APPROACH TO THE SWOLLEN PATIENT

Keith E Swanson MD
ND Academy of Family Physicians
Family Medicine Update
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Disclosures

• Speaker’s bureau: BMS-Pfizer
  • Should not affect this subject.

• I “borrowed” many of the images off the internet
Objectives

• Review basic underpinnings of edema development
• Provide a comprehensive look at the various causes of edema
• Identify key clinical features to “narrow the differential”
• Brief management pearls
Case

• 45 y/a healthy male active member of the armed forces
• CC: leg swelling
• Over 3 months, sudden onset ankle edema; gradually progressive. R>L
• Never with similar symptoms prior
• About 10 days prior, had RLE standard venous duplex → non-compressibility PTV (1/2)
• Started on appropriate anticoagulation however...
• edema progresses!!
• Any thoughts?
What’s going on here?

- Small “distal” unilateral DVT ≠ Bilateral progressive edema!!
- Random urine protein to creatinine Ratio of 3.
- The REAL reason for his swelling is...

Nephrotic Syndrome
Why is Swelling Important?

• “Am I going to die”?
• Unattractive, uncomfortable
• Certainly, in Top 3 reasons for VM consult
  • Mayo VM as well
What’s Behind the Swelling?

• An increase in the interstitial component of extracellular volume
  • Generalized edema not clinically apparent until interstitial volume has increased by 2.5-3 liters

• 2 overriding factors:
  • 1. altered capillary hemodynamics
  • 2. retention of Na and Water by the kidneys

• The interplay b/t these 2 factors much more complex than previously thought
20 L out

17 L in

3 L lymphatics
Contemporary Understanding of Edema Formation

- A more complex interstitial space
  - NOT simply space where a protein free ultra-filtrate of plasma hangs out
  - Actually, a “triphasic” system of free floating fluid, a gel phase, AND a collagen matrix

- Capillary lumens are very sophisticated
  - Lined with glycocalx composed of complex network of GAG molecules forming a filtration barrier that is interrupted by clefts through which capillary filtration occurs

- Capillary beds differ substantially depending on organ

Sterns, RH. Pathophysiology and etiology of edema in adults. 2016 UpToDate
• Detailed History
• Sound physical exam
• Basic labs and imaging
• Rarely, advanced labs/imaging.
Welcome to Scotland Yards!!

“The causes [of edema] may be obvious and easily recognized, or occult and taxing to the ingenuity of the most experienced clinician.”

William F Ruschhaupt
Pivotal Points
It’s all in the history!

• Abrupt vs gradual (timing)
• Unilateral vs bilateral
• Pain vs painless
• Newman’s 1st Law of Medicine
Timing

- Abrupt, Acute swelling (< 72 hours)
  - DVT, cellulitis, ruptured popliteal cyst, acute compartment syndrome
  - Often unilateral

- Systemic process
  - Begins simultaneously in each leg and advances to the same degree in each leg
  - Upper limb/facial edema clinches

- Duration
  - Appears dramatically and disappears completely with recurrences of similar pattern
    - Infectious, recurring injury, idiopathic/cyclic edema
    - NOT Venous insufficiency or chronic lymphatic obstruction

- Edema behavior can evolve depending on chronicity
  - Lymphedema → worse longer one is up on the limb but later, it may diminish.
Pain + Edema?

**Painful**
- Cellulitis
- DVT
- Baker’s cyst rupture
- Gastroc rupture

**Painless**
- Lymphedema
- Systemic causes
  - Usually, more generalized
Laterality

**Unilateral**
- More possibilities
- Big 3: DVT, CVD, Lymphedema
- Pelvic obstruction
  - Intrinsic OR extrinsic
  - Retroperitoneal fibrosis
- Fictitious
  - Look clues of constrictive device
  - h/o of underlying psychiatric disease

**Bilateral**
- Usually systemic
  - The 3 “osis”
- No associated precipitating event
- If supine, look at sacrum
  - Surrogate for leg swelling in supine
- Pain unlikely
# Common Causes of Bilateral Edema

