A Diagnostic Dilemma: Primary Sclerosing Cholangitis with High IgG4 Vs. IgG4-Related Sclerosing Cholangitis

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Background

Two etiologies of sclerosing cholangitis with overlapping features are IgG4-Related Sclerosing Cholangitis (IgG4-SC) and Primary Sclerosing Cholangitis with high IgG4 (PSC).

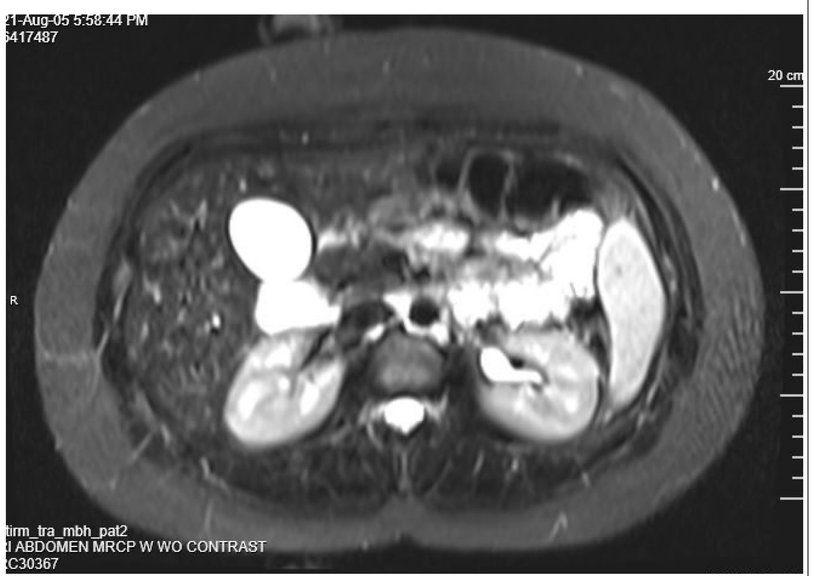
We present a case of a young female with overlap of features of both diseases, highlighting the diagnostic difficulty of delineating between the two pathologies.

Presentation/Clinical Course

A 25-year-old caucasian female with a medical history of diabetes and no previous pancreatic disease was incidentally found to have an AST and ALT in the low 200s, total bilirubin 2.6, and alkaline phosphatase of 1130 concerning for cholestatic obstruction on routine labs.

She was asymptomatic and not jaundiced at the time.

MRCP revealed a dilated common bile duct. The patient underwent ERCP/EUS demonstrating a common bile duct stricture . A plastic stent was placed, and cells for cytology/FISH analysis were unyielding for dysplasia malignancy.



Biopsies to evaluate the indeterminate stricture yielded IgG4+ plasma cells up to 14/HPF.

Based on the findings suspicious for IgG4-SC, she started prednisone therapy for one month.

Subsequent labs demonstrated mild improvement in alkaline phosphatase to 450, total bilirubin 0.2, and a normal IgG4 level but with persistent elevation of total IgG 1.5 times the upper limit of normal.

Repeat ERCP demonstrated resolution of the distal biliary stricture. She never developed abdominal pain, jaundice, weight changes or loss of appetite.

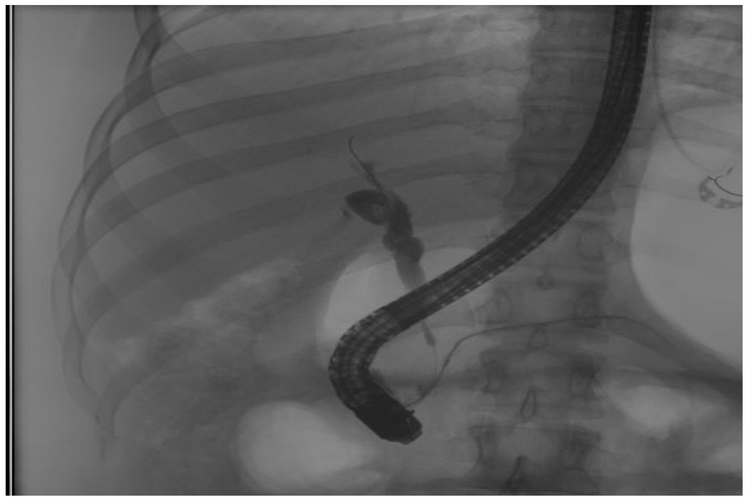
Imaging/Clinical Course

Six months later, LFTs began to uptrend and a third ERCP/EUS demonstrated new distal biliary stricture.

