Disclosure

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Complications of Cirrhosis

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Cirrhosis is an Extrahepatic Disorder

Muscle wasting
Swollen abdomen and legs
Yellow eyes, mucous membranes and skin

TIP: Examine patients carefully for telltale signs of liver disease
Muscle Wasting
Protein Calorie Malnutrition

TIP: The patient’s back may be more revealing than the front
The Spider Nevus is a dilated spiral arteriole.
Spider nevi disappear when the liver disease resolves, as with successful liver transplantation.
Changes in the Hands in Cirrhosis
- palmar erythema
More changes in the hands.....

Terry's nails

Muerhcke's nails

Palmar erythema

Finger clubbing
Another Side Effect of Estrogen/Androgen Imbalance: Gynecomastia:
Portosystemic Collaterals: Esophageal Varices
....in the stomach
- Gastric Varices -
....in the rectum
- Rectal Varices -
... Peristomal Varices -
.... and as the legendary - Caput Medusa -

collaterals from a recanalized umbilical vein

TIP: Reserve the term varices for mucosal collateral that can bleed
Ascites and Renal Dysfunction

TIP: Protect umbilical hernias that can erode; repair hernias electively when ascites controlled, avoid emergency operations
Hepatic Encephalopathy

Pathogenesis

Bacterial action

Protein load

Failure to metabolize NH$_3$

NH$_3$ Shunting

Bacterial action

Protein load
TIP: No Point in Measuring Blood Ammonia Levels

“Blood ammonia levels cause as much confusion in those requesting the measurement as in the patients in whom they are being measured”

Adrian Reuben
Hepatology 2002;35:983
TIP: Correct Dose of Lactulose

Head clear …
No diarrhea
Hepatopulmonary Syndrome

(Type I) Diffusion-perfusion defect

(Type II) Anatomic shunt

Excess perfusion (Low Ventilation/Perfusion ratio)

TIP: Type I responds to 100% inspired oxygen, Type II does not.

precapillary and capillary dilatations
Portopulmonary HTN
Spectrum of Pulmonary Vascular Pathology

- In-situ thrombosis
- Proliferation/Plexogenic change
- Normal
- Fibrosis
- Platelet aggregates

TIP: Get Doppler Echocardiography in all cirrhotics to detect pulmonary hypertension
Cirrhosis is not just a liver disease
- but a complex multi-organ syndrome
- with widespread extrahepatic effects
Caused primarily by circulatory dysfunction

- Dermatologic (microcirculatory)
- Endocrine

- Circulatory
- Cardiac
- Renal
- Gastrointestinal
- Pulmonary
- Neurologic
- Infectious (?)
VASODILATATION: THE ROOT OF ALL EVIL

Splanchnic Circulation 

Renal Circulation 

Systemic Circulation 

Pulmonary Circulation 

Cerebral Circulation*

Vasodilatation 

Secondary Vasoconstriction 

Vasodilatation 

Vasodilatation 

Vasodilatation 

Initiated by local factors

Blood Flow
Portal Hypertension
Variceal bleeding

- Na/H₂O Retention
- Hepatorenal Syndrome

↑ Cardiac Output
High Output Heart Failure
d receptor function
⇒ Cirrhotic cardiomyopathy

- Arterial hypoxemia
- Hepato-Pulmonary Syndrome
- Also primary - vasoconstriction

Brain Edema

Initiated by local factors

*Acute Liver Failure

Groszmann 2007
Varices Increase in Diameter Progressively
Risk of Bleeding Increases with Variceal Size

2-year probability of first bleed:
- Small varices: 7%
- Large varices: 30%
...And with the Presence of Red Marks

...And with the severity of liver disease
Evolution of Varices

Cirrhosis with no varices

Level of Intervention

Pre-primary prophylaxis

Management Recommendations

- Repeat endoscopy in 2-3 years
- No specific therapy
**Evolution of Varices**

- **Cirrhosis with no varices**
- **Small varices**
  - No hemorrhage
  - **Level of Intervention**: Pre-primary prophylaxis
  - **Management Recommendations**
    - Repeat endoscopy in 2-3 years
    - No specific therapy
- **Medium / large varices**
  - No hemorrhage
  - **Level of Intervention**: Primary prophylaxis
  - **Management Recommendations**
    - Non-selective β-blocker to prevent enlargement
    - Medium/Large varices
      - Non-selective β-blockers
      - Endoscopic Variceal Ligation (EVL) in those who are intolerant of drugs
SUMMARY OF MANAGEMENT OF VARICES AND VARICEAL HEMORRHAGE

**Evolution of Varices**

- **Cirrhosis with no varices**
  - Small varices
    - No hemorrhage
  - Medium / large varices
    - No hemorrhage
  - Variceal hemorrhage
  - Recurrent variceal hemorrhage