<table>
<thead>
<tr>
<th>Acute</th>
<th>Chronic</th>
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<tbody>
<tr>
<td>Venous insufficiency</td>
<td>Pulmonary Hypertension</td>
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<tr>
<td>Heart Failure</td>
<td>Idiopathic edema</td>
</tr>
<tr>
<td>Drugs</td>
<td>Premenstrual edema</td>
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<tr>
<td>Pregnancy</td>
<td>Obesity</td>
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## Less Common Causes of Bilateral Edema

<table>
<thead>
<tr>
<th>Acute</th>
<th>Chronic</th>
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</thead>
<tbody>
<tr>
<td>Bilateral DVT</td>
<td>Renal disease (nephrotic syndrome or nephritis)</td>
</tr>
<tr>
<td>Acute CHF, Renal disease</td>
<td>Liver disease</td>
</tr>
<tr>
<td></td>
<td>Secondary Lymphedema (tumor, XRT, infection)</td>
</tr>
<tr>
<td></td>
<td>Pelvic tumor or lymphoma (extrinsic compression)</td>
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<tr>
<td></td>
<td>Dependent edema</td>
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<tr>
<td></td>
<td>Diuretic induced</td>
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<tr>
<td></td>
<td>Pre-eclampsia</td>
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<td></td>
<td>Lipedema</td>
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</table>
## Rare Causes of Bilateral Edema

<table>
<thead>
<tr>
<th>Acute</th>
<th>Chronic</th>
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</thead>
<tbody>
<tr>
<td>Primary Lymphedema</td>
<td>Protein losing enteropathy</td>
</tr>
<tr>
<td>Protein losing enteropathy</td>
<td>Restrictive Pericarditis</td>
</tr>
<tr>
<td>Restrictive Pericarditis</td>
<td>Restrictive cardiomyopathy</td>
</tr>
<tr>
<td>Beri Beri (Thiamine deficiency)</td>
<td>Myxedema</td>
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</tbody>
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<table>
<thead>
<tr>
<th>Acute (&lt; 72 hours)</th>
<th>Chronic</th>
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<tbody>
<tr>
<td>DVT</td>
<td>Chronic Venous Insufficiency, DVT?</td>
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<th>Chronic</th>
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<tr>
<td>Ruptured Baker’s Cyst</td>
<td>Secondary Lymphedema</td>
</tr>
<tr>
<td>Ruptured Medial Head of the Gastrocnemius</td>
<td>Extrinsic venous compression (tumor/ lymphoma)</td>
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<tr>
<td>Compartment Syndrome</td>
<td>Reflex Sympathetic Dystrophy</td>
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<tr>
<td></td>
<td>Congenital Venous Malformations</td>
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<tr>
<td></td>
<td>May-Thurner Syndrome</td>
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</tbody>
</table>

Other Key Questions...

- Do you sleep in the recliner?
- s/s OSA
  - Snoring, apneic spells, large neck, daytime somnolence
- What has your weight done in the past few years?
- Anything that may have disrupted groin lymphatics
  - Ab surgeries/lymph node resection
  - Recurrent leg infection
  - h/o groin irradiation
- h/o VV, DVT
- Activity level
DVT

- Onset rapid and UNI-lateral
- Swelling, warmth, slightly reddish, cyanotic hue, tenderness along the deep veins
- Look for provoking factors
- h/o of previous DVT OR Thrombophilia
- Pretest probability → Wells score
  - Low to moderate? → D dimer. If negative follow closely
    - 1.4% incidence of DVT at 3 months
  - High: Compression Ultrasound
Chronic Vein Disease

- Most often due to Incompetent venous valves
  - DVT most commonly implicated
  - Other causes include genetic and obesity
- Should be obvious on exam but can be subtle initially
  - Hemosiderin deposition, sclerotic changes, atrophy blanche, ulcer (most commonly just above the medial malleolus) varicosities
- Early: soft pitting edema
- Later: Above
Worldwide

USA

![Image of a sperm cell]

![Image of a McDonald's logo]
Lymphedema

- Classification... Great for cocktail parties or playing Trivial Pursuit
  - Primary (idiopathic)
    - Congenital= present at birth or becomes evident by age 2; if familial → “Milroy” syndrome.
    - Lymphedema praecox= presents at age 2-35. F:M ratio 10:1; if familial → “Meige” disease
      - Most common form of primary lymphedema
      - Usually unilateral and limited to the foot and calf
  - Secondary (obstructive) → Much, much more common than primary
    - Usually, not a mystery
      - h/o of previous groin irradiation
      - h/o of cancer
      - h/o of recurrent infection/travel (Filariasis)
      - h/o of surgical manipulation/removal of lymph nodes
Obesity likely most common cause of secondary lymphedema
74% of morbidly obese wound pts also had lymphedema
21 pt severe lymphedema → 100 obese, 91% morbidly
Lymphedema Characteristics

