

Turning Your Clinical Cases into Scholarly Work

Course Syllabus & Readings Fall 2011

Contact Information

Course Director

Vineet Arora, MD, MA, FACP
Associate Professor
Assistant Dean, Pritzker School of Medicine
Associate Program Director, Internal Medicine Residency
Department of Medicine, W-216
varora@medicine.bsd.uchicago.edu
773-702-8157

Student Contacts

Michael Huber
Email: michaelhuber@uchicago.edu

Kyle Karches
Email: kkarches@uchicago.edu

Schedule for Turning Your Clinical Cases into Scholarly Work

Please note that all classes will be held from 5-7pm in L316

BEFORE Class, review this packet, focusing on what makes a good case, and then select a case (can start using worksheet at end to organize your work)

- **Monday Sept 12 5-7pm CASE SELECTION & VIGNETTE PRESENTATION (REQUIRED)**
 - Share case ideas & artifacts/consultants needed – (Group)
 - Intro to MRView
 - How to present a clinical vignette (Arora)

- **Monday Sept 19 5-7pm ABSTRACT WRITING & PRESENTATION REVIEW (REQUIRED)**
 - Draft slide review (group)
 - How to write a clinical vignette abstract (Arora)

- *Wednesday Sept 21 5-7pm Practice presentations (OPTIONAL)*

- **Due date for power point presentations: Thursday September 22nd**

- **Friday, Sept 23rd 1pm – 5pm Present in Internal Medicine Interest Group Clinical Vignette Competition (REQUIRED)**

- **Due date for abstracts: Thursday September 29th (due to ACP conference on October 1st)**

****required in-person activity.**

Note, the bulk of the activity for this course takes place outside of formal class through preparing an abstract and presentation. To receive credit for this course, students must turn in an abstract and do a power point presentation on Friday September 23rd.

POSSIBLE PREWORK FOR CLINICAL VIGNETTE
Turning Your Clinical Cases Into Scholarship
Vineet Arora MD
September 2011

Dear students, here are some tips on how to select cases as you think about the course. You may come with several you are thinking about. Here are some very rough guidelines that we can think about.

Selecting a Case

- Uncommon presentation of common disease
 - Diabetic muscle infarction (uncommon presentation of diabetes)
 - Thyrotoxic periodic paralysis (uncommon presentation of hyperthyroidism)
- Unusual cause of common problem
 - Diarrhea caused by pellagra
 - Heart failure due to Takatsubo's cardiomyopathy (broken heart syndrome)
- Common presentation of uncommon disease
 - Yellow nail syndrome
 - Hemophagocytic syndrome
- A recent diagnostic or therapeutic advance
 - Use of ADAMTS-13 to diagnose TTP
- Clinical pearl or classic sign for physical exam
 - Muerkhe's nails in patients with low albumin

Consulting the literature (PubMed and Google)

- Is this common?
- How often is it reported?
- Are there any important associations relevant?

Preparing the Case (Some of this you will do during the course but you can get a head start if free)

- Consult with team to let them know you are interested
 - Ensure that you will take the lead on at least the IL ACP Vignette but that you are planning to include them as authors (may pose a problem if resident plans on using case. You could suggest that you would do IL ACP and they could submit to National which is in April since mot 4th years are unlikely to go to a medical conference in April based on my experience)
- Obtain H&P – save what you have
 - As part of this course, you will receive access to MR View which will enable you to access the H&P (confirmation to follow)
- Review Epic for any figures that are relevant (Obtain from Epic)
 - Imaging – CXR/CT/MRI etc.
- Consult with pathology or radiology to explain any images that need interpretation
 - May need assistance from attending in radiology or pathology to interpret
 - Pathology will occasionally help by taking pictures
- If you are taking care of the patient CURRENTLY
 - Consider photos of dermatology findings or exam findings
 - Obtain consent if patients is visible (will send a form)

Sample Clinical Vignette Products (on Chalk)

