RESEARCH LETTER

Transient CA19-9 Elevation Post-COVID-19 Vaccine and Infection: A Case Series

Since early 2019, the world has been affected by severe acute respiratory syndrome coronavirus disease 2019 (COVID-19), which has led to more than 6 million deaths globally. Apart from lockdowns, face masks, and social distancing rules, vaccinations seem to be the most effective protection against the highly virulent coronavirus.[1] Given the rapid development of COVID-19 vaccines, unexpected side effects have started to be reported. Enlargement of axillary and supraclavicular lymph nodes has been implicated as a difficult side effect to manage in the context of breast cancer screening and restaging, head and neck cancers, lymphoma, and melanoma of the back and upper extremities.[2,3]

Another unexpected adverse effect is pancreatic injury: A case report of acute pancreatitis occurring shortly after the mRNA vaccine has been published[4] and Pfizer reported additional episodes of pancreatitis related to their vaccine.[5] Beyond vaccination, pancreatitis has also been reported in association with COVID-19 infection: One study found a 17% pancreatitis rate among 52 patients admitted to the hospital for COVID-19.[6] Another study examined the effect of COVID-19 infection on tumor markers and found that in a series of 53 patients, 2 had elevated cancer antigen 19-9 (CA19-9).[7]

CA19-9 is synthesized in the pancreas and biliary tract but also in the epithelium of the stomach, colon, uterus, and salivary glands.[8] For pancreas cancer, it has been reported to have a sensitivity of 79% to 95% and specificity of 82% to 91% for diagnosis.[9] CA19-9 can be elevated in benign disease processes and without a known cause.[10] Despite its shortcomings and the absence of better markers, CA19-9 is the most common biomarker used in monitoring the development and progression of pancreatic cancer (PC).

This case series reports increases in CA19-9 after COVID-19 vaccination or infection in 3 patients (Figure). The cases described were identified in individuals at hereditary high risk for PC participating in a surveillance program between March 2019 and December 2022. Around 300 patients are seen annually in the surveillance program and have visits every 6 or 12 months for imaging studies and laboratory evaluation including CA19-9 and pancreatic enzymes.

Case 1

A 70-year-old woman who was followed in our pancreatic cancer high-risk clinic (PCHRC) since 2019. Her mother and maternal grandfather suffered from PC. She tested negative for a 13 gene PC Germline Mutations Panel (Appendix A). Despite this, given her strong family history, she was eligible and enrolled in screening at the MD Anderson PCHRC. Her baseline CA19-9 was 18.6 U/ml in 2019. She received the first 2 doses of the Moderna vaccine in early 2021 and a Moderna booster in October 2021. Her blood was drawn for the PCHRC screening program on 11/4/2021, only 10 days after the booster application, and she had a CA19-9 elevation to 321 (normal <35 U/mL) with normal amylase, lipase, and hemoglobin a1c levels. Under our screening program, magnetic resonance imaging (MRI)/magnetic resonance cholangiopancreatography (MRCP) was performed and did not exhibit any suspicious pancreatic lesion or findings suggesting pancreatitis. Before proceeding with more invasive studies, the CA19-9 was checked again. A week after the sudden elevation, her CA19-9 had decreased to 225 U/mL and one month later, her CA19-9 levels had returned to normal. She did not exhibit abdominal pain or other alarming symptoms throughout the course of the CA19-9 elevation.

Case 2

A 61-year-old male at high risk for PC due to germline breast cancer 2 gene mutation and a paternal uncle diagnosed with PC at age 62 was followed in the PCHRC since 2017 with a CA19-9 consistently <35 U/mL (normal upper limit). He underwent multiple screening laboratory tests and MRCP exams without any abnormality between 2017 and 2020. In early 2021, he received the first 2 doses of the Pfizer COVID-19 vaccine and a booster by the end of 2021 (November). At his early 2021 follow-up, he was found to have an abrupt and significant elevation in CA19-9 to 130 U/mL. Pancreatic enzymes also increased: Amylase to 126 (normal 28–100 U/L) and Lipase to 92 (normal 13–60 U/L). Despite slightly increased amylase and lipase levels, clinical pancreatitis was not considered because the patient denied acute abdominal pain and tenderness in the upper abdomen. He was followed closely and at a 3-month follow-up he still had an elevated CA19-9. A triple-phase computed tomography abdomen was obtained which showed a normal pancreas without any suspicious lesions or abnormal imaging related to acute pancreatitis. Three months later, the CA19-9 had decreased to 48.7 U/mL and the patient continues to be closely followed.