- Painless, lack of CVD skin changes
- “Finger-print” pivotal signs
  - “Kaposi-Stemmer” sign → unable to pinch 2nd digit dorsal skin fold
- Dorsal “Hump” sign
  - Prominent skin creases b/t toes and dorsal hump.
- Early on, difficult to distinguish from early CVD
  - Lymphoscintigraphy
- Later, a warty texture (hyperkeratosis), brawny induration, cobble-stoning (lymphostatic verrucosis), “ski jump” toe nails
Stemmer’s sign
Case

• 40 y/o active female, CC swelling end of the day, legs ache.
• Sometimes, her face and hands will feel puffy
• No sig PMH, no prescription/OTC meds
• Labs and venous incompetency study all WNL
• Notes that when supine, tends to urinate more
• PCP gave her stockings... more pain, swelling no better.
• Working diagnosis?
**Idiopathic Edema**

- **Sine qua non:**
  - Swelling upright/diuresis supine in women (20-30s)
  - All other etiologies ruled out
    - Heart, Liver, kidney, Meds

- Face and hands; DM, Obesity, “emotional problems” common.
  - Purging behaviors (diuretics, laxatives, vomiting)

- Abnormal response to assumption of upright posture
  - Normal: mild plasma volume depletion d/t pooling of ECF in LE → fall in U NA excretion and daytime wt gain of 0.5-1.5 kg
  - Idiopathic Edema: lose much more fluid from vascular space with standing → marked increased release of hypovolemic hormones (renin, norepi, ADH) → increased wt gain (up to 10# in severe cases)
Potential Mechanisms
Idiopathic Edema

- Capillary leak → not well understood.
  - Precap sphincter tone?
    - Humorally mediated
      - Often have impaired hypothalamic fn → abnormal release of prolactin, LH, other hormones.
  - Primary capillary injury?

- Increased capillary pressure → increased capillary permeability → movement out
  - Exaggerated by gravity in standing.
  - Also explains why JVP not elevated and also why pulmonary edema does NOT develop.

- Decreased dopamine release
  - Impaired regulation of hypothalamic hormone release
  - Could alter capillary hemodynamics directly
  - Dopamine is natriuretic by nature, thus deficiency would result in less Na excretion
Idiopathic Edema

Diagnostics

• Typically, gain over 1.4 kg (3.08 lbs) over course of day.
  • Normal → < 0.46 kg (1.04 lbs)

• AM/Evening Weights:
  • Wt upon arising prior to any food/fluids, nude, empty bladder
  • Wt at bedtime, nude, empty bladder
  • Diagnosis suggested if wt gain > 0.7 kg (1.54 lbs)

• Water load Test:
  • More complex
  • Must be off diuretics x 10 d
Idiopathic Edema Management

• Many potential Rx proposed
  • low salt diet, intermittent recumbency, avoidance of excessive heat, wt loss
  • If on diuretics, stop and wait 3 weeks, warn of rebound!
  • Still edematous → spironolactone, Ace I, dopamine agonists (bromocriptine, carbidopa levodopa)
    • Low dose amphetamine: constrict precap sphincter → decreased cap hydrostatic pressure → less movement o/o capillary.

• Compression stockings ineffective; not well-tolerated.
Swelling Mimickers
Knee Effusion
LIPedema

AKA: CG-CAPS killer

Abnormal fat deposition
Painful
Stockings → worse
Does NOT respond to wt loss
“cut off” sign
Torso: Leg “mismatch”
Klippel-Trenaunay Syndrome

1. Port wine stain
2. Abnormal veins
3. Limb hypertrophy
“When something bad happens (edema), a medication did it... until proven otherwise”
Medication related edema

- Common culprits
  - Thiazolidinediones (pioglitazone, rosiglitazone)
    - Na reabsorption in collecting tubules (same site as aldosterone)
    - May occur insidiously and over months
    - Underlying heart disease increases edema risk
    - Can take 4-6 weeks after stopping to see less edema
    - usually diuretic resistant
  - NSAIDs (~ 5% incidence)
  - Corticosteroids
  - Estrogen, testosterone, progesterone
  - Several anti-hypertensives
    - BB, Clonidine, Hydralazine, Minoxidil, Methyldopa
Calcium Channel Blockers

- Common but dependent on class/dose; vasodilating > chronotropic agents.