Sample Papers

Hemmige V, Jenkins E, Lee JU, Arora VM Toxic epidermal necrolysis (TEN) associated with herbal medication use in a patient with systemic lupus erythematosus. J Hosp Med.2010. Epub ahead of print. <http://onlinelibrary.wiley.com/doi/10.1002/jhm.639/pdf> (attached)

Clayburgh DR, Yoon JD, Cipriani NA, Ricketts PA, Arora VM. Clinical problem-solving. Collateral damage. N Engl J Med. 2008;359(10):1048-54.
<http://www.nejm.org/doi/full/10.1056/NEJMcps0708994> (attached)

Sample Abstracts

Yoon JD, Ricketts PA, Clayburgh DR, Arora VM. When Occam Triumphs Over Hickam: Acute Abdomen in a Patient with an Interior Vena Cava Anomaly. 2007 Society of General Internal Medicine, April 2007. (attached)

Sample Posters

Kapoor N, Nam T, VanderWheele D, Arora VM. TTP or Not TTP? 2008 Society of Hospital Medicine Meeting, San Diego, CA, April 2008. (attached)

Sample PowerPoints

Patel T, Pouch S, Griffith J, Arora V. Modern Version of an Ancient Disease Secondary Pellagra due to Microscopic Colitis and Hydralazine. 2009 Midwest Society of General Internal Medicine, September 18, 2009. (attached)

Sheth H. “Steal Your Heart Away” Myocardial Ischemia Resulting From Multiple Coronary Microfistulae Draining into the Left Ventricle. 2008 American College of Physicians Illinois Associates’ Day, October 17, 2008. (attached)

Other Products

Sanders L. Dizzying Symptoms. The New York Times Magazine. May 31, 2010.
<http://www.nytimes.com/2010/06/06/magazine/06FOB-diagnosis-t.html>

Web Resources

<http://familymed.uthscsa.edu/facultydevelopment/elearning/anatomy.html>

http://www.acponline.org/residents_fellows/competitions/abstract/prepare/clinvin_abs.htm

WHEN OCCAM TRIUMPHS OVER HICKAM: ACUTE ABDOMEN IN A PATIENT WITH AN INFERIOR VENA CAVA ANOMALY

Yoon¹ J.D., Ricketts¹ P.A., Clayburgh² D.R., Arora¹ V.M.

¹University of Chicago, Department of Medicine, Chicago, IL

²University of Chicago, Pritzker School of Medicine, Chicago, IL

Learning Objectives:

1. Appreciate an uncommon risk factor for idiopathic deep vein thrombosis
2. Consider how Occam's Razor can clarify a diagnostic dilemma related to acute presentations of uncommon medical conditions
3. Recognize a situation where acute abdomen may be safely managed as an outpatient thus avoiding unnecessary surgery

Case:

50 year old male with newly diagnosed left lower extremity DVT after a prolonged airplane trip presented with 2 days of worsening abdominal and back pain. While on anticoagulation, he developed diffuse abdominal pain aggravated by movement and associated with intermittent flank pain. Past medical history included a hypercoagulable work-up that had been previously unremarkable. Physical exam was notable for tender flank pain and bilateral lower quadrant abdominal pain with rebound and guarding. His labs were remarkable only for unexplained hematuria. Infused abdominal CT surprisingly revealed an absence of the infra-hepatic inferior vena cava with multiple retroperitoneal collaterals, including an atrophic left kidney. Hospital course was characterized by persistent peritonitis. Infused MRI of the abdomen further revealed a thrombus in the left ascending lumbar vein. Patient was diagnosed with thrombophlebitis of the retroperitoneal collateral veins associated with his IVC anomaly. Patient was managed conservatively with anticoagulation, leading to resolution of his presenting symptoms 2 months later.

