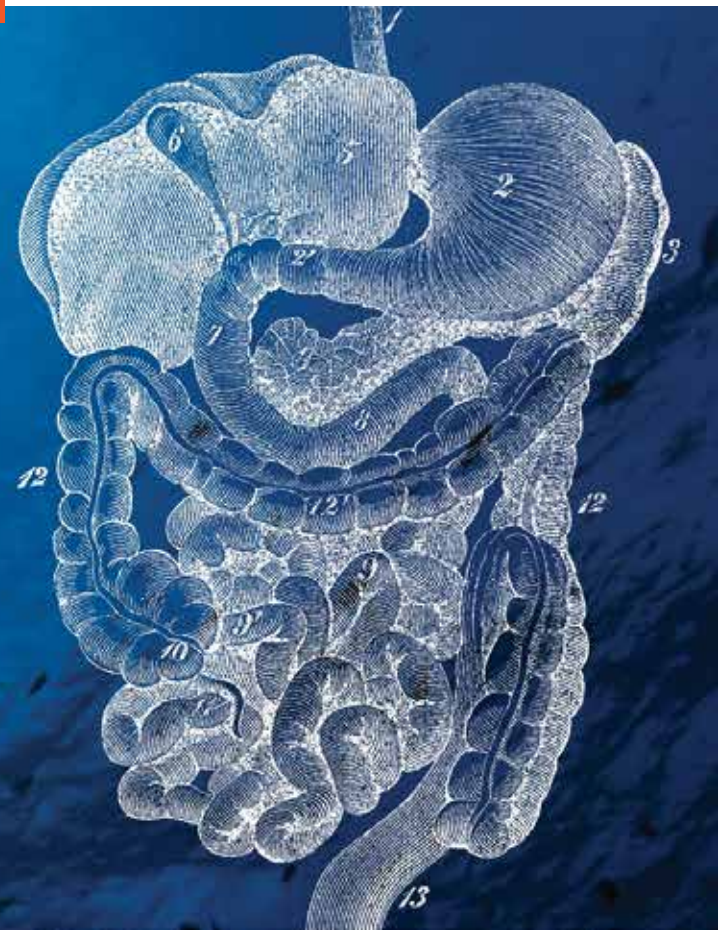
GUILD

Gastroenterology Updates • IBD • Liver Disease

GUILD CARIBBEAN
JANUARY 11-14, 2026
FAIRMONT EL SAN JUAN HOTEL
SAN JUAN, PUERTO RICO

Challenging Liver Cases



Led by Dr. F. Rodriguez Perez, MD
All Liver Faculty

Case #1

A 52-year-old woman is referred for US finding of steatosis and elevated liver enzymes.

- Labs: ALT 78 U/L, AST 68 U/L
- Alk phos normal, bilirubin normal, CK normal
- Platelets 180K
- A1c 7.9%
- LDL 118 mg/dL
- **Risk factors:** T2DM (8 years), BMI 34 kg/m^2), HT and dyslipidemia
- Medications: metformin, atorvastatin, lisinopril

- **Work-up for other causes of CLD are negative**
  - PEth 20 ng/dL

Noninvasive testing

- FIB-4: 2.1
- VCTE (FibroScan): 11.8 kPa and CAP: 330 dB/m

Diagnosis:
MASH with "at risk" fibrosis

What do you recommend?

- Focus on dietary changes and exercise for 6 months
- Refer for consideration of ESG
- Change from metformin to pioglitazone
- Vitamin E
- Semaglutide
- Resmetirom

