Rapid Symmetric Peripheral Gangrene of all Digits:

Is this DIC or CAPS?

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Learning Objectives

1.) To understand the classification criteria for Catastrophic Antiphospholipid Syndrome (CAPS)

2.) To recognize that it can cause symmetric peripheral digital gangrene

3.) To understand that clinical features of DIC (Disseminated Intravascular Coagulation) and CAPS can overlap. Making diagnosis difficult.

4.) To understand treatment must be initiated rapidly as mortality is high in CAPS
History of Present Illness

**CC:** 60 yo Caucasian F p/w one day of abdominal pain, nausea, vomiting and diarrhea.

**HPI:** History was obtained from patient’s family. Per mother’s report, the patient ate dinner then shortly after developed abdominal pain. Pain was diffuse and worsening over the course of the night with associated nausea and several episodes of non-bloody emesis. She also reported 1 episode of fecal incontinence of dark black stool. At baseline, the patient is able to perform ADLs, but has waxing and waning mental status on a daily basis. She is alert and sharp during the day but becomes confused and forgetful at night.

**Positive ROS:** chronic pain, residual L sided weakness

**Negative ROS:** no rashes, Raynaud’s, oral ulcers, hair loss, DOE/SOB, chest pain, fever, dysuria, burning with urination, or cough
History of Present Illness

**PMHx:** Multiple Sclerosis x 30 yrs w/residual L sided weakness- uses a cane to ambulate, dementia, dyslipidemia. No history of abortions or blood clots in the past.

**Allergies:** NKDA

**Medications:** Betaseron, Simvastatin, Multivitamin, Sertraline

**Social Hx:** smokes marijuana daily for body pain, drinks wine occasionally, lives at home with her husband, stopped working 1.5 yrs ago because of worsening Multiple Sclerosis (used to work in a pharmacy)

**Family Hx:** paternal uncle and maternal grandmother-DM, father- HTN, sister-deceased from complication of Wilm’s tumor. No known Rheumatological conditions in the family
Physical Exam

**Vitals:** T 36.5 oral, **Tmax 40.7** (rectal) in ER, **HR 118**, BP 142/73, R 16, O2 sat 96% RA

**General:** moderate distress, eyes closed, grimacing, holding R hand over abdomen

**HEENT:** NCAT, dry mucous membranes, no oral ulcers, normal sclera

**Lungs:** poor air movement, clear to auscultation

**CVS:** regular rhythm, tachycardia, no murmurs

**Abdomen:** distended, mild TTP in all quadrants (R>L)

**Extremities:** no edema, 2+ distal pulses bilaterally

**Skin:** no rashes

**Neuro:** AOx1 (to person only), unable to assess strength and sensation
Initial Workup

WBC 5.0, Hb 12.8, Hct 40.1, Plt 103

Na 137, K 3.2, Cl 102, Bicarb 20, BUN 20, Cr 1.12

AST 111, ALT 85, Alk phos 101, Tbilli 1.0, Tprotein 7.3, Alb 3.8

Lactate 7.6

FOBT Positive

UA: yellow, clear, spg 1.039, pH 7.0, trace protein, neg glucose, neg ketones, neg bili, large blood, trace LE, neg nit, WBC 111, RBC 143, no bacteria

PT 19.2, INR 1.63, PTT 45.8, Fibrinogen 409, FDP >/=20, Ddimer >9999, LDH 343, Haptoglobin 180, peripheral smear-no schistocytes
Initial Workup

**CXR:** No acute process is detected in the chest.

**CT Angio Head:** No acute intracranial disease.

**CT Angio A/P:** Obstructing stone seen at the right ureteropelvic junction measuring up to 1.0 cm with moderate hydronephrosis of the right kidney. Hyperenhancement of the right urothelium proximal to the stone is suspicious for superimposed infection. An additional 1.1 cm nonobstructing stone is seen in the upper pole of the right kidney. A wedge shaped hypodense region in the left kidney likely represents a region of hypoenhancement secondary to focal pyelonephritis versus a region of renal infarction. Thickening of the cecum and ascending colon are nonspecific, although can be seen in the setting of bowel ischemia versus other infectious/inflammatory etiologies. The visualized abdominal vasculature is widely patent without evidence of stenosis or occlusion.
Hospital Course

- **HD #1** - Urology consulted: Right percutaneous nephrostomy tube placed by IR, Continued resuscitation and abx. Lactate improved 7.6->3.1->2.7->1.7

- General Surgery consulted: abdominal pain and lactate improved w/nephrostomy tube, low suspicion for mesenteric ischemia. No surgical intervention needed.