Discussion:

The initial differential diagnosis of an acute abdomen is broad including appendicitis, perforated viscus, obstruction, renal colic, and mesenteric or renal vein thrombosis. In this case, however, the patient presented with apparent unrelated findings, including an idiopathic DVT, hematuria, tender flank pain, peritonitis, and a congenital IVC anomaly. Based on Occam's Razor, we looked for evidence supporting a single, unifying diagnosis. We discovered case reports of similar IVC anomalies presenting as a risk factor for idiopathic DVT, presumably from increased venous stasis despite collateral flow. Patients with these anomalies can also have unexplained hematuria and flank pain from dilated or thrombosed retroperitoneal collateral veins. Lastly we found a single case report of thrombophlebitis of pelvic vein collaterals associated with this IVC anomaly mimicking appendicitis-like pain, successfully managed with anticoagulation. Therefore we postulated that the patient suffered from a case of pelvic venous "hemorrhoids" due to an inflamed thrombus lodged in the pelvic collateral veins lining his retroperitoneum. This hypothesis was further supported by his MRI finding. This unifying explanation allowed us to take a conservative approach to what initially appeared to be acute surgical abdomen. Here we report a common presentation (acute abdomen) of an uncommon condition (pelvic collateral vein thrombophlebitis associated with an IVC anomaly). The presentation of multiple diagnoses in a patient is becoming more prevalent in an aging population with chronic conditions (*Saint's triad, Hickam's dictum*). Some therefore conclude that Occam's Razor is swiftly losing clinical power in the modern era. However, the acute constellation of symptoms in a healthy patient with an uncommon condition led us to invoke Occam's Razor to guide us through this diagnostic dilemma. Occam is not obsolete yet.



TTP or Not TTP?

Neena Kapoor, BA, Teresa Nam, MD, David VanderWheele, MD, PhD, Vineet Arora MD MA
Pritzker School of Medicine and the Internal Medicine Residency Program at The University of Chicago

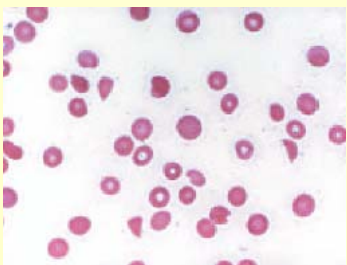
Objective

- Differentiate between malignant HTN and TTP as the cause for thrombotic microangiopathy in the setting of SLE
- Discuss the importance of ADAMTS13 functional and inhibitor assays in the diagnosis of TTP in patients with SLE

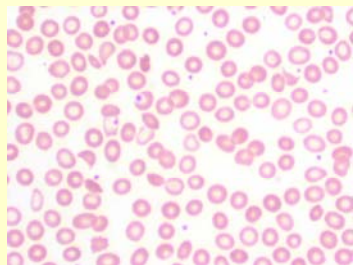
Case History

- A 25 year old female with a history of systemic lupus erythematosus (SLE), hypertension (HTN), and class IIIA lupus nephritis was admitted to the ICU for a generalized tonic clonic seizure
- Temperature 36.4 and BP 197/116
- Plasma exchange started for TTP (thrombotic thrombocytopenic purpura)
- Nitroprusside drip used to stabilize her HTN
- Patient eventually transferred to a rehabilitation facility

Hemopathology



Example of patient's blood smear prior to treatment demonstrating schistocytes¹



Actual blood smear of patient after plasma exchange

Imaging



Right basal ganglia and thalamic hemorrhage with intraventricular extension

Laboratories

Laboratory	Admission	Baseline
Hemoglobin (g/dL)	7.6	11.2
Platelets (K/uL)	39	325
Serum creatine (mg/dL)	6.8	0.8

- LDH 474U/L
- Haptoglobin <20mg/dL
- Direct Coombs antibody negative
- ADAMTS13 < 5%, normal >67%
- ADAMTS13 inhibitor 2.4 units, normal <0.4 units

Discussion

- Triad of ARF, microangiopathic hemolytic anemia (MAHA), and thrombocytopenia suggested thrombotic microangiopathy which could be due to TTP or malignant HTN

Symptoms	TTP	Malignant HTN
Fever	Uncommon ¹	Not associated
MAHA	Present	Present
Decreased platelets	Present	Present
ARF	Rare ¹	Not associated
Neurological changes	1/3 with no changes ¹	Not associated
ADAMTS13 antibodies	Present	Not present