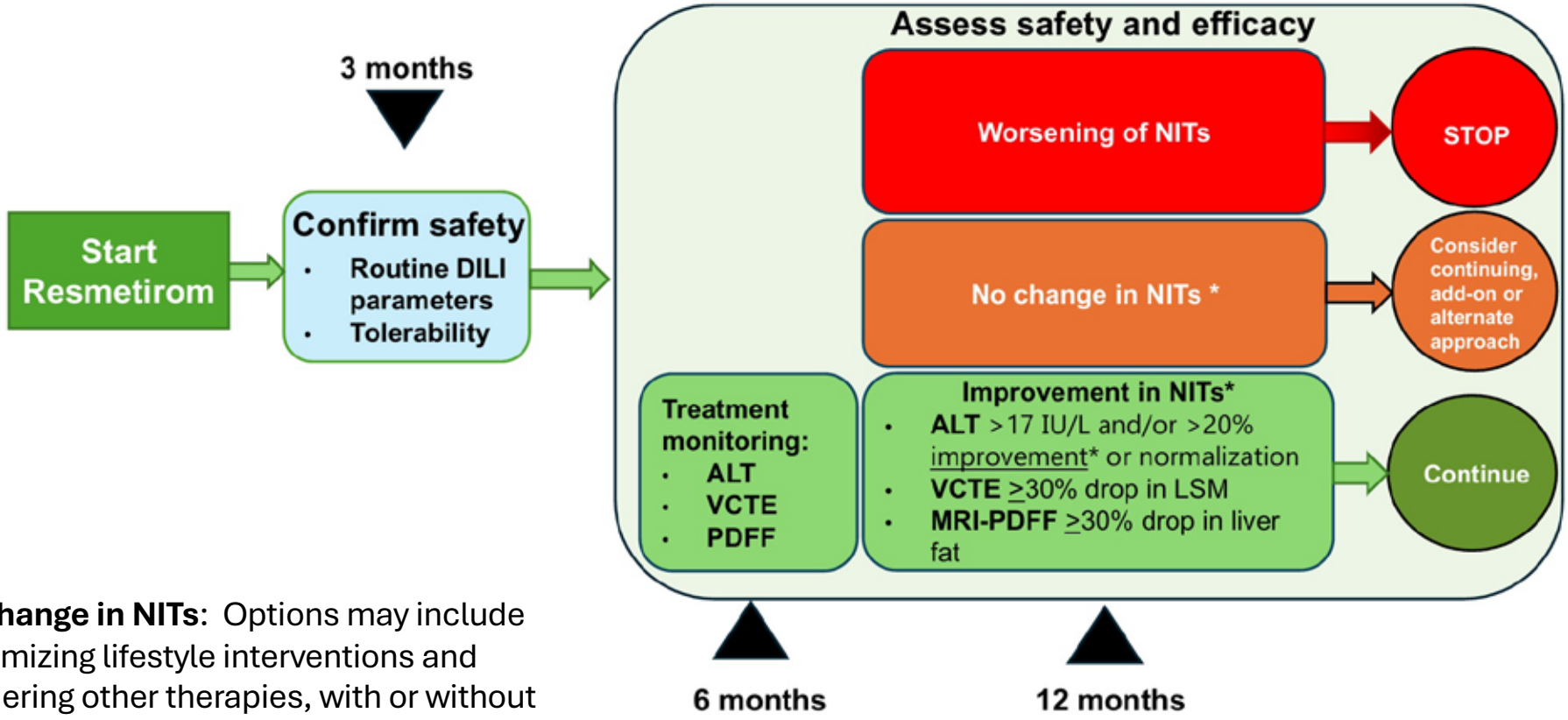
You refer to dietician and encourage her to join a gym. Start **resmetirom 80 mg daily.**

6 months later:

- Weight loss: 7%
- Intermittent diarrhea since start of treatment, tolerable
- ALT: 59 U/L (78), AST: 52 (68) U/L
- LDL: 82 mg/dL
- TSH: mildly suppressed, asymptomatic
- Repeat VCTE: LSM 10.9 kPa (11.8) and CAP 280 (330)

Continue, stop or change medication?

Assessment of Response to Resmetirom



If no change in NITs: Options may include re-optimizing lifestyle interventions and considering other therapies, with or without stopping resmetirom

Noureddin M, Clin Gastroenterol Hepat 2024

Key Take Aways:

Resmetirom side effects:

- GI symptoms (diarrhea most common), occas nausea
- Thyroid axis effects:
  - ↓ TSH (usually asymptomatic)
  - Monitor TSH and free T4
- Cardiac effects:
  - Mild increase in heart rate
- Lipids:
  - Typically reduces LDL and triglycerides (not increases)

On treatment monitoring:

- Month 3 – for tolerability
- Month 6– for early response
  - Improvements in ALT, lipids, and stiffness are expected early markers
  - Fibrosis regression takes longer
  - Mild TSH suppression without symptoms does not require discontinuation
- **Month 12 – decision time**

Case #2

- 40 year old white Hispanic female with history of elevated liver enzymes (cholestasis) documented for more than a year. No pruritus, no arthralgias.
- Lives in Mayaguez: west coast of Puerto Rico
- Has history of diabetes on metformin
- HTN on Losartan-low dose
- No toxic habits
- Some river bathing (very common in Puerto Rico)

FH: Grandmother and two aunts with “liver disease”. All died of non-hepatic etiologies

PH: BMI 29, no stigmata of CLD

Work-up done upon referral

- No medications other than those specified
- Negative AMA, ANA, ASMA
- Negative chronic viral hepatitis work up. Positive Hep A IgG.
- Normal iron and copper tests
- Negative schistosoma antibodies
- AST 68, ALT 72, Alkaline phosphatase 198
- US abdomen: fatty changes, normal gallbladder
- Fibroscan: LSM 5.3 kPa and CAP 298 dB/m

Next Steps?

Liver biopsy

- Minimal steatosis 5%
- Increased copper deposition in periportal hepatocytes
- No fibrosis
- Mild lymphocytic infiltrate
- No granulomas
- No periductal fibrosis
- No ductopenia
- No eosinophils

Not really helpful to establish a definite diagnosis


?
Now What?

