IgG4-related Autoimmune Pancreatitis Following mRNA-based COVID-19 Vaccination

Ankoor H Patel MD, Rajan Amin MD, Alexander T. Lalos MD

RUTGERS
Robert Wood Johnson Medical School

Introduction

IgG4-related disease (IgG4-RD) is a fibro-inflammatory disease that can affect multiple organs. Autoimmune pancreatitis type 1 is a manifestation of IgG4-related disease and can often mimic tumor-like masses. Autoimmune phenomena following COVID-19 mRNA vaccination are being increasingly reported. Currently, there are no cases in which IgG4-RD involving the hepatobiliary system have been reported following the COVID-19 vaccination. We present the first case of IgG4-RD and AIP type 1 to be associated with the mRNA-based COVID-19 vaccination.

Case Description

A 63-year-old African-American male was in his normal state until 2021. He received 2 doses of the mRNA-based COVID-19 vaccine in March/April 2021. In June, he presented to his PCP with complaints of fatigue and a rapid 20lb weight loss. He was diagnosed with diabetes mellitus (HgBA1C 10.9) and was started on metformin & repaglinide. However, his blood sugars remained uncontrolled. He denied any significant alcohol intake or history of illicit drugs, hepatotoxic medications, or liver disease. Physical exam was unremarkable.

In September, he was found to have liver enzyme abnormalities so repaglinide was stopped. However, he had worsening jaundice and developed pruritus. He was then referred to gastroenterology.

Lab Results

HgB 11.4 gm/dL
Thyroid studies normal.

ALT 154 unit/L
AST 86 unit/L
Alk phos 169 unit/L
Total Bilirubin 4.9 mg/dL
Direct Bilirubin 3.5 mg/dL
Hep B surface antigen, core antibody, & surface antibody negative
Hep C antibody was non-reactive.

IgG 1703 mg/dL (ref range: 600-1540 mg/dL)
IgG4 679.9 mg/dL (ref range: 4-86 mg/dL)
Ca 19-9 & CEA were normal.
Chromogranin A was within normal limits

