



UPMC

**University of Pittsburgh
Medical Center**

2019 Hepatology Update

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Clinical Vignette

- 68 yo F with PMH of GERD and MS referred from OSH to hematology at UPMC for severe iron deficiency anemia
- Denied overt bleeding
- Prior endoscopy notable for (GI?) AVMs
- Recent EGD and colonoscopy at OSH were normal
- Refused capsule endoscopy at OSH

Medical Histories

PMH:

Iron deficiency anemia
Breast carcinoma
GERD
Hypertension
Multiple sclerosis

PSH:

Tubal Ligation
CCY

Medications:

None

FHx:

M: Bleeding disorder, DM

F: Bled to death

7 siblings without bleeding diseases, brother with DM, no other known illnesses

2 children healthy

No GI, liver, or pancreatic diseases

SHx:

Waitress, married

No smoking,
EtOH, or illicit

PE and Laboratory Studies

- Vitals and PE unremarkable
- Labs: WBC 6.5, Hgb 9.1, MCV 75.2, RDW 31.8, plt 345; CMP unremarkable, iron 26, % iron sat 6, ferritin 19
- Started on IV iron with monitoring of her labs

Clinical Course

- ~1.5 years later she developed abdominal pain
- OSH CT chest/abd/pelvis with contrast: thyroid nodules and a 6 mm left lower lobe nodular density
- ENT: cauterization for epistaxis
- 6 months later: bleeding in her nose, throat, and teeth
- Heme PE note: “Broken blood vessels over the tips of her fingers” and “small red lesions” were noted on her tongue

Clinical Course

- Next two years: IV iron, aminocaproic acid not tolerated
- SOB
- OSH EGD: gastric and duodenal AVMs
- 2 months later: LE swelling
- Admitted later that month for LE and abdominal swelling
- CMP notable for AP 145, PT/PTT/INR 15.7/1.3/31.1, BNP 772
- EKG atrial flutter, TTE EF 55-60%, flattened septum, RVH, severe tricuspid regurgitation, small rt to lt shunt by saline (cardiac vs intrapulmonary)
- RHC: RA 19, RV: 61/3, PA 68/29/40, W: 28 Fick CO 8, Fick CI: 4.7.
- Doppler u/s and CT C/A/P with contrast

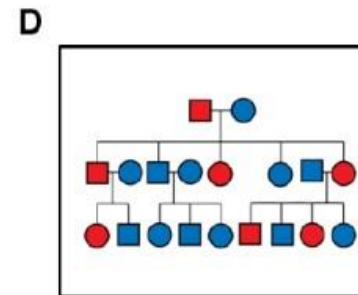
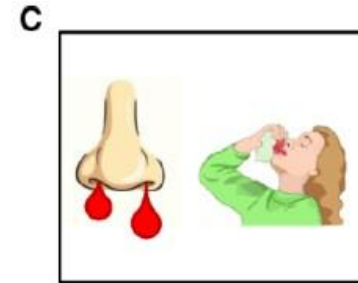
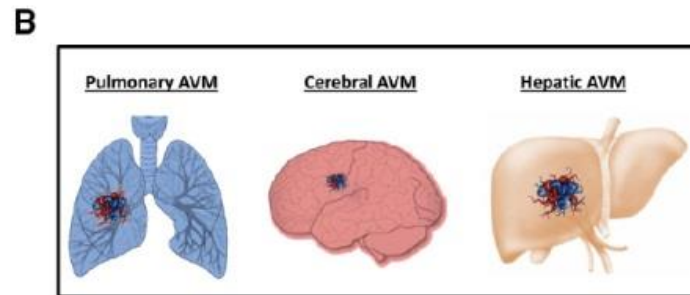
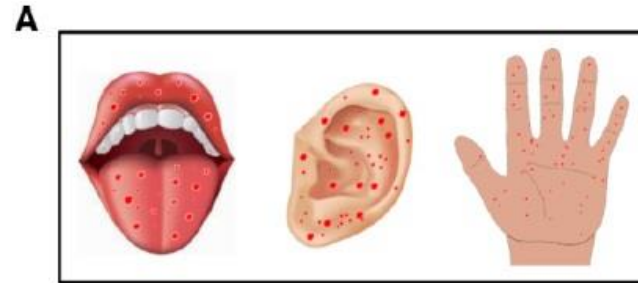
Diagnosis and Disease Course

- Diagnosis?
- What is happening in the natural course of disease?