Clinical course

- Woman with cholestasis but negative AMA test and non-diagnostic liver biopsy
- Empiric trial with ursodeoxycholic acid (12 mg/kg/day)
- Liver enzymes normalized in two months
- After one year the patient stopped ursodiol but liver enzymes(mainly ALKP) increased again
- Rechallenge with ursodiol led to normalization once again
- The patient has been followed every 6 months: enzymes and fibroscan have remained normal

Cholestasis in Puerto Rico

- Chart review of my clinic and another hepatology center in PR
- Out of 263 with autoimmune liver disease diagnosis:
  - 77 AIH
  - 118 PBC (AMA positive)
  - 68 AIH-PBC

  Nearly 32 % of population with cholestasis:
  AMA negative
  mostly women
  mild disease
  good response to ursodiol
  many from areas in West and North central cities of PR

AMA negative cholestasis in Hispanics from PR

- Consider genetic mutations associated to cholestasis
  - ABCB4 variants/PFIC3?
- Consider these genetic variants Hispanic patients migrating to different areas of US and who present with AMA negative cholestasis

Case 3:

- 32yoM with history of PVT, pancytopenia, esophageal varices referred for management
- Initial identification of PVT as GIB in Mexico – presenting w/ hematemesis 8 months prior. No history of abdominal surgery or trauma.
- Pancytopenia evaluated by hematologist -- BM biopsy normal, JAK2 negative, FV Leiden negative, anti phospholipid syndrome negative, PNH workup negative, slight deficiency of factor C and S activity likely secondary to a liver disease
- Medications: Nadolol, not currently on AC.
- Exam: central adiposity, no stigmata CLD, splenomegaly
- Work-up for causes of CLD largely negative

Labs:

- WBC 1.8, Hgb 14.3, Plt 40,
- albumin 4, ALP 76, ALT 48, AST 30, TB 1.2,
- BUN 21 creatinine 0.87, HbA1C 5.2, TG 68, TSH 0.96
- HBsAg neg, anti-HCV neg, HIV neg, ANA negative, IgG normal, ceruloplasmin and A1AT level normal, ferritin 9

Relevant data

- 4-phase CT scan:
  - Liver: Cirrhotic liver morphology with a mildly nodular contour and sequelae of portal hypertension including massive splenomegaly, extensive perigastric, gastric, esophageal, and paraesophageal varices.
  - Hepatic veins are patent with mild prominence of the IVC. Occlusive thrombus of the main portal vein, intrahepatic left portal veins, and SMV. Splenic vein is patent. Hepatic arterial anatomy is conventional.
  - No focal hepatic lesions or areas of suspicious arterial enhancement or venous/delayed washout.
- EGD: Esophageal varices, eradicated post banding. No gastric varices. Portal hypertensive gastropathy.

Next Steps?

PVT without cirrhosis

- Acquired hematologic disorders
  - Myeloproliferative syndromes
  - Antiphospholipid syndrome
  - PNH
- Inherited thrombophilia conditions
  - Factor V Leiden
  - Protein Cor S deficiency
  - ATIII deficiency
  - Factor II G20210A mutation
- Local factors or other systemic diseases
  - Bechet's' dz
  - Celiac dz
  - Obesity
  - Intraabdominal surgery (e.g. post bariatric surgery)
  - Blunt trauma
  - OCPs
  - Extrahepatic malignancy

PVT treatment options

- Thrombectomy/thrombolysis
- IR vascular procedures for portal vein revascularization
  - TIPS
  - Stents
- Anticoagulant therapy

- Factors influencing decision:
  - Chronicity
  - Extent and anatomy
  - Presence of cirrhosis and PHT
  - Symptoms
  - Response to or contraindication to AC
  - Transplant candidacy
  - Local expertise
  - Patient preference

IR Procedure: TIPS and stent placement

FINDINGS:

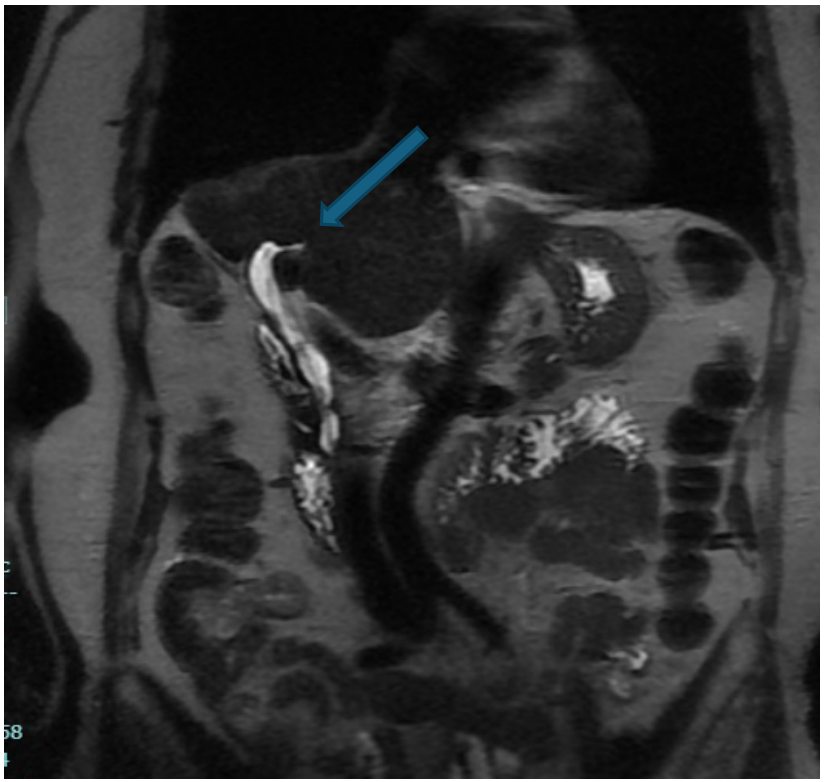
- Patent right hepatic vein by venography, suitable for TIPS creation.
- IVUS images demonstrate very small intrahepatic portal vein branches. Access needle advancement into a proximal right-sided portal vein branch is demonstrated.
- Initial splenic venogram demonstrates complete diversion of flow along the markedly enlarged coronary vein, which supplies extensive gastroesophageal varices. There is no hepatopetal portal venous flow.
- There is complete occlusion of the main portal vein and splenomesenteric venous confluence. There is overlying hilar and intrahepatic portal cavernous transformation.
- Following plug embolization, there is complete occlusion at the coronary vein trunk.
- Following TIPS creation and splenoportal venous stent extension/reconstruction, there is a widely patent splenoportal venous system with brisk flow through the TIPS into the IVC. No gastroesophageal varices are opacified.