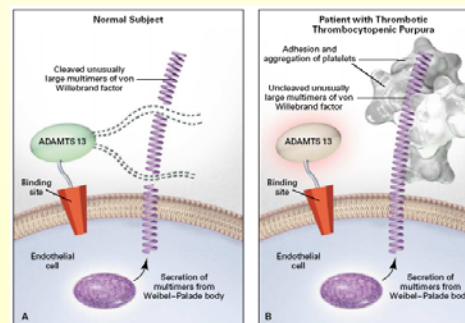
- ADAMTS13 functional and inhibitor assays used to differentiate between malignant HTN and TTP

- In 1998, researchers found that idiopathic TTP characterized by autoantibodies to ADAMTS13, a zinc-containing metalloprotease enzyme that cleaves von Willebrand Factor, rendering it inactive²

Mechanism of ADAMTS13

Panel A Normal: ADAMTS13 molecules attach to binding sites on endothelial cells and cleave unusually large multimers of vWF

Panel B TTP: Decreased activity of ADAMTS13 leads to large multimers of vWF, and induces adhesion and aggregation of platelets⁵



- ADAMTS13 inhibitor assay tests for autoantibodies by mixing heat treated patient plasma with normal plasma, and measuring residual ADAMTS13. Normal individuals have functional ADAMTS13 >67%, and ADAMTS13 inhibitor <0.4 units

- Because ADAMTS13 levels vary widely (22-172%) in SLE patients, functional assay should not be used alone to diagnose TTP³

- Therefore, ADAMTS13 inhibitor assay is used in conjunction with the functional assay to diagnose TTP in SLE patients

Conclusion

- While the annual incidence of TTP in the general population is only 4-11 cases per million, a much greater proportion of SLE patients (roughly 1-4%) will experience a TTP episode in their lifetime^{1,4}
- This prevalence, coupled with the near 90% mortality rate of TTP without plasma exchange, makes early recognition and treatment of TTP in SLE patients essential
- To diagnose TTP in SLE patients, both ADAMTS13 functional and inhibitor assays should be performed

References

1. George JN. Thrombotic Thrombocytopenic Purpura. NEJM 2006;354:1927-35.
2. Tsai HM, et al. Acquired deficiency of von Willebrand factor-cleaving protease in a patient with thrombotic thrombocytopenic purpura. NEMJ 1998;339:1585-94.
3. Rieger M, et al. ADAMTS13 autoantibodies in patients with thrombotic microangiopathies and other immunomediated diseases. Blood 2005;106(4):1262-65.
4. Stark M, et al. Acquired thrombotic thrombocytopenic purpura as the presenting symptom of systemic lupus erythematosus. Successful treatment with plasma exchange and immunosuppression - report of two cases. Eur J Haematol 2005;75:436-40.
5. Moake J. Thrombotic Microangiopathies. NEJM 2002;347:589-600.

Acknowledgements

- Patient and family
- Dr. Gurbuxani, Ph.D. Hematology

Modern Version of an Ancient Disease

Secondary Pellagra due to
Microscopic Colitis and Hydralazine

Tanvi Patel MSIV, Stephanie Pouch MD,
Jason Griffith MD, Vineet Arora MD

University of Chicago, Pritzker School of Medicine and
Department of Medicine

Midwest SGIM Regional Meeting
September 18, 2009



Case Presentation

- 56 year old African American male
 - CC: leg pain, diarrhea
- Diarrhea x 1 month
 - 10-12 watery, non-bloody BM/day
 - Persists with fasting
- Denies fevers, N/V, abd pain, weight loss
- No history of recent travel, laxative or antibiotic use, ingestion of sorbitol-containing products



Medical & Surgical History

- PMHx:
 - Chronic pancreatitis, DM2, HTN, pancreatic head mass, PVD
- PSHx:
 - PVD s/p bypass surgery in RLE c/b persistent leg pain
- All: NKDA
- Meds: Hydralazine and Labetolol
- ROS + for pruritic rash on hands and trunk

