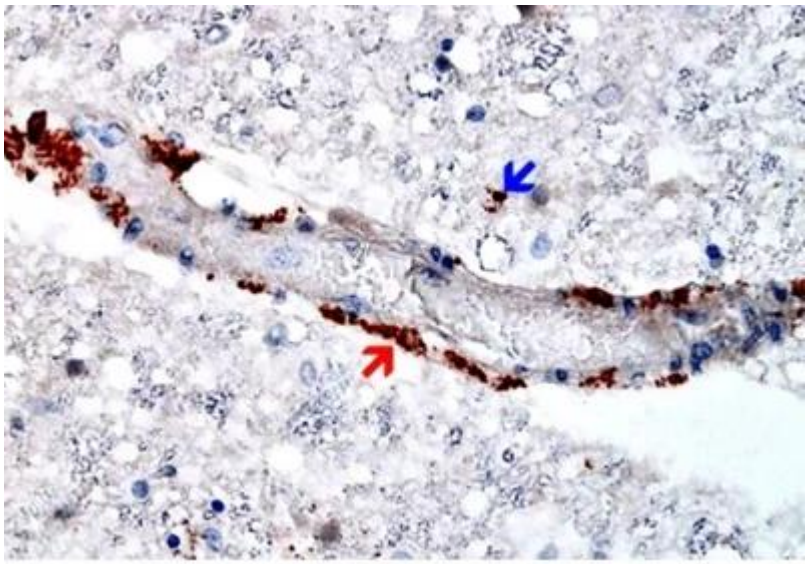
BNT162b2 (Pfizer- BioNTech) and mRNA 1273 (Moderna) vaccines were the first messenger RNA (mRNA)-based vaccines ever approved. In both vaccines, a mRNA sequence determines the structure and assembly of the immunogen, the SARS-CoV-2 spike (S) glycoprotein. The mRNA is protected from degradation by lipid nanoparticles (LNPs) and taken up by the cells as an LNP-mRNA complex through simple endocytosis. In this autopsy report, the German author presents a case of a patient aged 76 years with Parkinson's disease (PD) who died three weeks after receiving the third dose of the COVID-19 vaccine.

The official cause of death was recurrent aspiration pneumonia. However, a detailed autopsy examination revealed additional pathological findings, including multifocal necrotizing encephalitis, mild myocarditis, and pathological changes in small blood vessels (endothelitis).



Original figure from Mörz, M. Vaccines 2022, 10, 1651.

Case report

A patient aged 76 years received three doses of two different COVID-19 vaccines, the ChAdOx1 nCov-19 vector vaccine in May 2021, and the second and third doses of the BNT162b2 mRNA vaccine in July and December 2021.

On the day he got his first vaccine, the ChAdOx1 nCov-19 vector vaccine, he experienced cardiovascular symptoms that required medical care. After receiving the second vaccine, the BNT162b2 mRNA, the family noticed remarkable behavioral and psychological changes and a significant progression of his PD symptoms. He never fully recovered but he received

the BNT162b2 vaccine again. Two weeks later, he collapsed unexpectedly while eating, without signs of food aspiration. He partly recovered after intense resuscitation, but one week later he collapsed again. He was transferred to the hospital, where he died three weeks after receiving the second dose of the BNT162b vaccine. The clinical diagnosis was death due to aspiration pneumonia. Due to unclear symptoms after COVID-19 vaccinations, the family requested an autopsy. The patient had no history of COVID-19 infection.

Autopsy findings

A macroscopic examination of brain tissue showed a circumscribed segmental parenchymal necrosis in the right hippocampus. The brain's histopathology examination demonstrated the loss of pigmented neurons, pigment-storing macrophages, and scattered neuronal necrosis with glial debris reaction. These findings were suggestive of PD, confirming the clinical diagnosis.

Besides Parkinson's disease, brain histopathological examination demonstrated unexpected findings, such as multifocal necrotizing encephalitis of unknown etiology with pronounced inflammation, glial and lymphocytic reaction, and acute vasculitis (predominantly lymphocytic) in the frontal cortex, paraventricular regions, substantia nigra, and nucleus ruber of both hemispheres. In regions characterized by inflammation, evidence of apoptotic cell death was present in the endothelium of the cerebral capillaries. According to the author, these findings were indicative of multifocal necrotizing encephalitis.

Heart histopathological examination showed signs of chronic cardiomyopathy, mild acute lymphohistiocytic myocarditis, and vasculitis. The coronary capillaries and other small blood vessels exhibited mild acute vascular changes, like lymphohistiocytic infiltrates, prominent swelling and vacuolation of endothelial cells, multifocal myocytic degeneration and coagulation necrosis, and karyopyknosis of single endothelial cells and vascular muscle cells. Occasionally, the adherent plasma coagulates/fibrin clots were present on the endothelial surface, indicating endothelial damage.

The brain and heart findings demonstrated that small blood vessels were the most affected, especially the endothelium. The author cited previous studies that described endothelial dysfunction during viral infections, inducing a pro-coagulant state, microvascular leak, and organ ischemia.

Other findings included bilateral mild active nephritis, evidence of shock kidney disorder,

mild acute splenitis, bilateral chronic destructive pulmonary emphysema, and bilateral bronchopneumonia in the lower lobes at multiple stages of development.

Immunohistochemical Analysis

Even though the patient did not have a history of SARS-CoV-2 infection, the author performed an immunohistochemical analysis to investigate the presence of the SARS-CoV-2 antigens, the spike (S) and nucleocapsid (N) proteins, in the brain and heart tissue. In the brain tissue, the S1 subunit of the SARS-CoV-2 S protein was abundant in the necrotizing encephalitis lesions, in cells of the vessel walls, particularly within the cerebral endothelial cells, microglia and astrocytes from necrotic areas, and the nucleus ruber.

The S1 protein was also found in the endothelial cells of the heart's small blood vessels, in lymphocytic periarteritis of the thoracic and abdominal aorta, iliac branches, and cerebral basal artery. The N protein was not detected within the foci of inflammation in the brain and the heart and in endothelial cells of the small blood vessels, microglia, and astrocytes.

Conclusion

This autopsy report described a case of multifocal necrotizing encephalitis, mild myocarditis, and pathological changes in small blood vessels (endothelitis) that developed after a third COVID-19 vaccination (the first vaccine was the ChAdOx1 nCov-19 vector vaccine, and the second and third doses were the BNT162b2 mRNA vaccines). Immunohistochemical analysis detected the S1 subunit of the SARS-CoV-2 S protein, but not the N protein, within the foci of inflammation in the brain and the heart, and in endothelial cells of the small blood vessels.

Since only the S1 subunit was detected in the areas with acute inflammatory responses, the author stated that the S protein may have contributed to the development of these lesions and that the presence of the S protein in affected tissues was not the result of SARS-CoV-2 infection, but rather of vaccination.

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Journal References

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