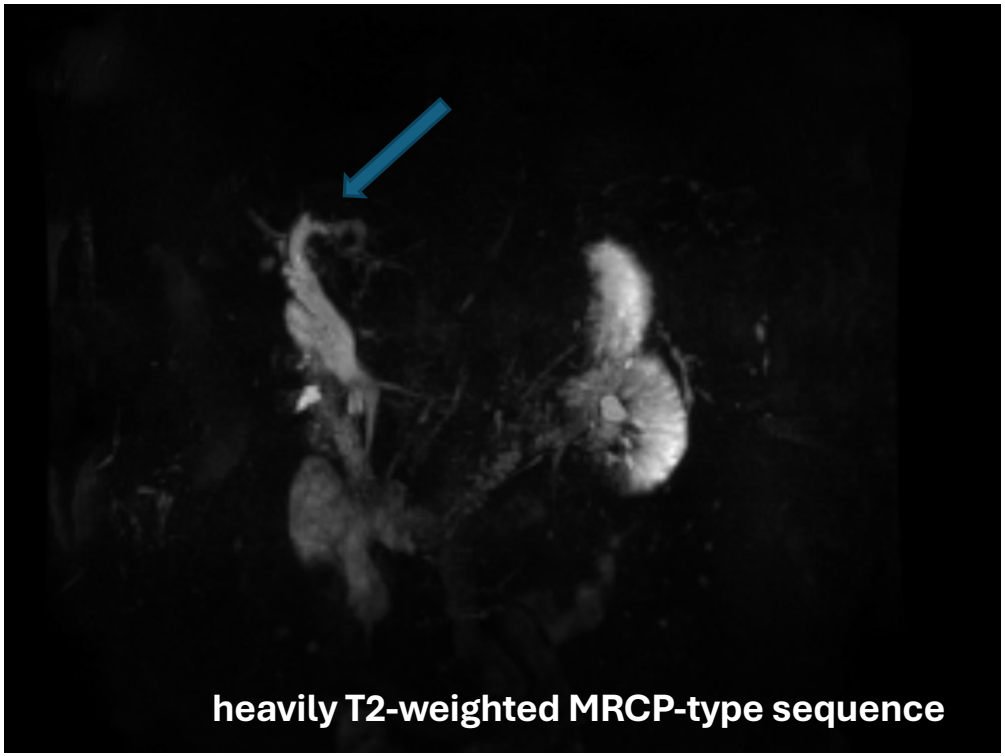
Case #4

- A 32-year-old man with a 16-year history of ulcerative colitis (moderate pancolitis, in remission) and 10-year history of PSC based on MRCP
- Presents with worsening pruritus and fatigue
- No new medications
  - Infliximab
  - Vitamin D
- PE: excoriations but otherwise normal

- **Laboratory Results**
- ALP: 620 IU/L (↑ from 400)
- GGT: 410 IU/L (↑ from 210)
- ALT: 95 IU/L (mild ↑ from 65)
- AST: 82 IU/L (mild ↑ from 60)
- Total bilirubin: 4.1 mg/dL (↑ from baseline 2.1)
- INR: 1.1
- CA 19-9: 45 U/mL (borderline elevated)

