Portal Hypertensive Gastropathy and Gastric Antral Vascular Ectasia

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Portal Hypertensive Gastropathy (PHG) Definition

- Macroscopic changes of the stomach associated with mucosal and submucosal vascular dilation

- Endoscopy:
  - Mosaic pattern
  - Red spots

References:
McCormack T, Gut 1985
Ripoll C, Garcia-Tsao, Clin Liv Dis 2010
Cubillas R Rockey DC, Liver Int 2010
Portal Hypertensive Gastropathy (PHG) Characteristics

- Mild or severe
- Characterized by a cobblestone / snakeskin appearance
- Distribution – fundus and body
- Bleeding responds to measures that reduce portal hypertension

Kalafateli M et al, Dig Dis Sci 2012
Cubillas R Rockey DC, Liver Int 2010
Portal Hypertensive Gastropathy (PHG) Prevalence

- Overall prevalence 20%-98%
- Highest prevalence in advanced cirrhosis and those with varices
- Prevalence seems to increase with EV obliteration

Primignani M, Gastroenterology 2000
Merli M, Am J Gastroenterol 2004
PHG: Natural History

N= 373 / 3 yr follow up

Primignani M, Gastroenterology 2000
Portal Hypertensive Gastropathy
Natural history / HALT C

- HALT C study → 1017 patients with bridging fibrosis/compensated cirrhosis were analyzed
- 37% had PHG
  - 34% mild changes, 3% severe changes.
  - Mosaic pattern - 33%, red marks – 15%, GAVE - 3%
- More prevalent in advanced disease and large EV

4 yr follow up → new onset PHG - 13% / yr
worsening PHG - 7% / yr

Fontana R, Am J Gastroenterol 2006
Fontana R, Am J Gastroenterol 2011
Portal Hypertensive Gastropathy
Pathophysiology

1. Increased portal pressure > 12mm Hg
2. Abnormal gastric mucosal blood flow
   Congestion $\rightarrow$ may lead to hypoxia
3. Mucosa susceptible to injury
   Impaired healing and mucosal defense
4. Local factors: overproduction of NO, endotoxemia and prostaglandins
   Role in microcirculatory changes

Kumar K et al, J Clin Gastroenterol 2010
Patwardhan VR, Cardenas A. APT 2014
Portal Hypertensive Gastropathy Pathophysiology

Degree of PHG is associated with severity portal hypertension
### Portal Hypertensive Gastropathy Classification

<table>
<thead>
<tr>
<th>New Italian Endoscopic Club for the Study and Treatment of Esophageal Varices</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MILD - Mosaic like pattern</strong></td>
</tr>
<tr>
<td>Mild: diffusely pink areola</td>
</tr>
<tr>
<td>Moderate: flat red spot in center of pink areola</td>
</tr>
<tr>
<td>Severe: diffusely red areola</td>
</tr>
<tr>
<td><strong>SEVERE - Red marks</strong></td>
</tr>
<tr>
<td>Red lesions of variable diameter, flat or slightly protuding</td>
</tr>
<tr>
<td>Discrete or confluent</td>
</tr>
</tbody>
</table>

*Spina GP, et al.. J Hepatol 1994*
Mild

Moderate

Severe

Mosaic like pattern
Red marks (severe)
# Management

Asymptomatic patients - no therapy

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduction of portal pressure</td>
<td>Beta blockers</td>
</tr>
<tr>
<td></td>
<td>Somatostatin/octreotide</td>
</tr>
<tr>
<td></td>
<td>Terlipressin</td>
</tr>
<tr>
<td></td>
<td>TIPS</td>
</tr>
<tr>
<td>Local therapy</td>
<td>Argon Plasma coagulation ?</td>
</tr>
<tr>
<td>Underlying liver disease</td>
<td>Liver transplantation</td>
</tr>
</tbody>
</table>

*Patwardhan VR, Cardenas A. APT 2014*
Portal Hypertensive Gastropathy
Acute bleeding

- Acute bleeding – occurs in 2-12% of cases
- Severe PHG and advanced liver disease
- Therapy –
  1. IV vasoconstrictors
  2. Antibiotics
  3. TIPS
  4. Endoscopic therapy?

Gostout C, Am J Gastroenterol 1993
Primignani M, Gastroenterology 2000
Zhou E, J Gastroenterol Hepatol 1998
Argon Plasma Coagulation (APC)

Noncontact thermal coagulation - applies high-frequency electric current that is passed through argon gas.

Scarse data in PHG and active bleeding

APC aimed to ablate specific lesions and/or the majority of mucosa at least 80% in diffuse lesions.

