Case Examples of DILI Superimposed on NASH

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Liver Forum Histology Series Session 5
Causality Assessment and the Role of Liver Biopsy as Part of the Evaluation of Suspected DILI in NASH Clinical Trials
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Case 1

• 43 Male with melanoma, previously treated with IFN alpha and surgery
• Received 3 cycles of a novel, first-in-human, monoclonal anti-CTLA4 (yet to be named ipilimumab)
• Virology and serology at event:
  • Anti HAV-IgM (-), anti-HCV (-), anti-HBsAg (-)
  • ANA 2.4EU (+), ASMA, AMA and anti-LKM (-)
• Obesity, diabetes

Biochemical Data at Time of Event

Relative Days from Time 0
(defined as 1st time ALT>5x ULN)

-75 -50 -25 0 25 50 75 100 125 150

ALT/ULN
AST/ULN
AP/ULN
tBili
Case 2

- 62 F with juvenile rheumatoid arthritis with a long and varied medication history for controlling symptoms, currently on tocilizumab and methotrexate (4-5 years on this regimen)
- Diabetic, not obese (BMI 23)
- Stopped tocilizumab prior to shoulder surgery, after restarting, aminotransferases rose (next slide)
- ANA (+) at 1:160, ASMA, AMA negative, IgG normal
Time course of liver tests, interventions

- **Tocilizumab**: q2 wks, q1 wk
- **Biopsy**: q1 wk
- **Surgery**: q2 wks
- **Steroids**: q1 wk

Liver tests:
- ALT
- Alk Phos
- Bilirubin

Timeline:
- 1/15/2017
- 4/25/2017
- 8/3/2017
- 11/11/2017
- 2/19/2018
- 5/30/2018
- 9/7/2018
Case 3

- 46 F, morbid obesity, s/p gastric bypass 2 yrs prior
- Initially weight, but regained 50-75 lbs
- Took supplements marketed for weight loss, including Kava Kava
- Developed cholestatic elevations in liver enzymes, with jaundice
- Stopped supplements and recovered, but restarted Kava Kava about 2 months later, with recurrence of jaundice
- Biopsies after both events
Take Home Points

• It is possible to diagnose DILI in the presence of underlying steatohepatitis

• Pathologist should have a good understanding of the spectrum of expected injury in NASH

• If pre-treatment biopsies are available, they should be reviewed at the same time

• The pathologist should take advantage of all of the information known at the time of the biopsy