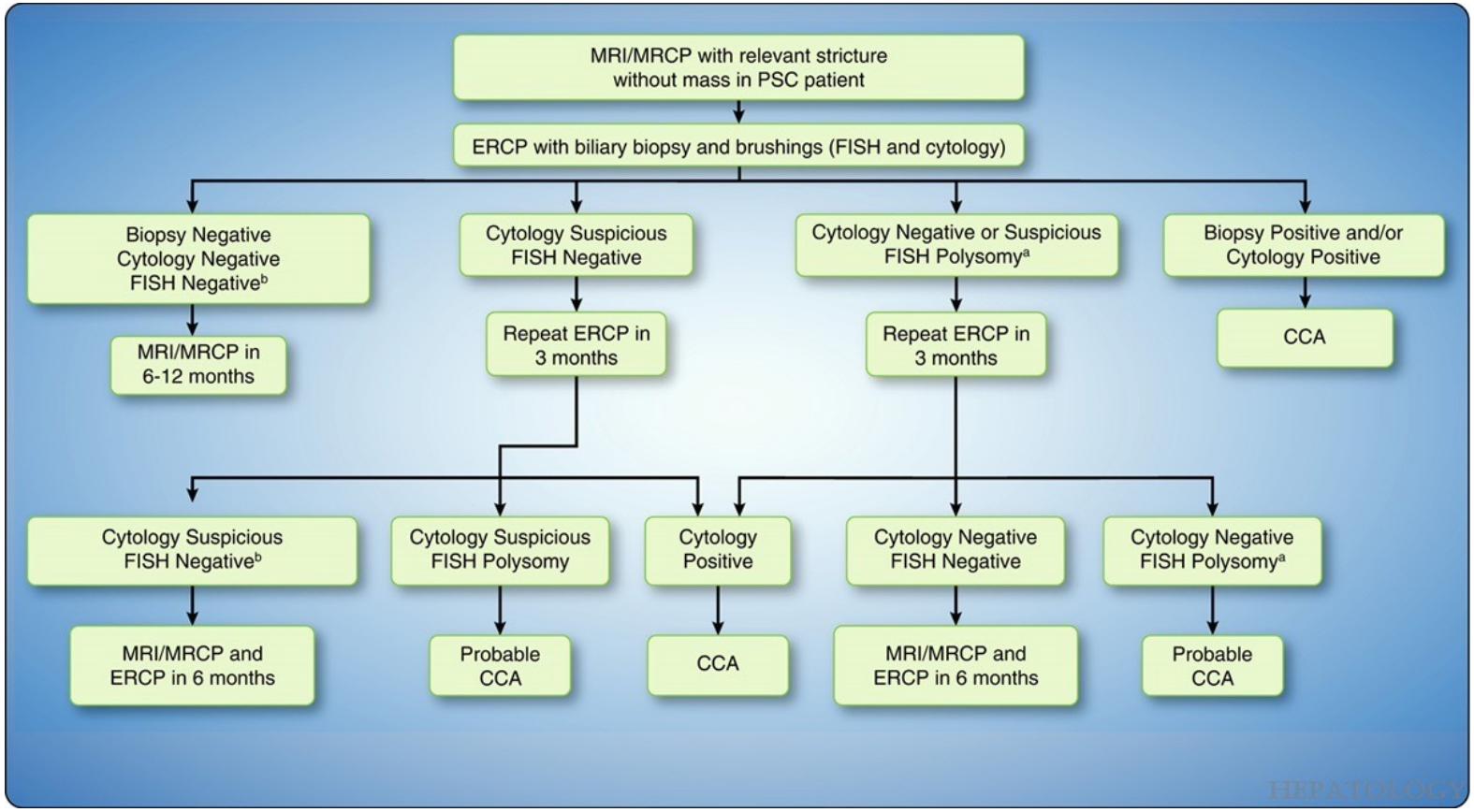
Repeat MRCP





L hepatic duct stricture, radiologic signs of cirrhosis

Approach to Stricture in PSC

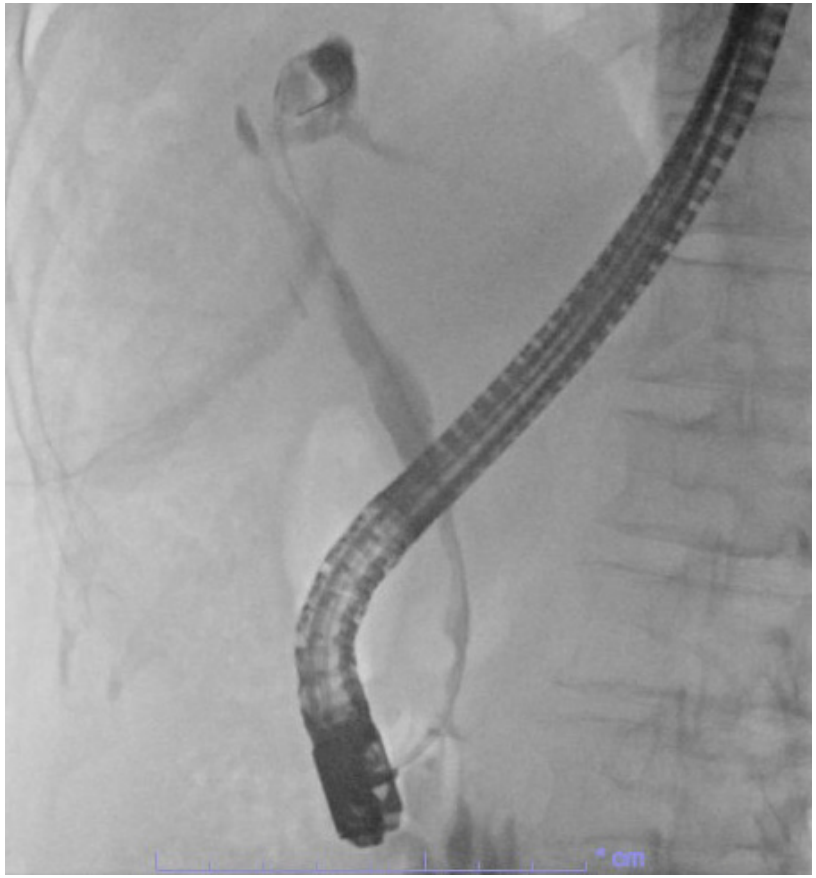


AASLD Guideline PSC 2022

Next Steps?