APC is administered at 40-60W and 1–2 L/min of flow
APC in PHG

- 11 patients with acute bleeding from PHG were treated with APC-
  (mean 2-3 sessions)
- 81% of the patients stopped bleeding or reduced transfusion requirements

Who?

Suboptimal control with IV vasoconstrictors
Poor candidates for TIPS

Herrera S, Gastrointestinal Endoscopy 2008
Hemospray

• Hemostatic powder licensed for endoscopic haemostasis (Europe and Canada.
• Easy to apply, non-contact method, which can cover large areas of mucosa, may benefit in acute bleeding from portal hypertensive gastropathy in case reports.

*J Hepatol.* 2014 Feb;60(2):457-60
Portal Hypertensive Gastropathy
Chronic bleeding

- Obscure / occult GI bleeding and anemia
- Occurs in up to 26% of cases
- Mainstay of therapy:
  - Iron supplementation / transfusions
  - Propranolol (20mg bid) or Nadolol (40 mg qd)
    - Decreases rebleeding ~ 60-80% cases
  - TIPS
    - Refractory cases / cirrhosis (Child < 12 points)

Perez-Ayuso, Lancet 1991
Kamath P, Gastroenterology 2000
GAVE

Watermelon Stomach

Diffuse Gastric Vascular Ectasia

Jabbari, Gastroenterol 1984
Ripoll C, Dig Liver Dis. 2011
Severe PHG may be difficult to distinguish from diffuse GAVE
# How to tease apart?

<table>
<thead>
<tr>
<th></th>
<th>PHG</th>
<th>GAVE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Associated with portal hypertension</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Distribution in stomach</td>
<td>Proximal</td>
<td>Distal</td>
</tr>
<tr>
<td>Mosaic pattern</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Associated with other diseases</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Response to therapies directed at decreasing portal pressure</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>First line therapy</td>
<td>Drugs</td>
<td>Endoscopy</td>
</tr>
<tr>
<td>Salvage therapy</td>
<td>TIPS</td>
<td>Other</td>
</tr>
</tbody>
</table>

*Patwardhan VR, Cardenas A. APT 2014*
### Biopsy (jumbo) helps tease apart PHG and GAVE

<table>
<thead>
<tr>
<th>Biopsy:</th>
<th>PHG</th>
<th>GAVE</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Thrombi</td>
<td>-</td>
<td>+++</td>
</tr>
<tr>
<td>- Vascular ectasia</td>
<td>-</td>
<td>+++</td>
</tr>
<tr>
<td>- Spindle cell proliferation</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>- Fibrohyalinosis</td>
<td>-</td>
<td>+++</td>
</tr>
<tr>
<td>- Dilated capillaries</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>- Submucosal edema</td>
<td>+++</td>
<td>-</td>
</tr>
<tr>
<td>- Thick submucosal vessels</td>
<td>+++</td>
<td>-</td>
</tr>
</tbody>
</table>

*Do you really want to do a jumbo biopsy in patients with advanced cirrhosis?*
Gastric Antral Vascular Ectasia Characteristics

- GAVE is distinct entity
- Occurs in < 5% of patients with cirrhosis
- Not related to portal hypertension
- Iron deficiency anemia due to chronic GI bleeding
- Other disease states associated with GAVE
  - autoimmune connective tissue disorders
  - systemic sclerosis
  - renal failure
  - bone marrow transplantation

Gostout, J Clin Gastroenterol 1992
Kalafateli M, Dig Dis Sci, 2012
Gastric Antral Vascular Ectasia
Pathophysiology

- Mainly unknown
- Related more to liver insufficiency
  - does not respond to BB or TIPS
  - Resolves after LT
- High levels of gastrin and prostaglandin E2 (vasodilators)
- Abnormal antral motility
- Mechanical stress

Quintero Gastroenterology 1987
Sparh, Gut 1999
Selinger, Digestion 2008
Gastric Antral Vascular Ectasia Therapy

• Indicated for bleeding
• Medical treatment?
  – Steroids, transxanemic acid, thalidomide – poor results

• Endoscopy
  – APC (standard of care)
  – ND:Yag laser (＞complications)
  – Band ligation (promising)
  – RFA (refractory cases)

Kwan Am J Gastroenterol 2006
Fuccio Digestion 2008
Wells, Gastrointest Endosc 2008
Sato Digest Endosc 2012
Gastric Antral Vascular Ectasia
APC

- 20120228_TRISTANY edited.avi

Settings: 40–60W / gas flow between 1 and 2 L/min
Gastric Antral Vascular Ectasia
APC

