GI Workshop
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Liver Function Tests – Case # 1

Application

- 49-year-old male, non-smoker, born in the US
- Partner in a law firm
- Applying for $3, 000,000 (US$) whole life policy

Insurance exam

- 5’10”, 205 lbs. (178 cm, 93 kg), BMI 29.2
- BP 124/84 Pulse 62
- Family history: mother died of breast cancer at age 75
- Total cholesterol 175 mg/dl (4.52 mmol/L), HDL 48 mg/dl (1.24 mmol/L)
- Glucose normal
- ALT elevated at 82 U/L (1.8 x normal), GGT and AST normal
- No reflex testing performed
- Urinalysis: WNL; negative for cotinine/nicotine

Liver Function Tests – Case # 1

Medical history

- Records dated back to 2017. Had been followed for “borderline” hypertension and cholesterol.
- Told to exercise more and watch his diet – initially not put on any medications.
- Despite this his repeat lipid levels in 2019 were total cholesterol 265 mg/dl (6.85 mmol/L), HDL 42 mg/dl (1.09 mmol/L)
- He was begun on atorvastatin in 2020.
- Prior liver tests during this time frame were all normal
- He has remained asymptomatic

Liver Function Tests – Case # 1

Questions

- What are the likely cause(s) of the ALT elevation?
- Would reflex testing with a CDT 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 been born and raised in Korea and entered the US 10 years ago?
- Would the risk potentially change if the ALT was low normal at 8 U/L?

Liver Function Tests –Alternate Scenario 1

- GGT elevated at 117 U/L (1.8 x normal), ALT and AST normal
- Other details are the same

Questions

- What are the likely cause(s) of the GGT elevation?
- Would reflex testing with a CDT 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 CDT 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 CDT alcohol marker reduce that mortality risk?
- Is there any risk with a GGT at the very low end of the normal range?

Liver Function Tests – Alternate Scenario 2

- ALT is elevated at 126 U/L (2.8 times normal) and AST is elevated at 65 U/L (1.97 times normal), GGT is normal
- Other details are the same

Questions

- What is the likely cause(s) of the elevations?
- Would reflex testing with a CDT 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 127 U/L (3.8 times normal) and ALT was 94 U/L (2.1 times normal)? If so, why?
- Would the probability of a positive CDT alcohol marker change?

Liver Function Tests – Alternate Scenario 3

- GGT is elevated at 210 U/L (3.23 times normal), ALT is elevated at 132 U/L (2.93 times normal) and AST is elevated at 92 U/L (2.8 times normal)

Questions

- What are the likely cause(s) of the elevations?
- Would reflex testing with a CDT 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 5’10”, 270 lbs. (178 cm, 122.7 kg)
  - Alkaline phosphatase is 260 U/L (2.08 times normal)
  - Bilirubin is 2.8 mg/dl (42.8 umol/L)
  - Serum albumin 3.1 mg/dl (31 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.

Ulcerative Colitis– Case # 2a

- Application
  - 23 year old female, non-smoker
  - Recent college graduate, starting new job as communications director for non-profit organization
  - Applying for 150,000 USD term life (convertible to whole of life without underwriting in first 10 years)

- Insurance exam
  - Self-reported: 5’3” (160 cm), 132 lbs. (60 kgs), BMI 23.4.
  - Diagnosed with ulcerative colitis at age 19.
  - Treated with mesalamine rectal suppositories, but no treatment for almost a year. Doing well, no symptoms.
  - Family history: father and mother both alive and well. Older brother with ulcerative colitis since age 15, controlled on medication. Younger sister without medical history.
  - Oral fluids negative for HIV, cotinine, and cocaine.

Ulcerative Colitis– Case # 2a Questions

1. Do you have enough information in which to assess mortality risk
2. Do you think a questionnaire or discretionary APS would be necessary or useful?
3. What is the main mortality risk in this case?

Ulcerative Colitis– Case # 2b

Application

- 32 year old male with history of ulcerative colitis (pancolitis) diagnosed at age 20 while in college.
- APS indicates on treatment with 5-ASA and infliximab.
- Last flare approximately 3 years ago.
- Colonoscopy 2 years ago with random biopsies every 10 cm from the cecum to the rectum revealed no evidence of dysplasia.

Questions

1. What two major risk factors determine the likelihood of developing colorectal cancer (CRC) in individuals with ulcerative colitis?
2. How often does this individual require surveillance colonoscopy?
3. What is his risk of developing colorectal cancer over time?
4. What is his current overall mortality risk?

Ulcerative Colitis– Case # 2b Alternate Scenario

- Applicant's colonoscopy 2 years ago demonstrated low grade dysplasia in one of the biopsies.
- He was to return for follow up colonoscopy in 6 months, but did not do so.

<u>Questions</u>

5. What is the recommended management of low-grade dysplasia?
6. What is the risk that he might have CRC at the time of underwriting?
7. How would you assess his mortality risk?
8. If he underwent total proctocolectomy with ileostomy or IPAA (ilial pouch-anal anastomosis) vs simple colectomy with ileorectal anastomosis, how would you assess this mortality risk?

Ulcerative Colitis– Case # 2b Alternate Scenario

- Applicant's most recent colonoscopy 2 years ago was normal.
- Fecal calprotectin and CRP are elevated as per LOV three months ago.
- Current insurance labs: KFTs normal, ALT 45 U/L normal, AST 38 U/L normal, GGT 110 (1.7x ULN), alkaline phosphatase 140 U/L (1.2x ULN).

Questions

9. Are you concerned at all with regard to the low-grade liver enzyme elevations? Why or why not?
10. What is the significance of fecal calprotectin elevation?
11. How would you assess his mortality risk?