- Women > Men
  - Perhaps women just more aware of their cosmesis?
  - Possible pharmacokinetic difference suggested at least for some classes (verapamil)
    - This has NOT been seen in other classes

- Mismatch b/t arteriolar resistance and venule resistance → increased hydrostatic pressure

- LE redness, warmth and non-blanching rash may occur
  - RBC leakage from capillaries

- Do:
  - Stop, decrease dose, or consider alternate class
  - Stockings
  - Consider administering at night
  - Add Ace inhibitor
    - Of course, as BP falls, may be able to decrease CCB as well

- Don’t:
  - Give diuretic (not salt/water issue)
Diuretic-induced Edema

- Persistent diuretic-induced hypovolemia activates several Na retaining mechanisms
- Once diuretic stopped, pt may be unable to acutely shut off this hormonal adaptation
- Result: rapid edema formation and the mistaken assumption that chronic diuretic therapy is indicated.
  - If wait 3-4 weeks, often spontaneous diuresis occurs with resolution of edema
- Study in elderly all taking diuretics solely for ankle edema
  - 75% able to discontinue without persistence of edema
  - Transient rebound common, took about 3 wks to resolve.
- Chronic high-dose diuretics→ commonly develop nephrocalcinosis
  - Chronic renal insufficiency
  - All can be partially reversed after diuretic stopped.
“Play the odds”

• Most common age > 50: Chronic Vein Disease
• Females menarche to menopause: Idiopathic edema
• Common but unrecognized: PAH/OSA
Sleep Apnea and Edema

- Poorly understood
  - changes in right sided heart pressures slowing venous return.
- PH NOT a prerequisite for edema
  - In group with edema:
    - 2/3 had OSA but only 1/3 had pulmonary htn
  - Usually, not accompanied by other signs of volume excess
- Unclear whether edema resolves on Rx
Labs/Imaging

- Simple, readily available labs can rule out/in multiple causes
  - My “edema” filter: UA (proteinuria); BNP (CHF). Cr (renal failure); TSH (hypothyroidism); albumin, PT (synthetic liver function)

- Imaging:
  - Venous Incompetency Study
    - DVT, venous valvular incompetency, proximal venous waveforms, baker’s cyst
  - MRI/V pelvis in certain cases
  - Echo → EF, pulmonary pressures
  - Sleep study
  - Venography
Respirophasic Flow  Pulsatile Flow
Right CFV

Left CFV
Valsalva
Swanson’s Guide to Edema Management

1. Find the cause
2. Rx the cause
3. if no better, see #1
Compression Pearls

- Often, not enough
- Inelastic vs elastic
- Surround yourself with experts...OTR/L
  - Call them, pick their brains
  - Learn from them!
- Almost all edema can be made better with a compression program...not just lymphedema
  - CVD, DVT, dependent edema, combination
  - NOT effective in Lipedema, Idiopathic edema
- Safe, even with rather severe PAD
  - In fact, may augment arterial flow!
- Stockings AFTER lymphedema therapy i.e. maintenance
  - Wear while up, on first thing AM (before legs swell)
Swanson’s Secret Weapon...

MOHAMMED RAHMAN, MD

SPECIALTIES
Nephrology

To schedule an appointment, please call 701-780-6400
In Summary

- Edema is common and presents a vast differential to the office clinician
- Using low tech readily available skills, the diagnosis can usually be identified
- Spending a bit of time up front on the H/P pays big dividends on the back-end
- Some causes are common yet often go unrecognized
  - Idiopathic edema
  - OSA
  - Diuretic induced edema
  - Newman’s first Law (Medications)
- Effective Rx is dependent on accurate diagnosis
  - My core: OT, Stockings, Nephrology
- Little in medicine is more gratifying that effectively treating edema!!
THANK YOU!

kswanson@altru.org