

## INTRODUCTION

### Liver Transplantation:

- Hepatitis C infection is the most common indication for liver transplantation in the U.S.
- HCV infection of the liver allograft occurs within hours from circulating virions.
  - Serum RNA levels are observed in the first several weeks.
  - Acute hepatitis occurs in 2-6 months.
  - Chronic hepatitis occurs in 3-9 months.

**\*\*\*Persistence of HCV infection is the rule after transplantation due to immune suppression.**

### Chronic recurrent HCV infection post transplantation

- There are four distinct patterns of recurrent chronic HCV in the liver allograft.
  - Usual chronic HCV (>70%)
  - Fibrosing Cholestatic Hepatitis C (5-10%)
  - Plasma cell-rich HCV
  - HCV overlapping with rejection or autoimmune hepatitis

## CASE PRESENTATION

### History:

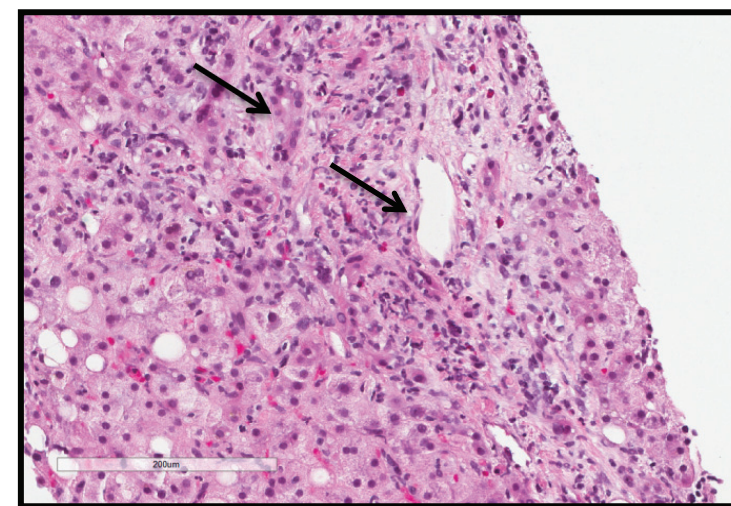
- 54 year-old woman with a history of chronic HCV infection complicated by cirrhosis and hepatocellular carcinoma.
- Liver transplantation (August 2014) from a CMV+, HCV+ donor.
- Post-transplant liver biopsy (11/11/13) showed recurrent HCV with mild activity (grade 2/4) and periportal fibrosis (stage 2/4).
- On January 19, 2014 presented with worsening malaise, fatigue, and jaundice.

### Physical Exam and Labs

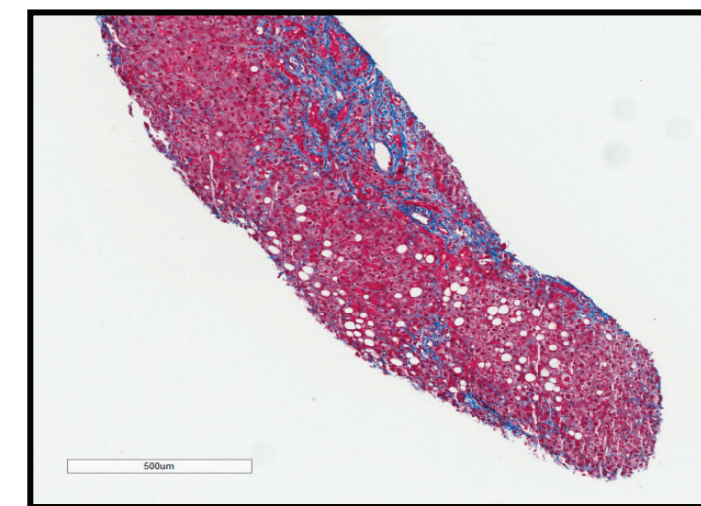
- Afebrile, lethargic, jaundiced with scleral icterus
- Hepatic Function Tests (1/21/14) :
 

Albumin:	2.6 mg/dL	(normal 3.5-5)
ALP:	602 U/L	(normal 30-120)
AST:	46 U/L	(normal 0-35)
ALT:	128 U/L	(normal 4-36)
Bilirubin:	15.6 mg/dL	(normal 0.3-1)
Direct bilirubin:	14.1 mg/dL	(normal 0.1-0.3)
- HCV Viral Load (1/20/14): 854,000 IU/mL

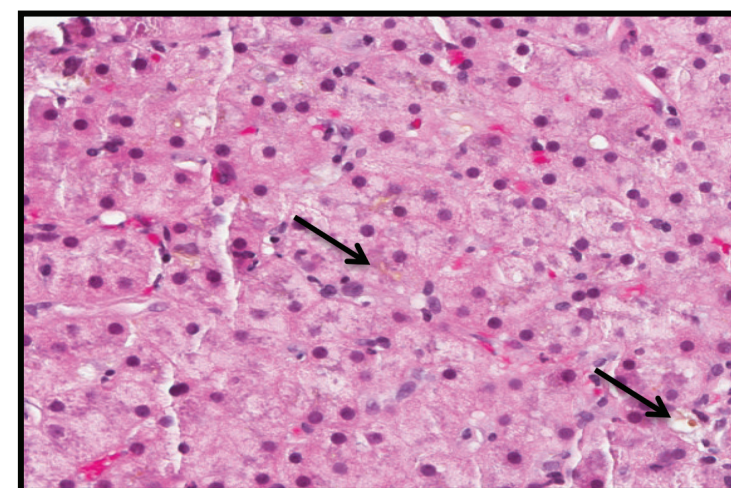
## Transjugular Liver Biopsy (1/24/14)