Crohn's Disease– Case # 2c

Application

- 38 yo M for $2M, nonsmoker
- Hx of CD, dx at age 8
- Multiple treatment regimens, currently on Humira (adalimumab), Imuran (azathioprine) and mesalamine
- Hx of perianal fistulas
- Last colonoscopy 2 years ago: quiescent colitis, benign 3 mm polyp

Questions

1. Is the CRC risk for Crohn disease the same as it is for ulcerative colitis?
2. Are there different surveillance recommendations for Crohn disease compared with ulcerative colitis?
3. What is the risk of developing PSC with Crohn disease compared with ulcerative colitis?

Barrett's Esophagus – Case # 3

- Application
  - 57 year old male, smoker
  - Works as an accountant
  - Applicant admits to occasional alcohol use
  - Applying for $1 million (US$) survivor policy

- Insurance exam
  - 5'10", 232 lbs. (178 cm, 105.5 kg)
  - BP 128/84, pulse 70
  - Family history: father died of hepatocellular cancer at age 60; mother had a heart attack at 62 and died of heart failure at age 71. Brother and a sister in good health.
  - Total cholesterol 198 (5.12 mmol/L), HDL 50 (1.29 mmol/L)
  - Blood profile normal
  - Urinalysis: within normal limits; positive for cotinine/nicotine

Barrett's Esophagus – Case # 3

- Medical history
  - Applicant has a long history of esophageal reflux symptoms without dysphagia.
  - An upper endoscopy 8 years ago showed salmon colored mucosa in the distal esophagus compatible with Barrett's esophagus that extended 5-6 cm from the gastro-esophageal (GE) junction.
  - Biopsies at that time showed intestinal metaplasia with goblet cells and no dysplasia.
  - Subsequent endoscopies 4 years and 1 year ago showed similar findings on examination and pathology with no dysplasia
  - Applicant has been treated with the proton pump inhibitor drug omeprazole which has largely controlled his symptoms.

Barrett's Esophagus – Case # 3 Questions

1. What are the main risk factors for development of Barrett's here?
2. What is the main mortality risk in this case?
3. Does this risk vary with age?
4. Does the use of the proton pump inhibitor drug lower the risk?
5. Is the follow-up regimen adequate here?
6. How would you assess the mortality risk?

Barrett's Esophagus – Case # 3 Alternate Scenario

- Applicant's endoscopy showed a short segment (< 3 cm of Barrett's)

Questions

7. Does the length of the Barrett's mucosa change the prognosis here?
8. What are other risk factors for progression?

Barrett's Esophagus – Case # 3 Alternate Scenario

- Applicant's initial biopsy showed reactive changes and possible low grade dysplasia
- Two subsequent biopsies show no dysplasia

Questions

9. Does the presence of low-grade dysplasia change the risk?
10. Is it likely that low grade dysplasia was present in this case?
11. How would you assess the mortality risk here?
12. What is the AGA recommendation for surveillance in those with low grade dysplasia?

Barrett's Esophagus – Case # 3 Alternate Scenario

- Applicant's most recent biopsy showed high grade dysplasia
- He was treated with endoscopic laser ablation of the distal esophagus
- Two subsequent endoscopies with biopsy showed no evidence of Barrett's or dysplasia

<u>Questions</u>

13. How does the presence of high-grade dysplasia change the risk?
14. Has the Barrett's and dysplasia been cured in this case?
15. What are other forms of treatment for high grade dysplasia?
16. How would you assess the mortality risk with this scenario?

Hepatitis B – Case # 4

Application

- 38-year-old male, works as a landscaper, current smoker
- Born and raised in Thailand, now lives in the United States
- Applicant denies alcohol use
- Applying for 150,000 USD term life with waiver of premium

Insurance Para-medical

- 5’8” (172 cm), 156 lbs. (70.9 kgs), BP 142/84 , pulse 70
- Family history: father died of stroke at age 60, mother died of hepatocellular cancer at 65, brother has cirrhosis; other 2 brothers and 3 sisters are in good health
- Total cholesterol 180 mg/dl (4.66 mmol/L), HDL 53 mg/dl (1.37 mmol/L), urinalysis normal, positive for cotinine/nicotine

Hepatitis B – Case # 4

- ALT 137 U/L (3.1 x normal), AST 92 U/L (2.8 x normal), GGT, alkaline phosphatase and bilirubin are all normal
- Hepatitis B surface antigen, hepatitis B core antibody (total) and hep B e antigen are all positive, hep B surface antibody is negative
- Urinalysis is normal, positive for cotinine

Hepatitis B – Case # 4

Medical History

- Applicant was diagnosed with hepatitis B in 2017
- His liver enzymes were initially normal but have been elevated for at least the past 6 years
- He was treated with interferon in 2020 but did not tolerate it
- His last viral DNA level was 450,000 IU/ml
- The viral genotype was C

Hepatitis B – Case # 4

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 woman and not a man?
- Would the mortality risk change if the e antigen was negative and the viral DNA was still elevated at 450,000 IU/ml?
- How would the presence of a Basal Core Promoter mutation affect the risk?

Hepatitis B – Alternate Scenario 1

- Applicant is a known hepatitis B carrier since 2018
- His ALT and AST readings have been consistently normal
- Viral DNA levels have been followed regularly with the most recent value 5050 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 2

- Applicant was diagnosed with hepatitis B in June of 2022
- ALT and AST were initially elevated at 2-3 x normal
- Applicant was started on entecavir (Baraclude) in December of 2022 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?

Thank You!

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