Biliary biopsies showed dense lymphoplasmacytic infiltrates and fibrosis with an average of 10 IgG4 positive plasma cells/HPF. Liver biopsies showed periductal fibrosis and a fibro-obliterative duct lesion.

Given the concern for PSC, colonoscopy was performed with biopsies showing mild crypt distortion, mild eosinophilia, and rare neutrophils in the lamina propria.

The patient remained asymptomatic throughout the disease course but had persistent biochemical hepatitis despite being on steroid therapy.



Discussion

In this case, the patient's epidemiologic, clinical, and histological factors were more consistent with PSC, and the decision was made to hold immunologic therapy.

Conversely, the mild biochemical and stricture steroid-responsiveness were initially more suggestive of IgG4-SC.

It is imperative to delineate between the two, as prognosis, treatment-responsiveness, and anticipated comorbidities differ.

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IgG4-SC VS. PSC

Category	IgG4-SC	PSC
Epidemiology	Most common in elderly men.	Slight male pre-dominance, most common in age 20-30 in western countries.
Presentation	Often present with jaundice, abdominal pain, and nausea. Often have extra-biliary manifestations consistent with IgG4-RD, such as: pancreatic masses, retroperitoneal fibrosis, kidney lesions, and lacrimal swelling.	Patients were diagnosed as having PSC with no evidence of any symptoms, but with an elevation in liver chemistries.
Comorbidity	38-72% of patients have concurrent Autoimmune Pancreatitis.	40-80% of patients have IBD.
Steroid responsiveness	Very responsive	Not steroid responsive
Laboratory data/Imaging	Shows elevated serum IgG4 concentration (≥135 mg/dL) Imaging Biliary tract imaging reveals diffuse or segmental narrowing of the intrahepatic and/or extrahepatic bile duct, associated with thickening of the bile duct wall.	Roughly 10-15% have elevated IgG levels. Imaging shows multiple segmental narrowing of the biliary tree i.e. "beaded" appearance.
Histology	Marked lymphocytic and plasmocytic infiltration and fibrosis Infiltration of IgG4-positive plasma cells (>10 cells per high power field) Storiform fibrosis and Obliterative phlebitis	Obliterative cholangitis with substantial periductular fibrosis, referred as "onion-skin fibrosis," is a typical finding, although this is found only in 20% to 40% of patients.
Management	Biologics, steroids, immunosuppressive therapies.	No medication has been approved to improve transplant free outcomes.
Prognosis	Not clearly defined but improved with treatment.	Transplant free, life expectancy from diagnosis is 12-21 years.

LITERATURE REVIEW

Tanaka A. IgG4-Related Sclerosing Cholangitis and Primary Sclerosing Cholangitis. Gut Liver. 2019 May 15;13(3):300-307. doi: 10.5009/gnl18085. PMID: 30205418; PMCID: PMC6529173..
Manganis CD, Chapman RW, Culver EL. Review of primary sclerosing cholangitis with increased IgG4 levels. World J Gastroenterol. 2020 Jun 21;26(23):3126-3144. doi: 10.3748/wjg.v26.i23.3126. PMID: 32684731; PMCID: PMC7336326.
Tanaka A. IgG4-Related Sclerosing Cholangitis and Primary Sclerosing Cholangitis. Gut Liver. 2019 May 15;13(3):300-307. doi: 10.5009/gnl18085. PMID: 30205418; PMCID: PMC6529173.