GI Workshop
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Liver Function Tests

CASE #1

Application

- 52 year old female, non-smoker, born in the US
- Vice president of a marketing firm
- Applying for $1, 000,000 (US$) with waiver of premium

Insurance exam

- 5’3”, 165 lbs. (160 cm, 75 kg), BMI 29.2
- BP 128/80 Pulse 68
- Family history: father died of prostate cancer at age 75
- Total cholesterol 182 mg/dl (4.71 mmol/L), HDL 48 mg/dl (1.24 mmol/L)
- Glucose normal
- ALT elevated at 75 U/L (1.7 x normal), GGT and AST normal
- No reflex testing performed
- Urinalysis: within normal limits; negative for cotinine/nicotine

Liver Function Tests

Medical history

- Records dated back to 2018. Had been followed for "prehypertension" and "borderline cholesterol".
- Told to exercise more and watch her diet – initially not put on any medications.
- Prior liver tests were normal
- Total cholesterol 256 mg/dl (6.62 mmol/L), HDL 44 mg/dl (1.14 mmol/L)
- She was begun on atorvastatin in 2021 .
- She has remained asymptomatic

Liver Function Tests

Questions

- What is the likely cause(s) of the ALT elevation?
- Would reflex testing with an alcohol marker or hepatitis studies likely be helpful?
- Which would be more helpful?
- How would you assess the mortality risk relative to the elevated ALT?
- Would a normal reflex test(s) affect your mortality assessment?
- Would the assessment change if the applicant had entered the US from Korea 10 years ago?
- Would the risk change in the original case if the ALT was low normal at 8 U/L?

Liver Function Tests

Alternate Scenario

- GGT elevated at 75 U/L (1.7 x normal), ALT and AST normal
- Other details are the same

Questions

- What is the likely cause(s) of the GGT elevation?
- Would reflex testing with an alcohol marker or hepatitis studies likely be helpful?
- Which would be more helpful?
- How would you assess the mortality risk related to the elevated GGT?
- Would the risk increase if the GGT was 3 times normal (135 U/L)?
- Would the probability of a positive alcohol marker change with this degree of elevation?
- Would the risk change if the HDL was 90 mg/dl (2.33 mmol/L)
- Would a normal alcohol marker reduce the mortality risk?
- Is there any risk with a GGT at the very low end of the normal range?

Liver Function Tests

Alternate Scenario

- ALT is elevated at 126 U/L (2.8 times normal) and AST is elevated at 53 U/L (1.6 times normal), GGT is normal
- Other details are the same

Questions

- What is the likely cause(s) of the elevations?
- Would reflex testing with an alcohol marker or hepatitis studies likely be helpful?
- Which would be more helpful?
- How would you assess the mortality risk related to the abnormal liver tests?
- Would the risk change if the AST was 109 U/L (3.3 times normal) and ALT was 72 U/L (1.6 times normal)? If so, why?
- Would the probability of a positive alcohol marker change?

Liver Function Tests

Alternate Scenario

- GGT is elevated at 158 U/L (3.5 times normal), ALT is elevated at 108 U/L (2.4 times normal) and AST is elevated at 75 U/L (2.5 times normal)

Questions

- What is the likely cause(s) of the elevations?
- Would reflex testing with an alcohol marker or hepatitis studies likely be helpful? Which would be more helpful?
- How would you assess the mortality risk related to the abnormal liver tests?
- Would your assessment change with any of the following additional scenarios?
  - Build is now 5'8", 270 lbs. (173 cm, 122.7 kg)
  - Alkaline phosphatase is 255 U/L (2.04 times normal)
  - Bilirubin is 2.8 mg/dl (42.8 umol/L)
  - Serum albumin 3.2 mg/dl (32 g/L)
  - Applicant sees a gastroenterologist who orders an anti-smooth muscle antibody, anti-mitochondrial antibody, ceruloplasmin level, anti-nuclear antibody (ANA), serum ferritin, iron saturation, alpha 1- antitrypsin level, all of which are normal.

Hepatitis B

Case #2

- 38 year old female homemaker, current smoker
- Born and raised in Taiwan, lives in the United States
- Applicant denies alcohol use
- Applying for 150,000 USD term life (convertible to whole of life without underwriting in first 10 years)

Insurance Para-medical

- 5’5” (165 cm), 145 lbs. (65.9 kgs), BP 142/84 , pulse 70
- Family history: father died of hepatocellular cancer age 60, mother had MI at 62, died of CHF at age 71, brother had cirrhosis; other brothers and sisters in good health
- Total cholesterol 198 mg/dl (5.12 mmol/L), HDL 50 mg/dl (1.29 mmol/L), urinalysis normal, positive for cotinine/nicotine
- ALT 122 U/L (2.7 x normal), AST 77 U/L (2.3 x normal), GGT, alkaline phosphatase and bilirubin are all normal
- Hepatitis B surface antigen, hepatitis B core antibody (total) and hepatitis B e antigen are all positive, hepatitis B surface antibody is negative