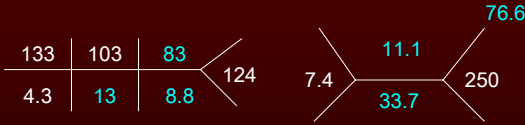


Physical Examination

- T 36.8, BP 77/37, HR 60, RR 17, O₂ 99% RA
- Orthostatic
- CV: RRR; normal S1, S2; diminished peripheral pulses with stasis dermatitis on LE bilaterally; no LE edema
- Resp: CTAB
- Abdomen: NABS, soft, NT, ND
- Integument: hyper-pigmentation, hyper-keratotic plaques on dorsum of hands bilaterally



Initial Laboratory Studies



- ESR: 45
- Lipase were amylase normal
- FOBT negative
- Serial cardiac enzymes negative
- EKG: NSR, no evidence of ischemia

- Anemia markers
 - Serum iron: 11
 - TIBC: 130
 - % sat: 8
 - Ferritin: 139



Initial Management



- Patient was managed for dehydration and acute renal failure
- BP was 77/37, requiring greater than 10 L of 0.9 NS with bicarbonate to stabilize
- Home anti-hypertensives held
- Potassium & magnesium repleted
- Derm consultation for skin biopsy



Diagnostic Evaluation

- Chronic diarrhea work-up:
 - Stool analysis
 - No leukocytes, fat or organisms
 - O&P negative
 - EGD, colonoscopy and mesenteric duplex were grossly normal
 - Biopsies taken for follow-up



Evaluation of Diarrhea

- Calculation of a stool osmotic gap to narrow the differential for chronic diarrhea
 - $Gap = \text{stool osmolality} - [2 \times (Na + K)]$
- Stool osmolality= 380
- Osmotic gap= 42
 - <50 suggests secretory diarrhea
 - >100 suggests malabsorption
- Stool electrolytes
 - Na 32
 - K 92
 - Cl 67
 - Mg 13



Secretory diarrhea

- Common causes:
 - Laxative use
 - Artificial sweetener use
 - Infection
 - Hyperthyroidism
 - Celiac sprue
- Ruled out with a thorough dietary history and laboratory studies
 - TSH and TTG both within normal limits



Workup: Rarer causes

- Given patient's known pancreatic mass, neuro-endocrine tumors were included:
 - VIPoma
 - Gastrinoma
- VIP, Gastrin, and 5HIAA all WNL



Workup: Rarer causes

- Rarer causes, such as deficiencies of:

- Niacin
- Folate
- Zinc
- Vitamins B6 and B12



- Nutrition labs:

- Vitamin B6 level: 2 (ref: 5-50)
- Zinc: 0.65 (ref: 0.66-1.10)



Case Resolution

- Acute renal failure resolved with aggressive hydration
- Dermatologic pathology:
 - Psoriaform rash consistent with clinical diagnosis of *acrodermatitis enteropathica*, which can be seen with vitamin deficiency
- Colon biopsy revealed collagenous colitis
- Diarrhea and rash resolved with B6 supplementation



Vitamin B6 Deficiency & our Patient

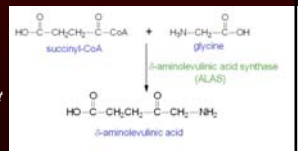
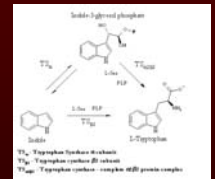
- Common – ¼ of all elderly patients
- Elderly African American men are a group at higher risk
- While diarrhea can cause mild B6 deficiency, severe B6 deficiency may infrequently cause a severe diarrhea due to secondary pellagra



Morris MS et al. J. American Journal of Clinical Nutrition, 2008; 87: 1446.

