say.

Experts have long observed that the COVID-19 coronavirus increases the likelihood of having a heart attack or stroke for up to a year after infection, particularly for those who already have underlying heart conditions. However, the specific mechanisms that account for these risks had until now remained unclear.

Led by researchers at NYU Grossman School of Medicine, the study explored how the coronavirus behaves in those with atherosclerosis, a disease in which plaque collects in major arteries and prompts chronic inflammation.

As part of the findings, publishing online Sept. 28 in the journal *Nature Cardiovascular Research,* the team detected the virus within the arteries of eight men and women with a history of atherosclerosis who had died of COVID-19. Besides colonizing arterial heart tissue itself, the coronavirus was also spotted inside local immune cells called macrophages, which normally protect the heart by "swallowing" and disposing of excess fat molecules in arteries.

The experiments further showed that in response to the infection, the macrophages released inflammatory signaling proteins called cytokines that promote a chronic immune response. Notably, the researchers say,

two of the identified cytokines, interleukin-1 beta and interluekin-6, have already been linked to heart attacks.

"Our findings provide for the first time a direct mechanistic link between COVID-19 infection and the heart complications it provokes," said study lead author Natalia Eberhardt, Ph.D., a postdoctoral fellow in the Department of Medicine at NYU Langone Health. "The virus creates a highly inflammatory environment that could make it easier for plaque to grow, rupture, and block blood flow to the heart, brain, and other key organs."

Past research has revealed that the coronavirus stirs up a massive immune response throughout the entire body. This cytokine storm, as it is called, is suspected to contribute to heart issues, says Eberhardt. However, the new study was designed to uncover more direct mechanisms that could be at play as well.

For the analysis, the research team collected 27 artery tissue samples from autopsies of patients who had died of severe COVID-19 between May 2020 and May 2021. All had been previously diagnosed with heart disease.

Next, the authors trained an artificial intelligence computer program to measure coronavirus levels in plaque cells, noting that while viral genetic material was detected using fluorescent dyes viewed under a microscope, the program was able to count thousands of viral features on a cell-by-cell basis.

The team also examined samples of plaque-covered tissue collected from patients who had received surgery to remove the fatty buildup from their arteries. Using a new technique that allowed them to study coronavirus infection of live tissue in the lab, the researchers showed that exposing plaque to the virus boosts inflammation levels in blood vessels.

Together the experimental findings revealed that macrophages rich in engulfed fat were invaded more frequently and for longer periods than those containing less fat. According to the researchers, this suggests that the coronavirus flourishes more easily in people who already have large amounts of plaque buildup in their arteries, explaining in part why those with atherosclerosis are more vulnerable to COVID-19.

"These results shed light onto a possible connection between preexisting heart issues and long COVID symptoms," said study senior author and cardiologist Chiara Giannarelli, MD, Ph.D. "It appears that the immune cells most involved in atherosclerosis may serve as a reservoir for the virus, giving it the opportunity to persist in the body over time."

As a result, the research team next plans to more closely explore this potential link between the coronavirus's behavior during atherosclerosis and long COVID, which includes heart palpitations, chest pain, and fatigue, among other issues.

Giannarelli, an associate professor in the Departments of Medicine and Pathology at NYU Langone, adds that because current investigation analyzed tissue infected with viral strains that spread throughout New York City early in the pandemic, the authors intend to repeat the study in those exposed to newer variants.

More information: SARS-CoV-2 infection triggers pro-atherogenic inflammatory responses in human coronary vessels, *Nature Cardiovascular Research* (2023). DOI: 10.1038/s44161-023-00336-5

Provided by NYU Langone Health