Hereditary hemorrhagic telangiectasia (Osler-Weber-Rendu syndrome)

- Epistaxis, gastrointestinal bleeding, and iron deficiency anemia
- Characteristic mucocutaneous telangiectasia
- Arteriovenous malformations (AVMs) commonly occur in the pulmonary, hepatic, and cerebral circulations



Diagnostic Criteria: Curaçao diagnostic criteria

- Spontaneous and recurrent epistaxis
- Multiple mucocutaneous telangiectasias at characteristic sites
- Visceral involvement (e.g., gastrointestinal telangiectasia; pulmonary, cerebral, or hepatic arteriovenous malformations)
- A first-degree relative with HHT

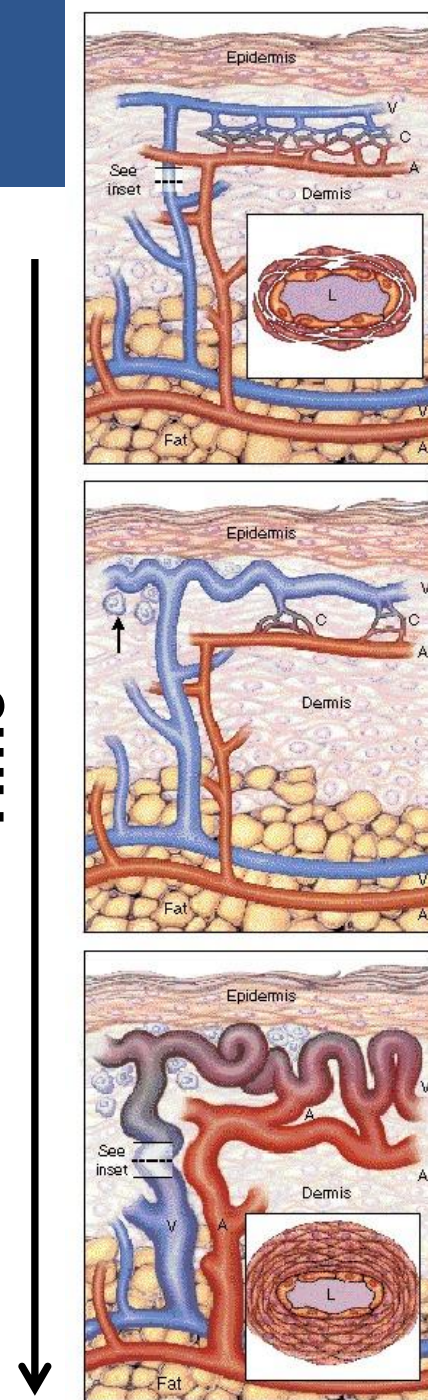
Definite (3+ criteria), suspected (2 criteria), and unlikely (1 criterion)

Pathophysiology

- AD disease with varying penetrance, progressive
- 1:5000 to 1:8000 individuals
- 600 mutations described: *ENG* (endoglin), *ACVRL1* (activin receptor-like kinase 1, ALK-1), *SMAD4*
- Result in diffuse defects in vascular structure (telangiectasias and AVMs)

N Engl J Med 1995; 333:918-924

Time



Management

Site	Incidence	Presentation patterns	Evaluation	Treatment
Nasal telangiectasia	>90%	Nose bleeds are usually the first manifestation of HHT, frequently commencing in childhood.	History, inspection	<ul style="list-style-type: none"> ■ Routine therapy includes nasal lubrication and treatment of iron deficiency when needed. ■ Laser treatment is generally preferred over cauterization. ■ Surgery in expert hands offers good results for selected patients. ■ Medical (systemic) treatments are an alternative and may be highly beneficial, but carry risks of prothrombotic side effects. ■ Emergency treatments such as packing may be required.
Mucocutaneous telangiectasia	50 to 80%	Increase in size and number with age. Main concerns are cosmetic. May hemorrhage.	Inspection (oral, mucosa, conjunctivae, face, trunk, extremities, nail beds)	<ul style="list-style-type: none"> ■ Generally not indicated, but laser therapy can be used.
Gastrointestinal telangiectasia	11 to 40%	Onset generally over 30 years: Iron deficiency anemia, occasionally acute gastrointestinal	Flexible endoscopy, endoscopy angiogram, capsule endoscopy	<ul style="list-style-type: none"> ■ Iron supplementation and transfusion are the mainstays of treatment. ■ Medical (systemic) treatments are available and may be highly beneficial, but they carry risks of prothrombotic side effects.