Results

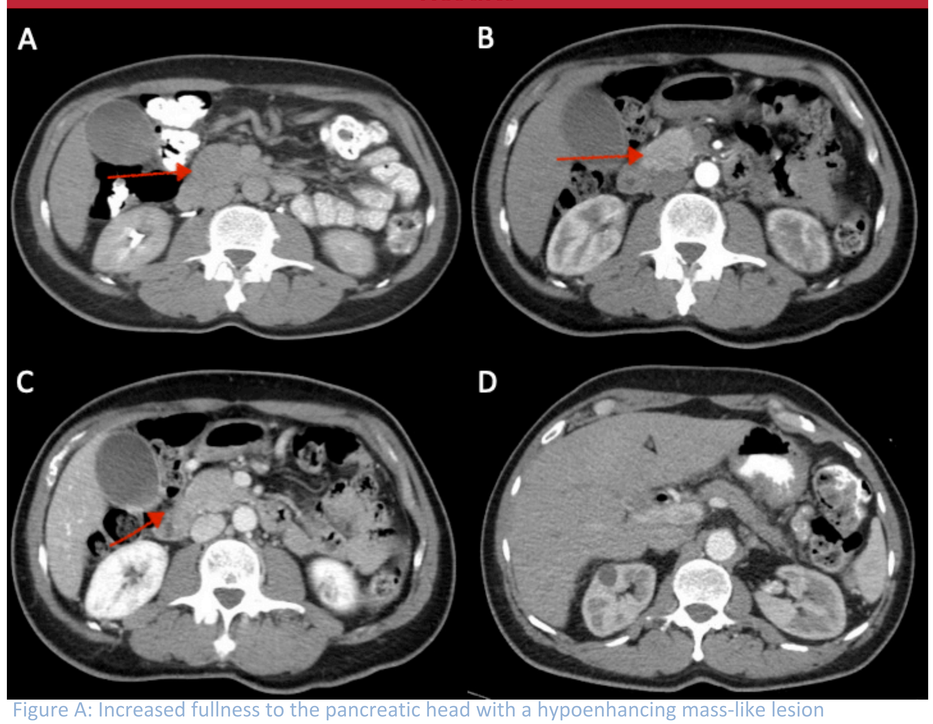

Figure A: Increased fullness to the pancreatic head with a hypoenhancing mass-like lesion measuring up to 3 cm.
Figure B, C: Hypervascular arterial enhancing pancreatic head mass measuring up to 3.6 x 2.6 x 5.5 cm in the largest dimensions

Contrast enhanced CT abdomen/pelvis revealed a hypervascular arterially enhancing pancreatic head mass measuring up to 5.5cm with moderate intrahepatic biliary dilatation and mild common bile duct dilatation to the pancreatic head.
A subsequent CT chest and neck was completed and did not demonstrate mass or adenopathy.
He underwent an ERCP with biliary stent placement as well as endoscopic ultrasound-guided pancreas biopsy. The biopsy specimen was diffusely positive for IgG4 but was “over-stained” and felt to be non-diagnostic. Liver biopsy was not obtained.

Diagnosis & Follow up

He was seen in our clinic at that time and given the absence of malignancy on the biopsy, normal Ca 19-9 and CEA levels, and the very elevated IgG4 level, a **diagnosis of IgG4-related autoimmune pancreatitis was strongly suspected**. He was **started on prednisone 40mg daily with a tapering schedule**. Within two weeks there was complete normalization of the liver enzymes.
Follow up imaging at six weeks demonstrated resolution of the pancreatic mass with continued normal liver transaminases with prednisone reduced to 15mg per day dosing. The patient felt well and had gained ten pounds. Biliary stent removal was planned.

Discussion

IgG4-RD is an uncommon, systemic autoimmune disease characterized by infiltration of IgG4-expressing plasma cells into involved organs resulting in chronic inflammation and fibrosis.

- Type I AIP is the most common of its organ-specific manifestations.
- Patients are typically in their 6^{th}-7^{th}, and are predominantly male
- Most common presentation is painless obstructive jaundice (up to 70% of patients with AIP) (1)

Patients will typically have significantly elevated titers of IgG (> 1800mg/dL) and its subset IgG4 (> 140 mg/dL). (2)

- IgG4 levels greater than 140 mg/dL were 86% sensitive and 90–96% specific for the diagnosis of AIP. (3, 4)
- IgG4 levels greater than two-fold of normal (> 280mg/dL) were only found in 1% of patients with pancreatic cancer and 53% in AIP. (5)

The patient had a normal blood sugar and LFT’s one year earlier. However, the patient developed insulin dependent diabetes shortly after the COVID-19 vaccination. Abnormalities in endocrine function of the pancreas and diabetes mellitus are seen up to 78% in patients with AIP. (10) Finally, when prednisone therapy was started there was a dramatic and complete response which further supports the diagnosis of IgG4 RD.

Autoimmunity linked to the mRNA-based COVID-19 vaccine has been reported.

- Several cases of autoimmune hepatitis with one case ending in fulminant liver failure requiring liver transplantation. (6)

Other vaccines, such as HPV, influenza, and HBV, have been suspected to trigger autoimmunity through molecular mimicry. (7)
Other studies have suggested that COVID-19 infection itself could trigger autoimmunity but this patient did not have the infection at any point to our knowledge.

Conclusion

Autoimmune phenomena following COVID-19 mRNA vaccination are being increasingly reported. We report the first case of IgG4-RD and AIP type 1 to be associated with the COVID-19 vaccine. Patients with new onset DM or cholestasis with or without signs of obstructive jaundice in the era of COVID-19 vaccination should be screened for IgG4-RD.

References

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