APPROACH TO THE SWOLLEN PATIENT

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ND Academy of Family Physicians
Family Medicine Update
January 2017

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

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

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 limbs/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 limbs 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
  • Intrinsc 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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</thead>
<tbody>
<tr>
<td>Venous insufficiency</td>
<td>Renal disease (nephrotic syndrome or nephritis)</td>
</tr>
<tr>
<td>Pulmonary Hypertension</td>
<td></td>
</tr>
<tr>
<td>Heart Failure</td>
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<tr>
<td>Idiopathic edema</td>
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<tr>
<td>Drugs</td>
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<tr>
<td>Premenstrual edema</td>
<td></td>
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<td>Pregnancy</td>
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<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></td>
</tr>
<tr>
<td>Acute CHF, Renal disease</td>
<td>Liver disease</td>
</tr>
<tr>
<td>Secondary lymphedema (tumor, XRT, infection)</td>
<td>Pelvic tumor or lymphoma (extrinsic compression)</td>
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<tr>
<td>Dependent edema</td>
<td></td>
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<tr>
<td>Diuretic induced</td>
<td></td>
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<tr>
<td>Pre-eclampsia</td>
<td></td>
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<tr>
<td>Lipedema</td>
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</table>
Rare Causes of Bilateral Edema

<table>
<thead>
<tr>
<th>Acute</th>
<th>Chronic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Lymphedema</td>
<td></td>
</tr>
<tr>
<td>Protein losing enteropathy</td>
<td></td>
</tr>
<tr>
<td>Restrictive Pericarditis</td>
<td></td>
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<tr>
<td>Restrictive cardiomyopathy</td>
<td></td>
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<tr>
<td>Beri Beri (Thiamine deficiency)</td>
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<tr>
<td>Myxedema</td>
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</tbody>
</table>

Common Causes of Unilateral Edema

<table>
<thead>
<tr>
<th>Acute (&lt; 72 hours)</th>
<th>Chronic</th>
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</thead>
<tbody>
<tr>
<td>DVT</td>
<td>Chronic Venous Insufficiency, DVT?</td>
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</table>

Less Common Causes of Unilateral Edema

<table>
<thead>
<tr>
<th>Acute</th>
<th>Chronic</th>
</tr>
</thead>
<tbody>
<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>
</tr>
<tr>
<td>Compartment Syndrome</td>
<td>Reflex Sympathetic Dystrophy</td>
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</table>

Rare Causes of Unilateral Edema

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<tbody>
<tr>
<td>Primary Lymphedema</td>
<td></td>
</tr>
<tr>
<td>Congenital Venous Malformations</td>
<td></td>
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<tr>
<td>May-Thurner Syndrome</td>
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Other Key Questions...

- Do you sleep in the recliner?
  - Us 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 surgery/ lymph node resection
  - Recurrent leg infection
  - No groin irradiation
  - No UV, 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 vs Wells score
  - Low to moderate vs 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

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

Worldwide USA

Obesity Rates 2015

CDC website
Obesity likely most common cause of secondary lymphedema
74% of morbidly obese wound pts also had lymphedema
21 pt severe lymphedema 220 obese, 94% 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, cobblestoning (lymphostatic verrucosis), "ski jump" toe nails
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 of pooling of ECF in LE → fall in U/Na excretion and daytime wt gain of 0.5-1.5 lb
  - Idiopathic Edema: lose much more fluid from vascular space with standing → marked increased release of hyperadrenalic 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
    - Other have impaired hypothalamic function: abnormal release of prolactin, LH, other hormones.
  - Primary capillary injury?
  - Increased capillary pressure → increased capillary permeability → movement out of extracellular fluid
  - Also explains why AP 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 at bedtime, nude, empty bladder
  - Wt upon arising prior to any food/fluids, nude, empty bladder
  - Diagnosis suggested if wt gain > 0.7 kg (1.54 lbs)
- Water load Test:
  - More complex
  - Must be off diuretics x 22 d

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!
  - Stilbenes (spironolactone, Ace inhibitor)
  - Dopamine agonists (bromocriptine, carbidopa levodopa)
  - Low dose amphetamine: constrict precap sphincter → decreased cap hydrostatic pressure → less movement out of capillary
- Compression stockings ineffective; not well-tolerated.
Swelling Mimickers

**LIPedema**

AKA: CG-CAPS killer

- Abnormal fat deposition
- Painful
- Stockings get worse
- Does NOT respond to wt loss
- "cut off" sign
- Torso: Leg "mismatch"

**Knee Effusion**

**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

"When something bad happens (edema), a medication did it... until proven otherwise"
Calcium Channel Blockers

- Common but dependent on class/dose, manifesting > chronotropic agents.
- Women > Men
  - Perhaps women more aware of their cosmesis?
- Maybe pharmacokinetic difference suggested at least for some classes (verapamil)
  - This has NOT been seen in other classes
- Mismatch between arteriolar resistance and venular 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
- ... (continue)

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

Diuretic-induced Edema

- Persistent diuretic-induced hypovolemia activates several Na retaining mechanisms
- 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, look about 1-2yrs 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 valvar incompetency, proximal venous waveforms, baker’s cyst
  - MRI/V pelvis in certain cases
  - Echo- EF, pulmonary pressures
  - Sleep study
  - Venography

CFA

No compression

With compression
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…OTRL
- 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…
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 than effectively treating edema!!

THANK YOU!

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