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Pulmonary AVMs	>50%	Usually silent. Cyanosis, clubbing, bruit, dyspnea, paradoxical embolism, cerebral abscess.	Chest radiography, blood gas measurement, helical CT, angiography, chest echocardiography	<ul style="list-style-type: none"> Therapeutic embolization. Antibiotic prophylaxis for dental and surgical procedures. Surgical resection may be indicated in highly selected cases.
Cerebral AVMs	10 to 15%	Usually silent. Headache, epilepsy, ischemia, intracerebral hemorrhage.	CT, MRI, Doppler sonography, angiography	<ul style="list-style-type: none"> Most do not require treatment. Therapeutic embolization, neurovascular surgery, or stereotactic radiosurgery in highly selected cases.
Hepatic AVMs	30 to 70%	Usually silent. Hepatic artery-hepatic vein AVMs: Hyperdynamic circulation. Portasystemic shunts: Ascites and encephalopathy.	Doppler sonography, CT, MRI	<ul style="list-style-type: none"> Most do not require treatment. For the small proportion of patients who develop symptoms, standard hepatic medical care is often sufficient to resolve symptoms. Liver transplantation in selected cases. Embolization is a higher-risk procedure; some centers do not perform embolization unless the patient is accepted into a liver transplantation program.

Thorax 1999; 54:714; Uptodate 2019; Management of hereditary hemorrhagic telangiectasia

Clinical Course

- Diuresed with milrinone
- V/Q scan low probability
- Head MRI without cerebral AVM
- Hepatology: Discussed transplant, patient declined
- Heme: bevacizumab if no transplant
- Hepatic embolization thought too high of risk
- Palliative care consulted
- Discharged on diuretics and PPI with multidisciplinary follow up

Clinical Course

- ~6 months later she presented to OSH with 2 days of melena found to have to be hypotensive with a Hgb of 5.4, received two units PRBC, Hgb to 7.7
- EGD OSH 11/11/17:
 - A few 10 mm non bleeding angioectasias were found in the stomach
 - Nd:YAG laser therapy was performed on the greater curvature of the gastric antrum, in the duodenal bulb and in the first part of the duodenum with 20 watts, 5 pulses, and 5 joules.
- She was lost to follow up

Summary: Hereditary hemorrhagic telangiectasia

- AD dominant vascular disease (AVMs and telangiectasias)
- Variable penetrance
- Clinical symptoms develop with increasing age
- Epistaxis earliest and most frequent symptom
- Iron deficiency anemia, GI bleeding, mucocutaneous telangiectasias and AVMs in the pulmonary, hepatic, and cerebral circulations are common
- Management with iron transfusions, local therapy, systemic therapy, and screening for PAVMs, +/- cerebral AVMs
- Hepatic AVMs and cardiac failure, if medical management fails consider transplantation

Thank you

Questions

Fun Fact Pittsburgh Trivia

What was invented (or first) in greater Pittsburgh

- A. The pound sign
- B. The Big Mac
- C. The hepatitis B vaccine
- D. The first commercial television station
- E. The first movie

Fun Fact Pittsburgh Trivia

What was invented (or first) in greater Pittsburgh

A. The pound sign -> emoticon at CMU

B. The Big Mac

C. The hepatitis B vaccine -> polio vaccine developed in Pittsburgh

D. The first commercial television station -> radio station - KDKA 1920 (CBS radio Pittsburgh)

E. The first movie -> first nickelodeon in Pittsburgh in 1905

Screening

- Basic clinical examination
- Evaluation for anemia and iron deficiency
- Pulmonary AVM (PAVM) screening
- Discussion of screening versus non-screening for other systemic AVMs:
 - Cerebral AVMs
 - Hepatic AVMs – Screening is rarely performed
 - Spinal AVMs – Screening is performed in pregnancy and for patients undergoing surgery when epidural analgesia may be required