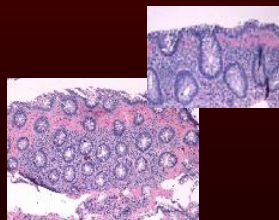
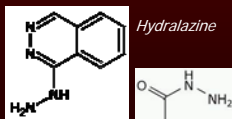
Pathophysiology

- Vitamin B6, pyridoxal 5'-phosphate (PLP), principal cofactor for many reactions
 - Niacin & heme synthesis
- B6 deficiency symptoms:
 - Diarrhea
 - Peripheral neuropathy
 - Microcytic anemia indistinguishable from iron deficiency anemia
 - Symmetric psoriasis



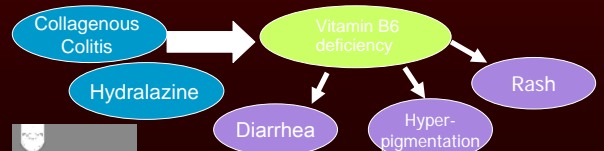
Clues to diagnosis...

- Isolated B6 deficiency occurs in patients taking pyridine inhibitors, such as INH or hydralazine
B6 repletion recommended
- Collagenous colitis is a microscopic colitis that may lead to a chronic diarrhea with multiple vitamin deficiencies



Conclusions

In our patient on hydralazine, the development of collagenous colitis likely resulted in a severe vitamin B6 deficiency and secondary pellagra, manifested by worsening diarrhea, hyperpigmentation and skin rash



Acknowledgements

- Our patient
- Patient's PCP, Dr. Kevin Thomas
- Dermatology consultant: Drs. Jessica Maddox & Christopher Shea





"Steal Your Heart Away"

Myocardial Ischemia Resulting From Multiple Coronary Microfistulae Draining into the Left Ventricle

Harshal Sheth, MD
Oral Clinical Vignette, ACP
Oct 7th, 2008



Case Presentation

- 36 yo AA male
 - CC: exertional chest pain, palpitations
- Denies associated SOB, leg swelling, calf tenderness, radiation of CP, pleuritic nature of CP
- No fever, chills or abdominal pain
- First occurrence of such pain
- No prior PMHx
- No medications
- Denies FHx premature CAD
- Occasional smoker, but otherwise, no illicit



Physical examination

- T 36.7, BP 120/75, HR 84, RR 18, O₂ 100%
- Heart exam: regular rate, rhythm; II/VI diastolic murmur heard best at apex with laterally displaced LV cavity
- Lungs clear to auscultation bilaterally
- Abdomen soft, nontender, nondistended; normoactive BS
- Peripheral pulses 2+ and symmetric
- No peripheral edema

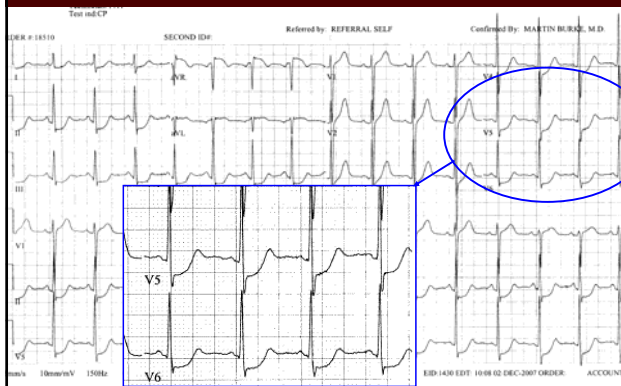


Laboratory studies

- Elevated WBC count of 18,000/ μ L
 - 75% neutrophils, 3% bands
- Hemoglobin 15.9g/dL
- Platelet count 199,000/ μ L
- Cardiac biomarker elevation
 - CK 326U/L (~2x ULN)
 - CK-MB 9.0ng/mL
 - Troponin T 0.15ng/mL (<0.10)
- Electrolytes within normal limits including K, Mg
- Total cholesterol 129
 - LDL 80
 - HDL 39
 - TG 49



EKG



Initial Management

Patient managed for acute coronary syndrome
Taken to cardiac catheterization for further evaluation