Follow-up

ERCP with stent placement

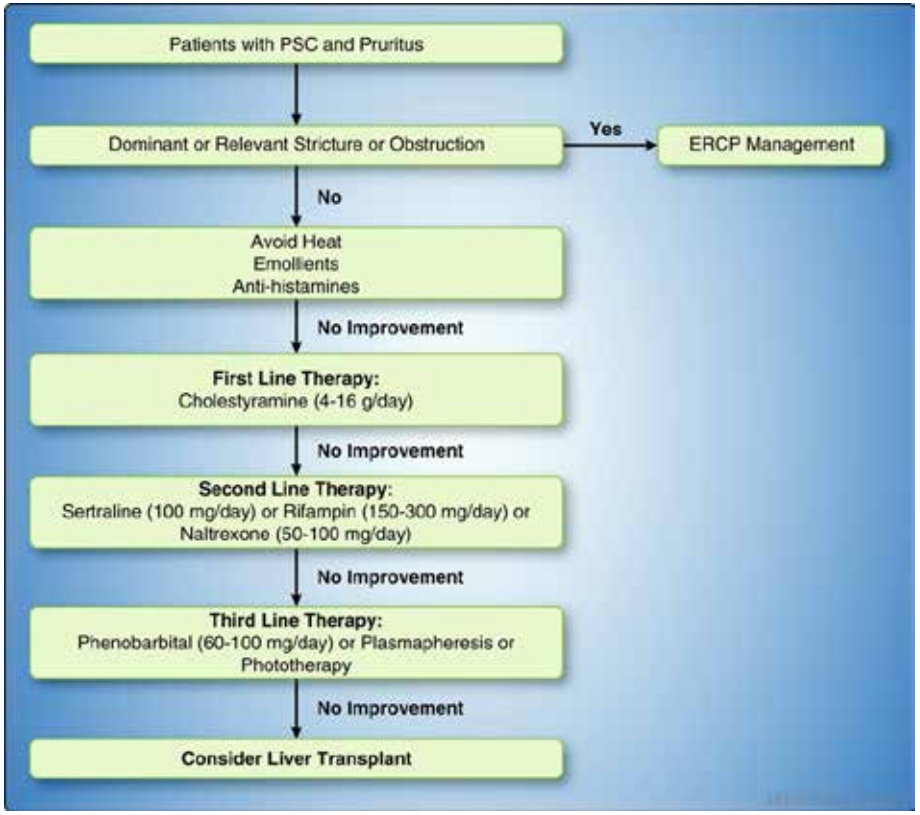


- Brushings – negative
- FISH: negative

- Repeat labs 1 month post-stent
- ALP: 454 IU/L (↓ from 620)
- GGT: 244 IU/L (↓ from 410)
- ALT: 75 IU/L (↓ from 95)
- AST: 61 IU/L (↓ from 82)
- Total bilirubin: 2.3 mg/dL (down from 4.1)
- INR: 1.1
- CA 19-9: 32 U/mL (prior 45)

- MELD 3.0 =12

What is best option for managing pruritus?



AASLD Guideline PSC 2022

2️⃣ **Rifampicin – Second line (if inadequate response)**

Dose: 150 mg daily → up to 300 mg twice daily

Monitoring: LFTs at baseline and periodically

Rationale:

Strong evidence for cholestatic pruritus

Reduces pruritogenic mediators (e.g., LPA)

3️⃣ **Third-line (if needed)**

Used if pruritus remains troublesome:

•**Naltrexone**

- 12.5–25 mg/day → up to 50 mg/day
- Warn about transient opioid withdrawal–like symptoms

•**Sertraline**

- 50–100 mg/day
- Helpful if sleep disturbance or mood symptoms coexist

✓ Either is appropriate if rifampicin fails or is contraindicated

Initial Data:

WBC 7.2, Hgb 14.4, plt 164, TP 7.1, albumin 4.2, INR 1.1

HBA1C 5.4, lipid panel normal

Lab View	2/12/2024 0:00	2/15/2023 0:00	2/8/2023 0:00	1/27/2023 0:00	5/12/2022 0:00	3/22/2022 0:00
ALT	50		44	44	19	26
AST	50 H		51 H	53 H	34	34

Today

Bilirubin Total	0.5	0.5	0.6		0.6 *	0.4 *
Alk Phos	70	70	77		72	70 *
ALT	125 * H	122 * H	112 * H		116 * H	102 * H
AST	94 H	93 H	93 H		102 H	90 * H

Case #5

- 74-year-old female referred for elevation in aminotransferases
- PMHx of HLD, HTN
- Feels well, no symptoms
- Non-contributory family history
- Medications
  - atorvastatin 10 mg (since ~2022)
  - cyclosporine 0.05% ophthalmic emulsion: years
  - Estradiol Patch 0.025 mg/24: years
  - hydrochlorothiazide-valsartan: years

PE: BMI=26, No stigmata CLD. Abdomen exam normal.