Hepatitis B

Medical History

- Applicant was diagnosed with hepatitis B in 2012
- Her liver enzymes were initially normal but have been elevated for at least the past 3 years
- She was treated with interferon in 2018 but did not tolerate it
- Her last viral DNA level was 550,000 IU/ml
- The viral genotype was C

Questions

- How would you assess the mortality risk?
- What are the key prognostic factors?
- Are there other test results you would be interested in reviewing?
- Would the mortality risk change if this were a man and not a woman?
- Would the mortality risk change if the e antigen was negative and the viral DNA was still elevated at 550,000 IU/ml?
- How would the presence of a Basal Core Promoter mutation affect the risk?

Hepatitis B

Alternate Scenario

- Applicant is a known hepatitis B carrier since 2012
- Her ALT and AST readings have been consistently normal
- Viral DNA levels have been followed regularly with the most recent value 6750 IU/ml
- Regular follow-up with alpha fetoprotein levels and abdominal ultrasound examinations of the liver have been normal
- Hepatitis B surface antigen, hepatitis B core antibody (total) and the hepatitis B e antibody are positive. The hepatitis B surface antibody and e antigen are negative

Questions

- What are the key prognostic factors?
- Is there a risk of reversion to hepatitis e antigen positive status?
- If the applicant was found to have a Pre Core mutation how would it affect the mortality risk?
- How would you assess the mortality risk?

Hepatitis B

Alternate Scenario

- Applicant was diagnosed with hepatitis B in June, 2019
- ALT and AST were initially elevated at 2-3 x normal
- Applicant was started on entecavir (Baraclude) in December, 2019 and has continued to take the medication regularly
- Viral DNA levels became undetectable after starting therapy and have remained undetectable
- Regular follow-up with alpha fetoprotein levels and liver ultrasound have been normal

Questions

- Is there any risk of relapse with higher viral DNA levels**?**
- What if the entecavir was stopped and the DNA levels were still undetectable?
- Is there any risk of hepatocellular cancer (a) if the DNA levels remain undetectable or (b) if the surface antibody was positive?
- How would you assess the mortality risk?

Case #3

- Baby Boomer born USA 1957: Male with clean medical hx.
  Requesting Life policy for 2.5 million

Agent asking for low substandard, possibly T2

Insurance paramedical

- BMI 27, BP 132/76, HR 72
- Family Hx unremarkable
- AST 33 (0-33), ALT 95 (0-45)
- GGT, T bili, Alk Phos , CDT neg, Alb 4.2 all normal
  HepBS Ag nonreactive, HepCAb reactive
- T.Chol 195, HDL 55
- UA normal, Neg cotinine

What is most likely etiology of elevated ALT? Would you make an offer with information you have here?

Hepatitis C

Confirmation that HCV RNA serology is positive.

Agent asking now for some offer, anything!!!

Questions:

- Would a liver biopsy be helpful?
- What is needed next in order to decide if an offer can be made?

Hepatitis C

Scenario #1

Obtains fibroscan with median results of **6.1 kPa**

Treated w/Harvoni for 6 months. 1 month after treatment, HCV RNA undetected with repeat 12 weeks after treatment, HCV RNA remains undetected. ALT has remained normal since treatment started.

Questions

- Can you assume SVR? sustained viral response
- How would you assess this risk?

Hepatitis C

Scenario #2

Obtains fibroscan with results of **11.5 kPa** suggestive of Fibrosis stage 3. Fibrosure 0.72

Subsequently, Treated w/Harvoni for 6 months and 12 weeks after treatment, HCV RNA is undetected and ALT returns to normal. AFP low and liver ultrasound without masses.

Questions

- Would you assess risk same as scenario #1?
- If not, what would you like to see in order to provide same or any offer for that matter?

Case #4 42 yo businesswoman applying for 5 million whole life

PMH: nonsmoker. 1-2 glasses wine 5xweek. Girls' night out may have 2-3 cocktails

Insurance Paramedical:

- 5'5" 155lbs BP 140/90 EKG normal
- Labs: BUN 25, Creatinine 1.2, Glucose 95, A1C 5.5%,Albumin 3.5, GGT 77(1.6 x nml) , AST 72 (2.1 x nml), ALT 40 (1.2x nml), hepCAb nonreactive. HBSAg nonreactive. Tchol 225, LDL 105, HDL 77

MVR clear

RX: None

PCP labs 1 yr ago: CBC - WBC 5.0, Hgb/HCT 12.5/38, MCV 110, platelets 135K (no clumping)
LFTs - AST 66, ALT 49, Alb 3.6,T bili 0.9 Lipids – HDL 82

Questions

- What are the concerns?
- How would you begin to underwrite her?