**Level of Intervention**

- Pre-primary prophylaxis
- Primary prophylaxis
- Secondary prophylaxis

**Management Recommendations**

- **Cirrhosis with no varices**
  - Repeat endoscopy in 2-3 years
  - No specific therapy

- **Small varices**
  - No hemorrhage
  - Non-selective β-blocker to prevent enlargement

- **Medium / large varices**
  - No hemorrhage
  - Non-selective β-blockers
  - Endoscopic Variceal Ligation (EVL) in those who are intolerant of drugs
  - Endoscopic/pharmacologic therapy
  - Antibiotics in all patients
  - TIPS or shunt surgery as rescue therapy

- **Variceal hemorrhage**
  - Non-selective β-blockers or EVL
  - Non-selective β-blockers + EVL?
  - TIPS or shunt surgery as rescue therapy
PATHOGENESIS OF ASCITES

Cirrhosis

- Hepatic venous outflow block
- Sinusoidal pressure (HVPG ≥ 10-12 mmHg)
- Ascites

- Arteriolar resistance (vasodilation)
- Effective arterial blood volume
- Activation of neurohumoral systems (renin, angiotensin, aldosterone)

- Sodium and water retention
WORSENING OF CIRRHOSIS LEADS TO WORSE ASCITES AND HEPATORENAL SYNDROME

Cirrhosis

- Intrahepatic resistance
- Sinusoidal pressure
  - Refractory ascites
- Hepatorenal syndrome
  - Sodium and water retention
  - Renal vasoconstriction
  - Activation of neurohumoral systems
- Systemic arteriolar resistance
  - Effective arterial blood volume
  - Worsening of liver disease
Treatment of Ascites

No ascites

Uncomplicated ascites

Refractory ascites

Hepatorenal syndrome

No specific therapy
Consider salt restriction
TIP: Easiest 2000 mg Sodium Diet

• All processed meat is poison
  – Ham, bacon, cold cuts, sausage etc

• Anything that is fresh is good
  – No salt in cooking and at table and no “lite” salt

• All packaged food has a label telling how much sodium in “mgs”
  – Maximum intake is the same number as the year: 2011, 2012, 2013 ….. etc
Treatment of Ascites

**Portal Hypertension**
- No ascites

**Uncomplicated ascites**

**Refractory ascites**

**Hepatorenal syndrome**

1) Salt restriction + diuretics
2) Large volume paracentesis (LVP) especially in hospitalized patients with tense ascites but also prior to initiating diuretics
Treatment of Ascites

1. LVP + albumin
2. TIPS
3. Peritoneo-venous shunt (in non-TIPS, non-transplant candidates), still used – LeVeen not available
Treatment of Ascites

Portal Hypertension
No ascites

Uncomplicated ascites

Refractory ascites

Hepatorenal syndrome

1) Liver transplant
2) Vasoconstrictors + albumin*
3) TIPS?
4) Terlipressin – not in USA
Natural History of Hepatorenal Syndrome (HRS)

Creatinine (mg/dL)

Type 2 HRS

THERAPEUTIC PARACENTESIS

Cefotaxime

Type 1 HRS

SBP

Arroyo et al., Gastroenterology 2002; 122:1658
TYPE-I HRS IS A MULTIORGAN FAILURE SYNDROME

Spontaneous bacterial peritonitis or other precipitating event

Increase in arterial vasodilation

*Decrease in cardiac output*

vasoconstrictors

resistance to portal venous flow

Aggravation of portal hypertension

Regional arterial vasoconstriction

<table>
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<th>Kidneys</th>
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<td>Adrenal dysfunction</td>
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Bacterial Infections Are Common in Hospitalized Cirrhotic Patients

“Spontaneous” infections are the most common type of infections in cirrhosis (n=572)

- Urinary tract infection: 32%
- Secondary peritonitis: 12%
- Cholangitis: 3%
- Cellulitis: 4%
- Secondary bacteremia: 6%
- Pneumonia / upper respiratory infection: 8%
- Other: 16%
- Other: 19%

Spontaneous infections:
- SBP (peritonitis)
- SB (bacteremia)
- SBE (empyema)

Fernández et al., Hepatology 2002; 35:140
Patient with SIRS and/or sudden hypotension, AKI, jaundice

Panculture, chest X-ray, Dx paracentesis

Start antibiotic

Creatinine > 1.0
BUN > 30
Bilirubin > 4.0

IV albumin

On admission
Dx paracentesis

Community-acquired
SBP: cefotaxime
amoxi-clavulanic
ciprofloxacin
(adapt to local patterns)

Nosocomial
Broader spectrum
antibiotics*

Modify (narrow) once culture results available

SBP:
* Particularly if recently hospitalized or on prophylactic AB
Late at night, and without permission, Reuben would often enter the nursery and conduct experiments in static electricity.