Work-up

- HBsAg neg, anti-HBc neg, anti-HCV neg
- ANA <1:80, ASMA (F-actin) <20, TTG IgA <1.0, iron sat 20%, ferritin 191, A1AT MM and level 147, IgG 1078, IgM 68

<u>MRI 4-phase</u>

- Liver: There are scattered hepatic lesions with imaging characteristics suggestive of hemangioma, essentially stable in size compared to prior study as follows:
  - -3.7 cm in the segment 7/8
  - -1.1 cm in segment 2
  - -4 mm segment 8
  - -6 mm in segment 5
- Spleen: No splenomegaly or mass.
- Pancreas: No mass or ductal dilatation

Next Steps?

Additional testing:

VCTE: Median Liver Stiffness: 5.6 KPa, 13% IQR; CAP: 267 dB/m

ALT	125 * H	122 * H	112 * H
AST	94 H	93 H	93 H
Bilirubin Direct			
CK Total	1,736 H	1,832 H	
Hemoglobin A1c			5.6 *
Est Avg Glucose (eAG)			114
LDH	351 H	338 H	

Aldolase	12.4 * H

Result Name	Result	Unit	Reference Value
High!! HMG-CoA Reductase Ab, S	148.7	CU	<20.0

ALT Elevation in Myopathies

- ALT can be elevated in significant muscle injury
- AST is present in liver as **cytosolic (20-40%) and mitochondrial** (60-80%) and ALT is present as **predominantly cytosolic** enzyme
- AST has shorter $t^{1/2}$ than ALT (14 vs 47 hrs)
- Both AST and ALT are distributed in other tissues but concentrations differ (decreasing order).
- AST: myocardium, skeletal muscle, kidney, pancreas, spleen, lung, and erythrocyte
- ALT: kidney, myocardium, skeletal muscle, pancreas, spleen, lung, and erythrocyte

- Anti-HMGCR myopathy is a form of **immune-mediated necrotizing myopathy (IMNM)** often linked to **statin exposure**
- **Anti-HMGCR antibodies** are identified through immunoassays (CIA or ELISA) and help diagnose autoimmune muscle disease, guiding therapy beyond statin discontinuation

Mohassei P, Muscle Nerve 2013

Case #6

- 46 year old male with history of MASLD and intermittently elevated AST/ALT.
- Obese -- but has achieved weight loss with diet and exercise
- DM – on metformin but now diet controlled
- Dyslipidemia – on statin

PAST HISTORY: T2 DM, HT, Dyslipidemia on statin; Chest pain and troponin increased post Moderna vaccination -- cath done and normal

FAMILY HISTORY: Mother: T2DM, Parkinson's disease, Alzheimer's disease; father CAD, stroke

SOCIAL HISTORY:

1 bottle wine per weekend – stopped with diagnosis of fatty liver
Born in India, in US 24 years

EXAM: BMI 28, No stigmata CLD, no hepatosplenomegaly

Work-up done by referring MD

- Cr 0.72, Glucose 116, creatinine 0.72, sodium 141, potassium 4.6, chloride 109, bicarb 24, total protein 7.6, albumin 5, total bilirubin 0.9, alkaline phosphatase 67, AST 46, ALT 60, PT 11.4.
- HBsAg negative, anti HCV negative, iron 116, iron saturation 26%, Ferritin 205, ceruloplasmin 10, and ANA negative, AMA < 20, anti actin antibody 3 (normal), A1 antitrypsin 107, phenotype MM,
- US abdomen -fatty change, liver 14.7 cm, PV patent with hepatopedal flow, no biliary dilatation, GB sludge and no stones.
- Fibroscan: LSM 10.5 kPa and CAP 188 dB/m

Additional Testing:

- Repeat labs confirm low ceruloplasmin and serum copper and mildly elevated urinary copper.
- Ceruloplasmin: 10 mg/dL Low
- Copper, 24-Hour Urine: 37 mcg/24hr High
- Serum copper, 41 mcg/dL (normal 70.0-140.0)
- Coombs test negative
- K-F rings not seen
- Genetic testing for APTB7 POSITIVE


What do you recommend?

Liver biopsy

- LIVER, CORE BIOPSY
  - Bridging fibrosis and early cirrhosis (Stage 3-4)
  - Minimal (approximately 5-10%) steatosis
  - Mild portal/ septal inflammation present
  - No hemosiderin deposition seen

- **Addendum:**
  Quantitative copper performed at Mayo clinic on FFPE tissue reports 461 mcg/g dry weight (High). This finding is suggestive of Wilson disease.