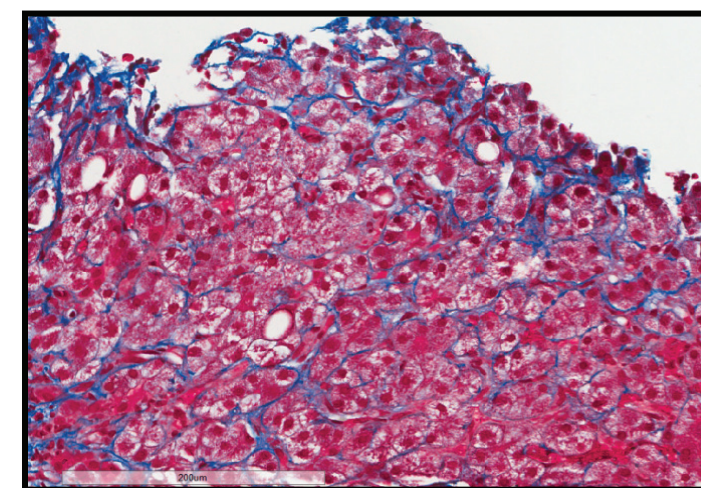
Portal tracts with ductular reaction and mild mixed inflammation; bile duct injury mediated by lymphocytes; no evidence of endotheliitis



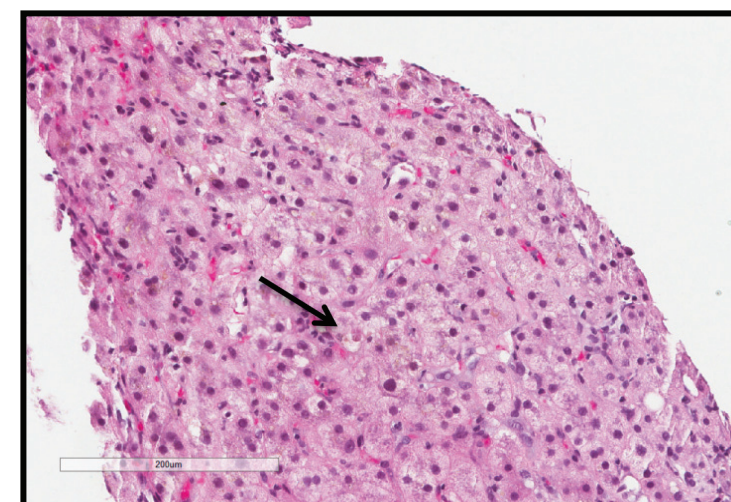
Bridging fibrosis to cirrhosis (stage 3-4 of 4)



Canaliculal and hepatocellular cholestasis



Pericellular (chicken-wire) fibrosis



Prominent lobular activity with apoptosis, hepatocyte feathery degeneration

### Diagnosis

- Fibrosing cholestatic hepatitis, Batts and Ludwig Grade 3 of 4, stage 3-4 of 4.

### Hospital Course:

Patient was treated with sofosbuvir and ribavirin (1/24/14) however suffered acute kidney injury. Medications discontinued (2/4/14).

HCV Viral Load (1/27/14) : 2340 IU/mL

### Repeat Biopsy (2/24/14)

Persistent canaliculal/hepatocellular cholestasis and ductular reaction. No endotheliitis. Minimal lobular activity. Bridging fibrosis to early cirrhosis (stage 3-4/4).

## FIBROSING CHOLESTATIC HEPATITIS C

- A rare and severe form of recurrent chronic Hepatitis C which presents within 1 year post-liver transplantation.
- Distinctive characteristics:
  - Rapidly progressive with high rates of graft loss and mortality within the first year of diagnosis.
  - Massive HCV RNA levels in the peripheral circulation.

### Risk Factors

- Over-immunosuppression
  - High dose cytotoxic therapy, HIV, other solid organ transplant
- High MELD score
- Older donor age

### Histology

- Prominent "ductular reaction" resembling biliary obstruction
- Cholestasis
- Hepatocyte feathery degeneration with lobular disarray
- Sinusoidal/pericellular fibrosis

### Criteria for Diagnosis

- At least ¾ of the characteristic histological features
- Timeframe of >1 month after liver transplantation

### Prognosis

- Mean survival time: 8 months before death or re-transplantation

### Treatment

- Successful treatment with conventional HCV therapy is rare.
- Sofosbuvir and simeprevir are FDA-approved only for chronic HCV infection in native livers but provide an avenue for future study in transplant patients.

## REFERENCES

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- 6.) Verna E.C., Abdelmessih R., Salomao M.A., et al. Cholestatic hepatitis C following liver transplantation: An outcome-based histological definition, clinical predictors, and prognosis. *Liver Transplantation*. 2013; 19 (1): 78-88.

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