San Francisco Hep B Free - Bay Area ECHO Notes

Session 14

January 16, 2022

I. Didactic Presentation: Hepatitis B Related Liver Cancer (Dr. Jennifer Guy, Director of the Liver Cancer Program, Transplant Hepatologist, California Pacific Medical Center) - presentation can be found at https://www.sfhepbfree.org/echo-program Password: Echo2020

II. Case Presentation: Dr. Catherine Moizeau - Clinician at Sacramento Community Clinic and Shingle Springs Health and Wellness

Case summary:

30 year old Vietnamese immigrant with eAg negative, eAb positive chronic HBV, on antivirals since age 19, currently TAF. HBV DNA 1 log (from <10 to 22 IU/ML), ALT range 66-141. HCV Ab negative, Delta Ab negative. HBV in mother, who is treated with NUC.

Underlying diabetes, on semaglutide and metformin, as well as dyslipidemia and obesity present with BMI 28.3 kg/m2. Also on oral contraceptive.

Liver biopsy July 2021 showed NASH: severe steatosis (80-90%, grade 3 of 3), mild-moderate inflammation (lymphocytes and neutrophils, grade 2 of 3) and ballooning (grade 1 of 2); bridging fibrosis was present (F3 of 4). US elastography also reported F3.

Clinical Questions and Responses

Q. What present and future steps can be taken to prevent further progression of liver disease?

Recommendations from Project ECHO panel:

Dr. Amy Tang – Primary Care (North East Medical Services)

Dr. Will Holt - Hepatology (Sutter Health)

Dr. Frank Trinh – Infectious Disease (San Mateo Medical Center)

Dr. Anita Chang – Primary Care (Asian Health Services)

NASH is the dominant disease here; the changes on biopsy are unlikely related to HBV given near-complete viral suppression as well as underlying risk factors for NASH and high NAFLD Activity Score on biopsy (NAS is 6 out of 8). Weight loss is the mainstay of treatment for NASH and this patient has obesity with BMI >27.5 kg/m2, which defines obesity in Asians.

Weight loss in NASH yields increasing benefit at several thresholds:

- 3% weight loss (5.1 pounds) associated with lower ALT
- 5% weight loss (8.5 pounds) associated with decrease in steatosis
- 7% weight loss (11.9 pounds) associated with NASH resolution
- 10% weight loss (17 pounds) associated with fibrosis regression

This patient started at 170 pounds and has already lost 6% of body weight – the liver biopsy was done prior to weight loss. She should be encouraged to lose an additional 7 pounds or more and aim for under 150 pounds – a rounder number that would represent a total of nearly 12% body weight loss (and bring her BMI to 26.5 kg/m2). The alarming degree of liver fibrosis at such a young age makes this degree of weight loss urgent – she is at risk of progression to cirrhosis if this does not happen in a period of months to years. It is likely that she has a genetic predisposition to rapid progression of liver disease (ie, PNPLA3 mutation) but there is no consensus recommendation to check for this mutation as it will not change clinical management.

Referral to hepatology is reasonable given underlying advanced fibrosis – both for higher level of care and to reinforce the message to the patient that this is a very serious condition. Our panel agrees with annual liver cancer screening with ultrasound and AFP – guidelines do not explicitly recommend this in noncirrhotic NASH, but bridging fibrosis is associated with an increased risk of HCC, even if not as high as in cirrhosis. (We would recommend annual HCC surveillance for this patient anyway based on chronic HBV infection, though this is also not explicitly laid out in the AASLD practice guidelines, given her female gender and age <50.)

Weight loss surgery should be discussed in patients with NASH and significant fibrosis who cannot lose weight. Pioglitazone, Vitamin E and GLP-1 agonists have shown improvement in NASH in histology in high-quality RCT's; we recommend semaglutide in patients like this and note that the patient is already on it – may even have already seen weight loss from it. Pioglitazone can cause adverse reactions including weight gain, and Vitamin E was not studied in diabetic patients.

Hepatology consultation would yield additional serologic workup, if not already done (alpha-1 phenotype, anti-actin antibody, ferritin + iron saturation, ceruloplasmin) as well as repeating a social history to screen for alcohol intake. This patient should abstain completely from alcohol, if not already doing so.

Based on the biopsy report and case presentation, the panel would not add a second antiviral medication to lower HBV DNA to 'undetectable' but hepatology referral would likely result in multidisciplinary review of biopsy to ensure HBV activity is not strongly suspected. However, if patient is able to get weight under 150 pounds and a convincing pattern of ALT improvement is not seen, would consider repeating biopsy or adding a second antiviral. Given that there are 2 chronic liver diseases present, threshold to repeat liver biopsy before making major clinical decisions should be low.

The fact that US elastography and liver biopsy were concordant is useful: if ALT falls with weight loss and HBV replication remains largely suppressed, would repeat elastography to look for expected improvement in liver stiffness. If improved, would use elastography every 1-3 years to monitor fibrosis with referral for liver biopsy if this test ever suggests regression back to F3 or progression to F4. If ALT falls with weight loss but elastography does not improve – allowing for up to 6-12 months of lag – would also consider repeating biopsy.