Trientine therapy initiated

Consider Alternative Diagnosis in SLD

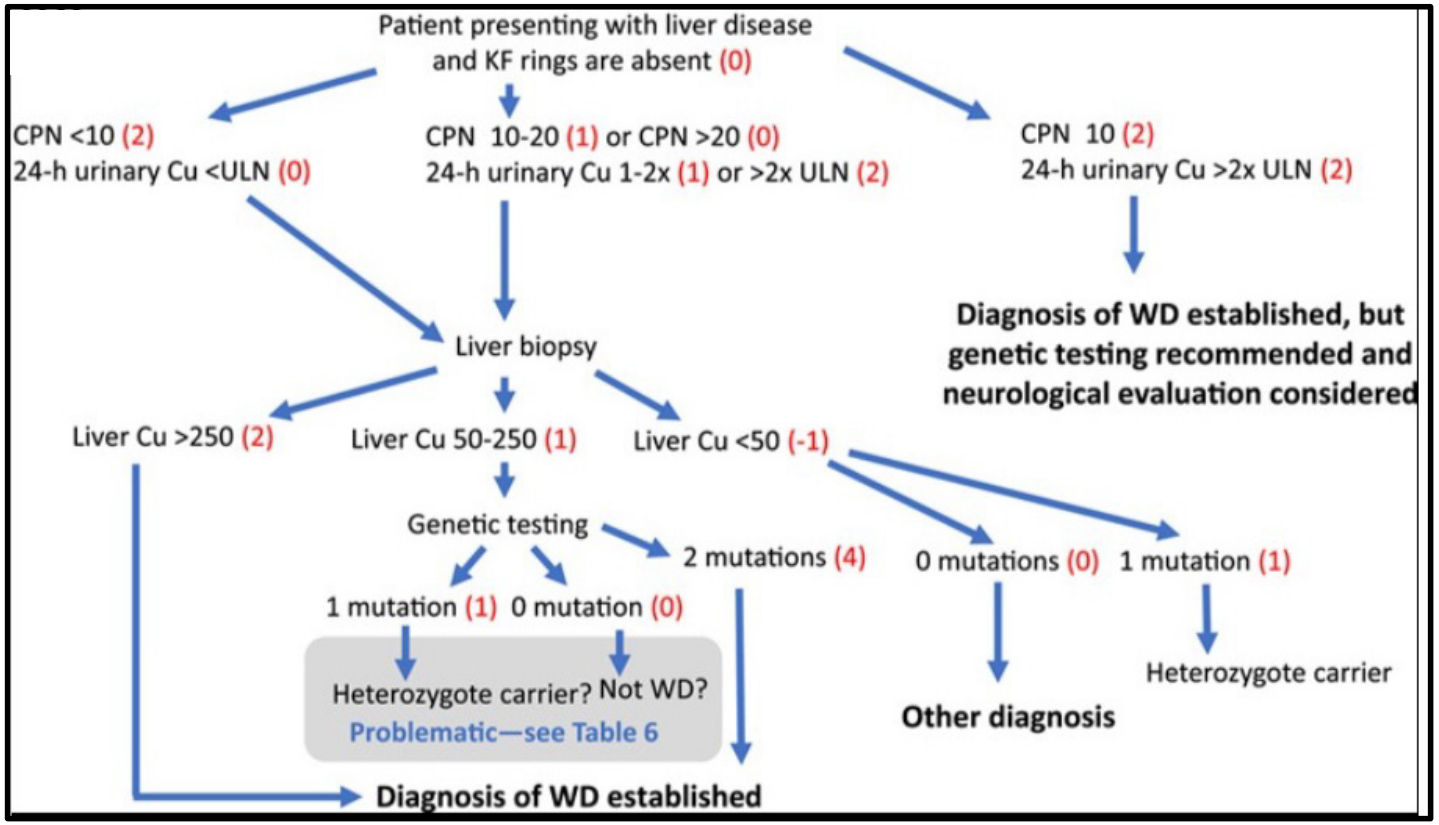
TABLE 2 - When to consider testing for less common causes of hepatic steatosis and steatohepatitis

Condition	Clinical scenario	Diagnostic test	Treatment
Hypobetalipoproteinemia	Low LDL, low triglycerides, fat malabsorption	ApoB level, genetic testing (MTTP, PCSK-9)	Low-fat diet, fat-soluble vitamin supplementation
LAL deficiency	Markedly elevated LDL-C and low HDL-C, elevated triglycerides, xanthelasma, hypersplenism, advanced fibrosis in young age, predominately microvesicular steatosis on liver biopsy	Enzyme assay, genetic testing	LAL replacement
Nutrient deficiency (eg, carnitine, choline)	Anorexia, short bowel, bypass surgeries	Nutrient levels	Supplementation
Wilson disease	Younger age, neuropsychiatric symptoms, low alkaline phosphatase, low ceruloplasmin	24-h urine copper; quantitative copper on liver biopsy	Chelation
Celiac disease	Iron deficiency, abdominal pain, bloating, vitamin D deficiency, bone loss, diarrhea, dermatitis herpetiformis	Tissue transglutaminase IgA, duodenal biopsy	Gluten-free diet

Abbreviations: ApoB, apolipoprotein B; HDL-C, high-density lipoprotein cholesterol; IgA, immunoglobulin A; LAL, lysosomal acid lipase; LDL-C, LDL cholesterol.

AASLD MASLD Practice Guidelines 2023

Diagnostic Algorithm for WD (if no K-F rings)



Numbers in parentheses indicate corresponding Leipzig score, where a **sum ≥4 indicates that WD is highly likely.**

AASLD Practice Guideline 2022