Bonacini Cirrhosis Discriminant Score

Platelets (x1000/mm3):

- >340 – zero points
- 280 to 339 – one point
- 220 to 279 – two points
- 160 to 219 – three points
- 100 to 159 – four points
- 40 to 99 – five points
- <40 – six points

ALT/AST ratio

- >1.7 – zero points
- 1.2 to 1.7 – one point
- 0.6 to 1.19 – two points
- <0.6 – three points

INR

- <1.1 – zero points
- 1.1 to 1.4 – one point
- >1.4 – two points

modified three parameter CDS by Dr. Maurizio Bonacini in 1997

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Do a quick Bonacini. Could the value be above 7 to suggest cirrhosis?

Platelets **135k**
ALT/AST = 49/66 = **0.74** if use current paramed values, ALT/AST = 40/72 = **0.55**
INR….. Don't have.
Question: If had an INR, is it be possible to get a score above 7?

Platelets (x1000/mm^3):
>340 – zero points
280 to 339 – one point
220 to 279 – two points
160 to 219 – three points
100 to 159 – four points
40 to 99 – five points
<40 – six points

ALT/AST ratio
>1.7 – zero points
1.2 to 1.7 – one point
0.6 to 1.19 – two points
<0.6 – three points

INR
<1.1 – zero points
1.1 to 1.4 – one point
>1.4 – two points

Case #5 **55** yo international businessman applying for 5 million whole life

PMH: smoker. Drinks socially. HTN on Lisinopril. HLD on Lipitor. GERD on Prilosec OTC. Last executive physical 6 months ago.

Insurance Paramedical:

- 6'2" 205lbs BP 140/90 EKG normal
- Labs: BUN 25, Creatinine 1.2, Glucose 95, A1C 5.5%, GGT 77(1.6 x nml) , AST 66 (2.1 x nml), ALT 49 (1.2x nml), CDT +, HepCAb nonreactive. HBSAg nonreactive. Tchol 225, LDL 105, HDL 77

MVR DUI 2011

Executive PE labs 6 months ago: CBC - WBC 5.0, Hgb/HCT 12.5/38, MCV 110, platelets 325K

Lipids – HDL 82

His brother is an MD and prescribes the Lisinopril and Lipitor

Questions

- What are the concerns?
- How would you begin to underwrite him?

Alcoholic Liver Disease

Do a quick Bonacini. Could the value be above 7 to suggest cirrhosis?

Platelets **325k**
ALT/AST = 49/66 = 0.74
INR….. Don't have.
Question: If had an INR, could it be possible to get a score above 7?

Platelets (x1000/mm^3):
- >340 – zero points
- 280 to 339 – one point
- 220 to 279 – two points
- 160 to 219 – three points
- 100 to 159 – four points
- 40 to 99 – five points
- <40 – six points

ALT/AST ratio
- >1.7 – zero points
- 1.2 to 1.7 – one point
- 0.6 to 1.19 – two points
- <0.6 – three points

INR
- <1.1 – zero points
- 1.1 to 1.4 – one point
- >1.4 – two points

Asks his MD brother to order Fibroscan, thinking he could get a better rating

Fibroscan Results 8.1 kPa
Any rate change

Stiffness	Indicates	Advice
> 18.7 kPa	Cirrhosis PPV = 90%	US and AFP every 6 months for surveillance of Liver cancer. Stop all alcohol
12.7-18.7 kPa	≥ F3 Advanced fibrosis PPV=92%	Stop all alcohol. Consider US and AFP every 12 months for surveillance of Liver cancer
> 8.2-12.6	≥ F2 Advanced fibrosis PPV = 100%	Stop all alcohol

What if Fibroscan report was 19.5 kPa?
Would you offer?
What other conditions could be present with cirrhosis due to any liver condition?

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Diagnostic Accuracy of Bonacini score

Bonacini CDS	# of studies	Total# of patients	# Patients w/cirrhosis	Sensitivity	Specificity	Positive LR/ P value	Negative LR/ P value
>8	5	613	113	0.25	0.96	13 / 0.003	0.77/ 0.01
>7	6	906	170	0.39	0.96	9.4/0.06	0.65/0.018
>3	5	756	196	0.90	0.32	1.4/<0.001	0.30/0.66

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CDT

What improves the predictive value of a positive test suggesting ingestion of more than 60 g etoh/day?

CDT

What improves the predictive value of a positive test suggesting ingestion of more than 60 g etoh/day?

if any of these 2/3 conditions are present with positive CDT, likelihood increases greatly on predicting heavy alcohol

1. HDL over 50
2. GGT over 65
3. Tobacco user

More concern if additionally, there is an elevated AST or SGOT of > 45

Thank You!

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