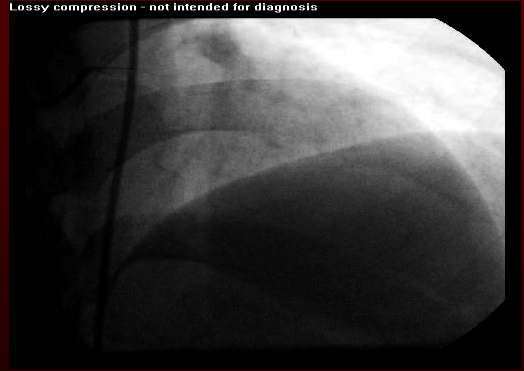
Cardiac Catheterization Images

Lossy compression - not intended for diagnosis



Cardiac Catheterization Images

Lossy compression - not intended for diagnosis

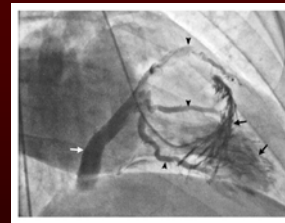


Management cont.

- Patient managed for acute coronary syndrome
 - Cardiac catheterization revealed nonobstructive coronary artery disease with multiple arterio-sinusoidal coronary microfistulae draining into LV
 - Subsequent treatment with oral nitrates and beta-blockers achieved reduction in symptoms
 - At 6 months, patient remains asymptomatic with good exercise tolerance



Discussion



Microfistulae in right ventricle
Singhal and Khoury, NEJM, 2008

- Multiple coronary microfistulae draining into LV is a *rare* phenomenon
- Anatomical, clinical and hemodynamic effects incompletely understood
- Communications generally classified into one of the following morphological categories:
 - Arterial-luminal
 - Arterio-sinusoidal
 - Arterio-capillary



Etiology



Dilated thin-walled Thebesian sinusoids (S) in the depth of the myocardium
Bellet, et al. Archives of IM, 1933

- Anomalies suspected to be congenital in origin
 - Partial persistence of embryonic myocardial sinusoids into intertrabecular spaces
 - Normally these structures regress
 - formation of Thebesian vessels of adult heart
 - Incomplete development results in microfistulae



Pathophysiology

- Up to 20% of total cardiac output can be shunted through these connections creating a "coronary steal" phenomenon resulting in symptoms of angina
- Diastolic murmur and LVH (both of which our patient had) suggest significant left-to-left shunt volume causing diastolic volume overload



Management

- Remains a controversial issue
- Surgical intervention warranted if shunting leads to hemodynamic significance
- Medical therapy alone often employed with calcium channel blockers, beta-blockers and/or nitrates has seen greatest success



Acknowledgements

- Patient and family
- Jim Woodruff, MD, Internal Medicine Residency Program Director
- Rajiv Swamy, MD, Chief Resident
- Vineet Arora, MD, FACP, Associate Program Director

Preparatory Checklist for Turning your Clinical Cases into Scholarship

Name _____

Potential Case

Brief one liner

Does it have a diagnosis? Yes No

Teaching Points

Classification

- Uncommon presentation of common disease
- Common presentation of uncommon disease
- A recent diagnostic or therapeutic advance
- Clinical pearl for physical exam or history

Literature Search

- PubMed (MeSH terms?)
- Google
- Other

Chart Artifacts

First need MRN

From MR View

- Admission H&P
- Relevant notes
- EKG

From Epic: Labs

- Routine Labs (CBC/ BMP/ LFTs)
- Coags and other heme labs (i.e. anemia workup)
- Endocrine or Nutrition Labs
- Relevant rheumatology labs

Preparatory Checklist for Turning your Clinical Cases into Scholarship

Name _____

- Microbiology
- ABG
- Other Labs

From Epic: Imaging

- CXR
- Other plain films
- CT
- MRI
- Other
- Need to discuss with radiologist?

From consultants: Other images

- Hematology (smears)
- Pathology (biopsies, surg path)
- Microbiology (cultures)
- GI imaging
- Cardiology (Echocardiogram /Angiogram)
- Other

Patient Pictures? Yes No

Notifications

- Contact Team Members to Discuss Writeup (invite as coauthors)
- Patient?
 - if considering publishing into a case report, need consent for some journals (do not need to do this for clinical vignette competition)
 - to take photos