- Effective in 85-90%
- Reduces transfusion requirements
- Increases Hb levels (mean 2-3g/L)
- Safe, easily applied
- Widely available

- Large areas can be treated
- Treatment every 2-4 weeks
- Approximately 3-4 sessions

Recurrence in 30-60%

Sebastian S, Dig Liver Dis. 2004
Kwan Am J Gastroenterol 2006
Fuccio, Digestion 2008
Herrera S, Gastrointest Endosc 2008
Gastric Antral Vascular Ectasia Banding

- Used given safety and efficacy of EBL in obliterating submucosal vascular plexus
- Involves banding a large area of antrum
- Maximum amount of bands placed (mean 7-12)
- Scarse data –
- 2 small studies with promising results

Wells, Gastrointest Endosc 2008
Sato Digest Endosc 2012
# Gastric Antral Vascular Ectasia Banding - summary of 2 studies

<table>
<thead>
<tr>
<th></th>
<th>APC (n=35)</th>
<th>Banding (n= 21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rebleeding</td>
<td>68-70%</td>
<td>8.3 - 33%</td>
</tr>
<tr>
<td>Transfusion</td>
<td>2.7-5.7</td>
<td>1-2.5</td>
</tr>
<tr>
<td>Cessation of bleed</td>
<td>56%</td>
<td>23%</td>
</tr>
<tr>
<td>Treatment sessions</td>
<td>3-4</td>
<td>1-3</td>
</tr>
<tr>
<td>Mean Hb level post</td>
<td>10</td>
<td>11</td>
</tr>
<tr>
<td>Deaths</td>
<td>33-39%</td>
<td>33-39%</td>
</tr>
<tr>
<td>Side effects</td>
<td>bleeding</td>
<td>bleeding, nausea, vomiting</td>
</tr>
</tbody>
</table>

Wells, Gastrointest Endosc 2008  
Sato Digest Endosc 2012  
Patwardhan, Cardenas APT 2014
### Gastric Antral Vascular Ectasia
#### Prospective study

<table>
<thead>
<tr>
<th></th>
<th>Banding (n= 21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical response</td>
<td>19%</td>
</tr>
<tr>
<td>Hb - Before EBL / After EBL</td>
<td>88 (101–118) vs109 (79–97) p&lt;0.001</td>
</tr>
<tr>
<td>PRBC (Before EBL / After EBL)</td>
<td>2.85 (2.03–3.6) vs 1.15 (0.3–2)p&lt;0.001</td>
</tr>
<tr>
<td>Sessions</td>
<td>2.28 ( 1-6)</td>
</tr>
<tr>
<td>Bands applied</td>
<td>16 (6-59)</td>
</tr>
<tr>
<td>Side effects</td>
<td>2  Transient abdominal pain</td>
</tr>
</tbody>
</table>

Zepeda – Gomez- Endoscopy. 2015
Radiofrequency ablation / HALO

• Delivers a uniform depth of ablation over a 3 cm$^2$ area, may theoretically allow for more reliable destruction of vascular ectasias and more surface area to be treated in a single session
In 6 patients with GAVE, 83% of patients had cessation of bleeding with improvement in haemoglobin after 1–3 treatments.

More recently, in a prospective study of 21 patients with bleeding GAVE refractory to APC, 86% of patients became transfusion independent after radiofrequency ablation (maximum of four treatment sessions).

_Gastrointest Endosc_ 2008; **67**: 324–7
_Gastrointest Endosc_ 2013; **78**: 584–8.
Gastric Antral Vascular Ectasia
Rescue therapy

- Endoscopic cryotherapy
- Surgical antrectomy in selected cases
- TIPS is not effective

Cho, Gastrointest Endosc 2008
Belle JM, Surg Laparosc Endosc Percutan Tech 2009
Kamath PS Gastroenterology 2000
PHG Treatment Algorithm

Acute bleeding

Treatment with somastostin / octreotide

antibiotics

Control ?

yes

Start treatment with
β-blockers

no

Consider TIPS

Not candidate

Consider APC sessions or
hemospray

uncontrolled or
cannot take
PHG Treatment Algorithm

Chronic bleeding

Iron therapy / transfusions prn
Treatment with β-blockers

Control ?

yes

Continue therapy

no

Consider TIPS

unable to take

Liver transplant

Not candidate
GAVE Treatment Algorithm

Chronic anemia or bleeding

Iron therapy / transfusions prn
Treatment with Argon plasma

Repeat sessions

No control after 3-4 sessions

Consider banding

Refractory case

Consider:
- RFA
- Surgical antrectomy

Follow up

response

response
Thank you