- **HD #2** - Spiked fever 38.1, Afib w/RVR HR 160s, DC cardioversion x1, amiodarone gtt initiated.

- ECHO: LVEF 35-40%, akinetic anterior septal wall, R ventricle enlarged, L atrium mildly enlarged, R atrium enlarged, moderate MR, PAP 39, moderate to severe TR

- Initial Blood Cultures: Proteus mirabilis and Enterococcus faecalis. Thought to be secondary to urinary source

- CXR: interval development of central pulmonary vascular congestion consistent w/mild CHF
Hospital Course

- **HD #3-** Change in lower extremities: 2+ pulses b/l, cold and clammy extremities. Skin: diffuse blue, violaceous reticular patches on b/l anterior LE

- **HD #4-** Hypoxic respiratory failure requiring intubation

- CT chest w/ Contrast: New bilateral pleural effusion and subjacent atelectasis. New patchy ground-glass opacities in bilateral upper and right lower lobes, suggestive of multifocal pneumonia versus pulmonary edema. Other etiologies such as pulmonary hemorrhage or drug toxicity are less likely.

- **HD #5-** Change in skin: blue discoloration of b/l toes to bases and finger tips to DIPs bilaterally. Heparin gtt started.

Differential Diagnosis of Symmetric Bilateral Digital Ischemia

- Vasospasm - Scleroderma
- Vasculitis - SLE, ANCA, cryoglobulinemia
- Thrombosis - APS, DIC
Hospital Course

- **Initial Treatment:** Nitropaste without efficacy
- **HD #5:** Steroids started, Solumedrol 125mg IV Q 12hours with taper
- **Rheum Work-up:**
  - ANA 1:640 homogenous, DSDNA neg, SM/RNP neg, C4 7, C3 27, Up/c 0.8
  - B2glycoprotein neg, Cardiolipin neg, **Lupus anticoag positive**
  - SSA/SSB neg
  - ANCA neg
  - Scl-70 neg, centromere neg, normal nailfold capillaroscopy
  - cryoglobulin neg
Hospital Course

- Hematology/Oncology consulted: concern for DIC (severe sepsis, elevated D-Dimer and FDP, low Fibrinogen (102), occasional Schistocytes on peripheral smear) versus CAPS.
  - Given high mortality associated with CAPS, recommended to continue heparin gtt and initiate:
    - Plasmapheresis x 3 days (HD # 7-9)

- Skin on Right Foot (Punch Biopsy) pathology report - microvascular thrombosis of arterioles and small veins. Overlying epidermal ischemia and surrounding dermal fibrosis

- Duplex Ultrasound of Upper Extremity - Occlusive deep venous thrombosis of right mid to distal brachial vein.

- IVIG at 400mg/kg x 5 days (HD # 12-16)
Diagnosis- CAPS

- 3 organ involvement
  1) Left kidney wedge shaped infarction
  2) Skin necrosis
  3) Right upper extremity DVT

- Development of manifestations simultaneously or in less than 1 week

- Lupus Anticoagulant positive

- Punch biopsy of skin with microthrombosis
Left Kidney: Wedge Shaped Infarction
Peripheral Digits: Skin Gangrene
Punch Biopsy of Skin on Right Foot

Path slide from skin on right foot: showing microvascular thrombosis of arterioles and small veins. Overlying epidermal ischemia and surrounding dermal fibrosis.
Outcome

- No further progression of digital ischemia
- Sepsis resolved
- Respiratory status improved
  - Extubated
- Transferred to outside hospital
  - Surgical amputation of digits
Catastrophic Antiphospholipid Antibody Syndrome (CAPS) is a rare and rapidly progressive form of Antiphospholipid Syndrome (APS) that involves multiple organs.

- It is often fatal
- Mortality approaching 50% without treatment

There are a wide variety of clinical manifestations of CAPS that can make a timely diagnosis difficult.

- The most common precipitating factor in CAPS is infection.

Disseminated Intravascular Coagulation (DIC) and APS do not commonly coexist except in cases of CAPS.

- Because of the overlapping characteristics in DIC and CAPS, the presence of Lupus Anticoagulant antibody can significantly help with diagnosis

Based on the CAPS Registry: CAPS was the first manifestation of APS in 49.1% of the patients.
Discussion

- Given the rarity of the disease, there are multiple hypothesis on pathogenesis.

- There is no standardized treatment for CAPS but based on review of published case reports, the highest survival rate was seen in patients that received combination of anticoagulation, corticosteroids and plasma exchange or intravenous gamma globulins.