Case 3

A 57-year-old woman with breast cancer 2 gene germline deleterious mutation enrolled in screening at the PCHRC. Her initial CA19-9 was 29.1 U/mL and baseline MRI/MRCP showed normal pancreas. The patient followed up 1 year later and was found to have an elevation in her CA19-9 to 77.4 U/mL. MRI/MRCP was performed and did not exhibit any suspicious pancreatic lesion or abnormal imaging related to acute pancreatitis. She described having COVID-19 3 months prior to obtaining this elevated CA19-9 level. Her CA19-9 normalized to 29 U/mL after a month and thus further diagnostic methods were not needed. A year later, MRI/MRCP and repeat labs were normal.

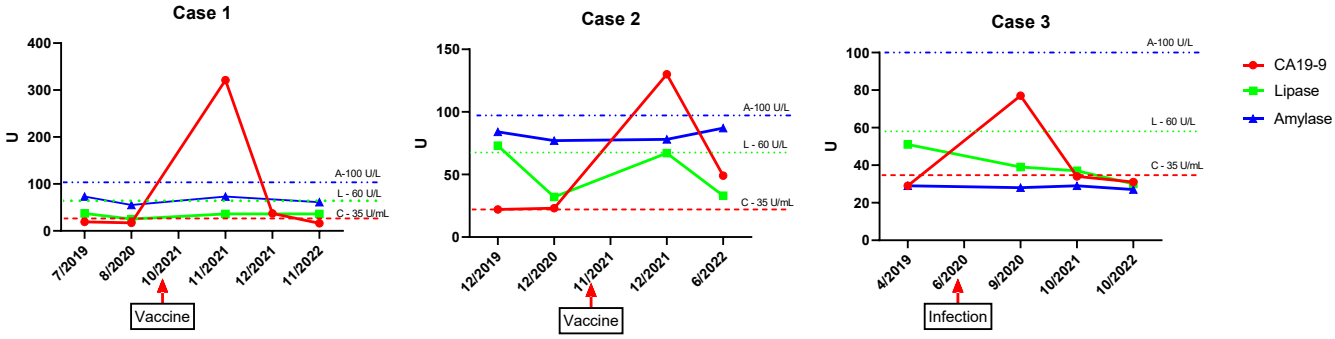

Figure. Biomarkers at various time points (CA19-9, amylase, and lipase) in the 3 cases. Case 1 and 2 had a change in CA19-9 related to vaccine administration and Case 3 had a change following COVID-19 infection. Dashed lines represent the upper limit of normal levels for each biomarker. Red arrow indicates COVID-19 vaccine or infection.

We have described a series of 3 cases of increases in CA19-9 and subsequent normalization (within 1–3 months) temporally associated with COVID-19 vaccination or actual infection in a cohort of ∼300 high-risk patients in a screening program for PC. This caused much anxiety and concern among the patients and the treating physicians regarding the possibility of PDAC developing in this high-risk cohort. The mechanisms underlying these changes are unknown and may be different. Pancreatitis in those who contract COVID-19 pneumonia has been postulated to be secondary to the expression of angiotensin-converting enzyme in pancreas cells, which are also expressed in the lung and allow entry of the virus into the cell.[6,7] Molecular mimicry has been hypothesized to cause pancreatitis after COVID-19 vaccination due to antibody formation that can also recognize cells of the pancreas in an autoimmune fashion.[4]

In patients undergoing PC screening, recent COVID-19 infection and vaccination should be taken in consideration when evaluating CA19-9 increases. These changes should also be carefully examined in patients with PC who are either being monitored for recurrence of disease or where changes in CA19-9 can impact treatment decisions during conventional chemotherapy or clinical trials. With the COVID-19 pandemic entering an endemic phase, physicians need to be aware of the transient elevations of CA19-9 due to COVID-19 vaccination or infection.

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Supplementary Materials

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Abbreviations used in this paper: **CA19-9, cancer antigen 19-9; COVID-19, coronavirus disease 2019; MRCP, magnetic resonance cholangiopancreatography; PC, pancreatic cancer; PCHRC, pancreatic cancer high-risk clinic**

Most current article

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Data and analytic methods are made available throughout the manuscript; however, no specific study materials will be made available to other researchers.

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